



Human Research Protections Program
Office of the Institutional Review Board

Standard Operating Policies

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GA 100 GENERAL ADMINISTRATION

GA 100	GENERAL ADMINISTRATION
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1. PURPOSE

The purpose of this SOP 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 assure that the rights and welfare of research participants are protected
- State the authority of the IRBs
- Define the scope of the IRBs
- Define the relationship of the IRBs to other committees and to officials within the University system

2. POLICY STATEMENT

2.1 Statement of Institutional Authority

The University of Pennsylvania's Institutional Review Boards (IRBs) are established and empowered under the authority of the Trustees of the University of Pennsylvania. The University of Pennsylvania requires that all research projects that meet the definition of human participants' research be reviewed and approved by one of the University of Pennsylvania's IRBs prior to initiation of any research related activities.

2.2 The Purpose of the IRBs

The IRBs purpose is to protect the rights and welfare of humans participating in biomedical and behavioral research conducted at the University of Pennsylvania. The IRBs review and oversee such research to assure that it meets ethical principles and that it complies with federal regulations that pertain to human participant protection at 45 CFR 46 and 21 CFR 50 and 56, and other pertinent regulations and guidance.

2.3 Governing Principles

The IRBs are guided by the ethical principles regarding all research involving humans as participants as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, entitled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "[Belmont Report](#)"). These principles are defined in the Belmont Report as follows:

- Respect for Persons – Individuals should be treated as autonomous agents; and persons with diminished autonomy are entitled to protection
- Beneficence – Maximize the benefits and minimize the possible harms
- Justice -- The burdens and benefits of research should be justly distributed

2.4 IRB Authority

2.4.1 The IRBs are established to review biomedical and social-behavioral research involving human participants that is conducted by faculty, staff and students of the University regardless of the source of funding and location of the study if :

- The research is sponsored by the Trustees of the University of Pennsylvania;
- The research is conducted by or under the direction of any employee, faculty, staff, student or agent of the University of Pennsylvania in connection with his/her/their institutional responsibilities;
- The research is conducted by or under the direction of any employee, faculty, staff, student or agent of the University of Pennsylvania using any property or facility of the University of Pennsylvania;

- The research involves the use of the University of Pennsylvania's nonpublic information to identify or contact human research participants; or,
- The research involves the use or disclosure of protected health information.

2.4.2 Each IRB has the authority to ensure that research is designed and conducted in such a manner that protects the rights and welfare and privacy of research participants. Specifically, each IRB may disapprove, require modifications, approve, or suspend studies based upon consideration of human participant protection aspects.

3. SPECIFIC POLICIES

3.1 Federally Funded Research

If the study is part of an application to a sponsoring agency, the human research protocol must be reviewed and approved by the IRB prior to expenditure of any grant funds.

3.2 State Law

3.2.1 Pennsylvania State Law

The IRBs recognize that Pennsylvania laws impose additional requirements. To ensure that the applicable requirements are met, the IRB members or administrative staff will consult with the Office of General Counsel of the University of Pennsylvania for guidance on additional legal requirements under Pennsylvania state law.

3.2.2 New Jersey State Law

The IRBs recognize that New Jersey laws impose additional requirements. To ensure that the applicable requirements are met, the IRB members or administrative staff will consult with the Office of General Counsel of the University of Pennsylvania for guidance on additional legal requirements under New Jersey state law.

3.3 Tribal Law

The IRBs recognize that local tribes may impose additional requirements. To ensure that the applicable requirements are met, the IRB members or administrative staff may request confirmation or other support of the conduct of the research.

3.4 Relationship of the IRBs to University Officials and Other Committees

3.4.1 Review of research by officials and other committees: Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials or other committees of the University of Pennsylvania. However, those officials or committees may not approve research if it has been disapproved by an IRB.

3.4.2 IRB relationship to university officials and other committees: The IRB functions independently of, but in coordination with, University officials and other committees.

3.4.3 For industry sponsored research, research may not begin until the contract is finalized.

3.4.4 When review is required by other University committees, the Principal Investigator and the research team are informed that research may not begin until the required committee reviews are complete.

3.5 Use of Policies and Procedures

Each IRB must maintain and follow all written policies and procedures consistent with federal regulations, good clinical practice, and research ethics when reviewing proposed research.

3.6 Number and Scope of IRBs

The Board of Trustees has authorized 9 IRBs to review research involving human participants conducted by faculty, staff and students of the University. The University consists of the undergraduate and graduate schools of the University of Pennsylvania, and the University of Pennsylvania Health System.

In general, IRB applications involving biomedical research or clinical trials are assigned to IRBs 1-7. Research involving social or behavioral sciences is reviewed by IRB 8. IRB 9 meets on an ad hoc basis to review unanticipated problems, incidents of noncompliance or other items requiring special considerations and is comprised of current IRB Chairs and Members, as well as representatives from other University offices, with specific relevant expertise, including background in issues related to privacy and confidentiality.

4. REFERENCES

[Provost HRPP Statement](#); [Belmont Report](#); [21 CFR 56.108](#); [21 CFR 56.109](#); [45 CFR 46.103\(b\)\(4\)](#), [45 CFR 46.113](#)

1. PURPOSE

The purpose of this policy is to describe specific activities that require IRB review and, conversely, those activities that do not require IRB review.

2. POLICY STATEMENT

No intervention or interaction with human participants in research, including recruitment, may begin until the IRB has reviewed and approved the research protocol. “Human participants research” is any activity that either: 1) meets the HHS definition of “research” involving “human participants” as defined in the HHS regulations or 2) meets the FDA definition of “clinical investigation” that involves “human participants” as defined in the FDA regulations.

All research involving human participants (as defined above), and all other activities which even in part, involve such research, regardless of sponsorship, must be reviewed and approved by a University of Pennsylvania IRB. The University does not apply 45 CFR 46 regulations to non-federally funded research. The IRB will provide for equivalent protections and apply the same policies and procedures to all human participant research.

Under certain conditions, the University may rely on another organization’s IRB. The reliance on another IRB will be outlined in an approved IRB Authorization agreement or under the conditions of an approved cooperative agreement. If the University agrees to rely on another organization’s IRB, the research will not be considered approved at Penn until the IRB authorization agreement has been fully executed and approval of the research and the addition of the Penn study site has been granted by the IRB of Record. The University may decline to rely on another IRB if the study is high risk to participants and/or the institution, or for other reasons as determined by institutional leadership.

Under certain conditions, another organization may rely on the Penn IRB. The reliance on the Penn IRB will be outlined in an approved IRB authorization agreement or under the conditions of an approved cooperative agreement. For multi-site trials, each participating site that is engaged in human participants’ research is responsible for obtaining IRB approval of their research activities from their local site’s IRB or the execution of a reliance agreement with the Penn IRB or another IRB.

3. SPECIFIC POLICIES

3.1 Activities that Require IRB Review

Specific activities that may require IRB Review can include, but are not limited to:

3.1.1 Any clinical investigation including: 1) an experiment in which a drug product is administered, dispensed to, or used involving one or more human participants; or 2) research involving one or more participants to determine the safety and/or effectiveness of a device.

3.1.2 Collection and use of data about a series of standard procedures or treatments for dissemination or generalization if the activity meets the definition of “human research”.

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

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

3.1.5 Systematic investigations involving innovative procedures, surgeries, or treatments, including new variations on accepted techniques, consistent with accepted principles and practices of surgery, but where clinical benefit is unpredictable or unknown. For example, if an 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.

3.1.6 Emergency Use of an Investigational Drug or Device. An emergency use of an investigational drug or device for an individual patient may proceed without prospective IRB review. However, the IRB should be notified of the administration of the product within 5 business days. When emergency medical care involves an investigational article, the research does not require prospective IRB review and approval, the patient is a research participant as defined by FDA regulations but may not be considered a research participant as defined by HHS regulations, and data generated from such care *cannot be included in any prospectively conceived report of an HHS regulated research activity*.

3.1.7 Treatment Use Requests. Prospectively planned non-emergency medicine research involving the use of an investigational agent under a treatment IND (also referred to as a single patient IND), compassionate use IDE, or treatment IDE for an individual patient requires prospective IRB approval.

3.1.8 Emergency Medicine Research. Prospectively planned emergency medicine research with investigational drugs, devices, or biologics requires IRB approval. If the researcher intends to waive the requirement for informed consent, additional requirements must be met including community consultation and public disclosure.

3.1.9 Data, Human Cell or Tissue Repository. Human cell or tissue (genetic tissue) research typically involves repositories that collect, store, and distribute human tissue materials for research purposes.

3.1.10 Investigator Initiated Research. Research, initiated and conducted (alone or with others), that is designed and/or written by the principal investigator, a sub-investigator, or a faculty member at the University of Pennsylvania or another academic institution, regardless of source of funding or support.

3.1.11 Student Research. Directed or independent human research projects which employ systematic data collection with the intent to contribute to generalizable knowledge. These activities include:

- i. All master's theses and doctoral dissertations that involve research with human participants; and
- ii. All projects that involve research human participants and for which findings may be published or otherwise disseminated.

3.1.12 Access to protected health information. Investigators conducting research with protected health information maintained within any of the covered entities of the University of Pennsylvania must provide the IRB with appropriate information to obtain approval of the activity prior to access of the protected health information.

3.1.13 Collaborative Research. Collaborative research requires IRB review by each performance site unless an IRB Authorization or Independent Investigator Agreement is in place or carried out under the terms of a cooperative agreement.

3.1.14 Clinical Trial. A research study in which one or more human participants 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.

3.1.15 Research involving Genetic Information. Genetic information means, with respect to any individual, information about:

- (a) such individual's genetic tests,
- (b) the genetic tests of family members of such individual, and
- (c) the manifestation of a disease or disorder in family members of such individual.

Genetic test includes any analysis of human DNA, RNA, chromosomes, proteins, or metabolites, that detects genotypes, mutations, or chromosomal changes.

Genetic test does NOT include:

- a) an analysis of proteins or metabolites that does not detect genotypes, mutations, or chromosomal changes; or
- b) an analysis of proteins or metabolites that is directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a health care professional with appropriate training and expertise in the field of medicine involved.

3.2 Activities Not Subject to IRB Review

3.2.1 Proposals determined not qualify as human participants' research may not require IRB review. Additionally, activities such as quality or performance improvement, quality assurance or quality control, program and fiscal audits, and certain disease monitoring as prescribed by the Public Health Department generally do not qualify as research but may require review to establish this or for a privacy board determination.

3.2.2 Case Studies. A single retrospective case report is a medical/educational activity and does not meet the Federal Policy for the Protection of Human Participants definition of "research" which is "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." In general, the review of medical records for publication of case reports of 3 or fewer patients is not considered human research and does not require IRB review and approval.

Under HIPAA, a single case report is an activity to develop information to be shared for medical/educational purposes. Therefore, the use of protected health information to prepare a paper for publication of a single case report does not require IRB review for HIPAA purposes. If the data are de-identified, no waiver or authorization is required. If, however, the investigator wishes to publish data with HIPAA identifiers an authorization signed by the patient is required.

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

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

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

3.2.6 Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. Investigators have the option to obtain from the IRB documentation that the activity is not subject to IRB review.

3.2.7 The use of a marketed drug or device in the course of standard medical practice.

3.2.8 Non-experimental innovative procedures, surgeries, or treatments which is a new variation on accepted techniques, consistent with accepted principles and practices of surgery, and regarded as having predictable clinically beneficial results for patients. IRB review is generally not required when the innovation is being made for the care and treatment of patient(s) and there are no plans to collect and analyze data for generalizable knowledge.

3.3 Collaborative Research with the Veterans Affairs Medical Center – Philadelphia

When all work is to be done at the VAMC and the only association with the research at Penn is the investigator's dual appointment, there is no requirement for submission or review by Penn's IRB. When research is conducted at both the VAMC and at Penn, the research must be reviewed and approved by both IRBs.

3.4 IRB Authorization Agreements

Under certain conditions, the University may rely on another organization's IRB as the IRB of Record or the University may agree to serve as the IRB of Record for another organization. The conditions of the reliance will be outlined in an approved IRB Authorization agreement or under the conditions of an approved cooperative agreement. An IRB Authorization Agreement, also called a reliance agreement or cooperative review agreement, is defined as an agreement that documents respective authorities, roles, responsibilities and communication between an organization providing the ethical review and a participating organization that is delegating IRB review to the IRB of Record.

Unless otherwise specified in the agreement, the role of the IRB of Record will be limited to providing review, approval, and continuing oversight that meets the requirements of the Federal Regulations governing human research. The IRB of Record will not assume all the responsibilities of the relying organization's Human Research Protections Program. Records must include documentation specifying the responsibilities that a relying organization and an organization operating an IRB each will undertake to ensure compliance with the requirements of the Common Rule.

Unless otherwise specified in the IRB Authorization Agreement, the IRB of Record will retain responsibility for the following activities:

- Reviewing potential non-compliance, including complaints, protocol deviations, and results of audits:
 - Identifying which organization is responsibility for deciding whether each allegation of non-compliance has a basis in fact
 - Identifying which organization's process is used to decide whether each incident of non-compliance is serious or continuing
- Ensuring that, should termination of a reliance agreement occur, one of the parties clearly is responsible for continued oversight of active studies until closure or a mutually agreed upon transfer of the studies.
- Determining whether the relying organization applies its FWA to some or all research, and ensuring the IRB or EC review is consistent with requirements in the relying organization's FWA.
- Determining which organization is responsible for obtaining any additional approvals from DHHS when the research involves pregnant individuals, fetuses, and neonates; or children; or incarcerated persons.
- Determining which organization is responsible for reporting serious or continuing non-compliance; unanticipated problems involving risks to participants or others, and suspensions or terminations of IRB or EC approval.

Unless otherwise specified in the IRB Authorization Agreement, the relying IRB or organization will retain responsibility for the following activities:

- Providing education to its organization's researchers and research staff
- Conducting scientific reviews required by the organization's HRPP
- Ensuring concordance between any applicable grant and the IRB or EC application

- Obtaining management plans for researcher and research staff conflicts of interest and providing the management plan to the IRB of Record in a timely manner
- Managing organizational conflict of interest related to the researcher
- If additional regulatory requirements, for example, those of Department of Defense (DoD) or Department of Justice (DoJ) must be applied due to the involvement of the relying organization, the relying organization will either apply the requirements or notify the IRB of Record that the external review must take them into account when reviewing the protocol.

3.5 Failure to Submit Project for IRB Review

The implications of engaging in activities that qualify as research that is subject to IRB review without obtaining such review are significant. If an investigator begins a project without prospective IRB review and approval and later learns of the review requirement, the investigator should promptly notify the IRB. The IRB may allow (with or without provisions) or deny use of the data.

If an investigator begins a project and later finds that the data gathered could contribute to generalizable knowledge, has changed in some fashion as to now require IRB review, or that he/she/they may wish to publish the results, the investigator should submit a proposal to the IRB for review as soon as possible. If the IRB does not approve the research, the IRB may determine that the data derived from the previously conducted research cannot be used as part of a study, thesis or dissertation nor may the results of the research be published.

4. REFERENCES

[Federalwide Assurance; 45 CFR 46.102\(d\)\(f\); 21 CFR 50.3\(d\)\(g\); 21 CFR 56.108\(b\)\(1\); 45 CFR 46.103\(b\)\(4\); 21 CFR 50.24; OPRR Reports, Emergency Medical Care, May 15, 1991; OPRR Reports: Informed Consent Requirements in Emergency Research, October 31, 1996; OHRP Guidance Research Involving Coded Private Information or Biological Specimens, Oct. 16, 2008; OHRP Issues to consider in the research use of stored data or tissues, Nov. 7, 1997; OHRP Guidance; Engagement of Institutions in Research, Oct. 16, 2008; FDA Guidance on Single Patient IND, Feb. 4, 2015; Genetic Information](#)

1. PURPOSE

The purpose of this section is to state the IRBs' commitment to maintain and follow up-to-date policies and procedures that adhere to regulatory mandates and ethical principles.

2. POLICY STATEMENT

Following federal regulations and guidance supported by institutional policies assures that the rights and welfare of the human participants of such research will be overseen and protected in a uniform manner, regardless of changes in personnel. Written procedures must be in place to insure the highest quality and integrity of the review and oversight of research involving human participants and for the adequate documentation of such oversight.

Standard operating policies (SOPs or Policies) and procedures provide the framework for the ethical and scientifically sound conduct of human research.

3. SPECIFIC POLICIES

3.1 Review and Revision of Policies & Procedures

3.1.1 Changes to regulations, federal guidelines, or research practice as well as the policies and procedures of the University of Pennsylvania may require a new policy or a revision to a previously issued policy.

3.1.2 Policies will be reviewed at least every three years, or as needed, by the Director for Human Research Protections and any appropriate IRB staff.

3.2 Policy Dissemination and Training

3.2.1 New or revised policies are approved by the Director for Human Research Protections and will be disseminated to the appropriate individuals and departments. If new or revised policies impact the status of any existing IRB authorization agreements, the Director will inform the reviewing or relying IRBs of the updated policies.

3.2.2 Training will be provided to all members of the IRB and IRB staff on any new or revised policy and or relevant procedure.

3.2.3 Each new IRB member or staff employee must review all applicable policies prior to undertaking any responsibilities at the IRB.

3.3 Forms

Forms including checklists and worksheets are used to ensure that policies are integrated into the daily operations of research and review throughout the University, and to assist IRB staff and IRB members in the review process. Forms are either controlled or non-controlled. Final versions of controlled forms are uploaded to the submission in the electronic submission system, Human Subjects Electronic Research Administration (HS-ERA) or maintained in the paper file.

3.3.1 Controlled Forms are regulatory documents that become part of the permanent record of IRB review.

3.3.2 Non-controlled forms are management tools designed to assist with the IRB review process and do not become a formal part of the IRB submission.

4. REFERENCES

[45 CFR 46.103\(b\)\(4\)\(5\)](#); [21 CFR 56.108](#); [21 CFR 56.115\(6\)](#)

1. PURPOSE

This policy describes the training and educational requirements and options for IRB members and staff.

2. POLICY STATEMENT

Training of IRB staff and members is critical if the IRB is to fulfill its mandate to protect the rights and welfare of research participants in a consistent manner throughout the University of Pennsylvania research community. IRB members, staff and others charged with responsibility for reviewing, approving, and overseeing human participant research should receive detailed training in the regulations, guidelines, ethics and policies applicable to human research protections.

The University of Pennsylvania has written policies and procedures requiring all individuals involved with the Human Research Protection Program to understand and apply their obligation to protect the rights and welfare of research participants. The University requires all researchers and other appropriate personnel to provide evidence of training and qualifications by submitting relevant documentation to the IRB, sponsor, or regulatory authorities.

3. SPECIFIC POLICIES

3.1 Training

3.1.2 Management level staff and members of any IRB who are overseeing research on human participants (human participants as defined in 46.102(f) and/or 56.102(e) that is managed, funded, or taking place in an entity under the jurisdiction of the Trustees of the University of Pennsylvania will receive initial and ongoing training regarding the responsible review and oversight of research and these policies and accompanying procedures.

3.1.3 The Director for Human Research Protections establishes the educational and training requirements for IRB members and staff who review biomedical and behavioral research at this institution and who perform related administrative duties. Initial and ongoing training is documented by the Associate Director in conjunction with IRB staff members.

3.1.4 Members of the IRB will participate in initial and continuing training in areas germane to their responsibilities.

3.1.5 Chairpersons will receive additional training in areas germane to their additional responsibilities.

3.1.6 IRB staff will receive initial and continuing training in the areas germane to their responsibilities.

3.1.7 IRB members and staff will be encouraged to attend workshops and other educational opportunities focused on IRB functions. The University will support such activities to the extent possible, and as appropriate, for the responsibilities of members and staff.

3.2 Evaluation of IRB Member Performance

The Director and Associate Director is responsible for periodic evaluation of the performance of IRB members and Chairs and for the periodic evaluation of the composition of the IRBs to meet regulatory and organizational requirements.

4. REFERENCES

[Terms of the HHS Federalwide Assurance](#); [45 CFR 46.107\(a\)](#); [21 CFR 56.107\(a\)](#)

1. PURPOSE

This section describes management policies and procedures to promote the long-term commitment of IRB administrative staff employees and ensure the efficient and effective administration and enforcement of IRB decisions.

2. POLICY STATEMENT

The IRB administrative staff provides consistency, expertise, and administrative support to the IRBs, and serves as a daily link between the IRB and the research community. Therefore, the highest level of professionalism and integrity on part of IRB staff is expected.

3. SPECIFIC POLICIES

3.1 Job Descriptions and Performance Evaluations

Members of the IRB staff should have a description of the responsibilities expected of their positions. The performance of IRB staff will be reviewed according to current university and IRB office policy.

3.2 Resources and Staff Positions

The University provides resources to the IRB, including adequate meeting and office space, and staff for conducting IRB business. Office equipment and supplies, including technical support, file cabinets, computers, internet access, and copy machines, will be made available to the IRB and HRPP staff.

Staffing levels and function allocation will be determined according to university policy, management assessment of support requirements and budget constraints. The Vice Provost for Research reviews the IRB budget with the Director for Human Research Protections periodically, and no less than annually, to ensure adequate allocation of resources to IRB administration.

3.3 Hiring and Terminating IRB staff

The human resource policies of the University of Pennsylvania determine the policies for recruiting and hiring staff. Delegation of specific functions, authorities, or responsibilities may be authorized by the Director of Human Research Protections for Human Participants Protections to an appropriate staff member.

3.4 Documentation

The HR policies of the University of Pennsylvania determine the policies for identifying, documenting and retaining formal staff interactions (such as performance reviews, termination procedures).

4. REFERENCES

<https://www.hr.upenn.edu/myhr/resources/policy/recruitment/staffrequisitioning>

<https://www.hr.upenn.edu/myhr/resources/policy/termination/termination>

<https://www.hr.upenn.edu/myhr/resources/policy/termination/separation>

<https://www.hr.upenn.edu/myhr/resources/policy/termination/resignation>

1. PURPOSE

This policy requires any IRB member, IRB staff, or consultant with a conflicting interest in a research protocol to disclose that information to the IRB Chair or IRB administrative staff.

2. POLICY STATEMENT

In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, conflicts should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated. This policy applies to all research protocols reviewed by the IRB, regardless of level of review.

The standard that should guide decisions about conflicting interests whether an independent observer could reasonably question whether the individual's actions or decisions would be based on factors other than the rights, welfare, and safety of the participants.

The Vice Provost for Research has the authority to determine when conflicts of interest (COI) exist as defined by institutional policy and to impose and enforce disciplinary action in the event that COI is not disclosed.

3. SPECIFIC POLICIES

3.1 Definitions

The definition of conflicting interest for IRB members, consultants and staff is aligned with the institutional policies on conflicts of interest for Investigators and the federal regulations, as referenced.

3.2 Disclosing, Managing, and Documenting Conflicts of Interest

No regular, alternate IRB member or consultant may participate in the review of any research project or protocol, in which the member has a conflict of interest, except to provide information as requested.

IRB members are expected to self-identify their conflicting interests for all reviews, including reviews by the convened IRB and reviews using the expedited procedure. These reviews include unanticipated problems involving risks to participants or others and non-compliance with regulations, laws, or the requirements of the IRB. For protocols reviewed by the convened IRB, the IRB will document the name of the IRB member with the conflict and will document that the IRB member left the room during the discussion of the protocol. IRB members with conflicting interests do not count towards quorum.

3.3 IRB Staff

Institutional staff whose job status or compensation is impacted by research that is reviewed by the IRB must be absent from IRB deliberations and voting. The IRB staff is required to both initially report possible financial interests, as well as update the appropriate IRB staff if attending a meeting with a submission for which they have a current financial interest and are required to be absent from IRB deliberations and voting on any research protocol, where a potential conflict exists. Any case of disclosure of conflict of interest by staff shall be referred to the Director for development of a management plan.

3.4 Education and Training in COI

IRB members and staff are required to participate in education and training activities related to conflict of interest issues.

4. REFERENCES

http://www.upenn.edu/almanac/volumes/v59/n02/pdf_n02/090412-Supplement-ConflictsInterest.pdf; 45 CFR 46.107(e); 21 CFR 56.107(e); FDA Information Sheets, FAQ, Section II, Question 12

1. PURPOSE

This policy is concerned with the processing of disclosures of conflicts of interest by research team members involved in the design, conduct or reporting of human research (hereinafter investigators) and their report of this to the IRB to ensure adequate protection of participants.

2. POLICY STATEMENT

The protection of human participants in research requires that conflicts of interest involving investigators be eliminated or managed so that the results of the research are free from bias. The management of conflicts of interest is the responsibility of the Vice Provost for Research as advised through the Conflicts of Interest Standing Committee (CISC). It is the policy of the IRB that review of the management, minimization or elimination of conflicts of interest involving investigators is an integral part of the review of human research.

In the interests of protecting human participants, the Institutional Review Board requires the following steps be taken to address such potential conflicts of interest in the conduct of human research.

3. SPECIFIC POLICIES

3.1 Submission of Confidential Financial Disclosure Statements

Principal Investigators submitting research applications to the IRB are required to certify:

- 3.1.1 They have reviewed the University policies on conflicts of interest with all research team members involved in the design, conduct or reporting of that specific research protocol (investigators) and,
- 3.1.2 As part of the current protocol application, all investigators have identified any significant financial interests requiring disclosure. In the event a significant financial interest requiring disclosure has been identified, the individual with the applicable interest must submit a disclosure in accordance with institutional policies. The IRB application and informed consent documents are available to the Conflict of Interest Standing Committee (CISC) for review.

3.2 IRB Review

It is not the purview of the IRB to reinterpret institutional conflict of interest policies or their implementation. Rather its function is to ensure that participant protection, the integrity of IRB review, and the conduct of a research are not jeopardized by an unidentified and unmanaged conflict of interest. When human research requires review by the CISC, the IRB will not approve the research until the CISC review is complete and any management actions required are agreed to by the Investigator(s). Representative(s) of the IRB will actively participate in the CISC discussions to inform the management strategies needed to ensure human participants are adequately protected, and where appropriate may require modification to the study documents, including the consent form, in response to review of any financial disclosures.

The IRB shall concentrate on those aspects of any conflict of interest that may reasonably affect human participant protection and may require changes to the protocol or consent form that may include, but are not limited to the following:

- 3.2.1 The IRB may require an enhanced data safety monitoring plan.
- 3.2.2 Where applicable, the informed consent will disclose the nature of an investigator's conflict using language approved by the IRB.

3.2.3 In the event that additional protections are required to ensure human participants protections that extend beyond those which have been incorporated in the management plan required by the Vice Provost for Research, a convened IRB will be required to review the plans for management and institute any required changes necessary to ensure that human participants protections have been appropriately addressed and the study meets the criteria for IRB approval. This could include any changes needed to the management strategies in response to an investigator appeal.

Please Note: In addition to individual investigator interests, any interests of the institution that could constitute a conflict of interest require review. The process for identification, review and management of these interests is outlined in the Charter for the *Human Research Advisory Committee (HRAC)* and its corresponding addendum related to *Institutional Conflicts of Interest*.

If the Penn IRB has agreed to rely on an External IRB per an IRB authorization agreement, the process described above should still be followed. The researchers must disclose this conflict of interest to the IRB of Record according to the process agreed upon between the Penn IRB and the IRB of Record and comply with any conflict of interest management plans that may result.

3.3 IRB Review of Conflicts of Interest at External Sites

If the Penn IRB is serving as the IRB of Record for another organization through an IRB authorization agreement or under the conditions of an approved cooperative agreement, the investigators will be subject to their institutional policies on conflicts of interest. They are not subject to the University of Pennsylvania's Conflict of Interest policies or to review by the Conflict of Interest Standing Committee (CISC).

Investigators at other relying organizations or Universities are required to identify any financial interests that they have disclosed according to their institutional policies and provide the Penn IRB with any applicable conflict of interest determinations and management plans conducted at the relying institution. The Penn IRB will then review the information provided according to Section 3.2. The Penn IRB retains the authority to impose additional prohibitions or conflict management requirements more stringent or restrictive than proposed by the relying organization or University if necessary. However, the Penn IRB will not modify or change any management plan or mandated disclosure to participants without discussion with an acceptance by the relying organization or University.

4. REFERENCES

- Principles of Responsible Conduct, *Almanac*, Volume 54, No, 27, April 1, 2008,
- University of Pennsylvania Policy on Conflicts of Interests Related to Research, revised November 21, 2022: <https://catalog.upenn.edu/faculty-handbook/iii/iii-f>
- University of Pennsylvania Policy on Patent and Tangible Research Property, Effective October 1, 2023: https://almanac.upenn.edu/uploads/media/101023-Patent_Policy_supplement.pdf

1. PURPOSE

This policy describes signature authority for IRB related activities.

2. POLICY STATEMENT

The Vice Provost for Research, IRB Chairs, Director for Human Research Protections, Associate Directors, and other appointed designees of the IRB Senior Staff are authorized to sign documents in connection with the review and approval of research projects involving the use of humans as participants, which have been reviewed and approved pursuant to University policies and procedures and upon decision of the IRB.

This policy also applies to IRB administrative staff, but only in the capacity of signing IRB correspondence that reflects decisions reached by either the convened IRB or one of the noted signatories above. In all cases individuals must sign their own name and no other and indicate their title under their signature.

3. SPECIFIC POLICIES

3.1 Authorization for Signatory Authority

Authorization to sign documents not described in this policy may be made in writing by the Director.

3.2 Results of Reviews, Actions and Decisions

The results of reviews and actions taken by the IRB via convened review may be signed by any designated member of the IRB staff. The results of reviews and actions taken by the convened IRB that result in a disapproval may be signed by the IRB Chairs, Director, or Associate Director in attendance at that Committee meeting. Communications regarding determinations of serious or continuing noncompliance or unanticipated problems may be signed by the designated member of the IRB Staff.

3.3 Routine Internal Correspondence

Any action, letter, memo or e-mail between the IRB or administrative staff and the faculty or staff of the University that provides information concerning the review of research protocols by the IRB or staff and which do not imply or appear to imply approval of this activity may be signed by the IRB staff member.

3.4 Correspondence with External Agencies

Official letters or memos sent to agencies of the federal government, funding agencies (whether private or public) or their agents will be signed by the Vice Provost for Research or designee.

3.5 Decisions Made by the Chair

Any letters, memos or email sent representing the decision or opinions of the Chairs of the IRBs or their respective designees, as long as such correspondence does not imply review and approval of research participants, may be signed by designated IRB staff if designated by the IRB Chair, or IRB majority in a convened meeting.

4. REFERENCES

[45 CFR 46.103\(b\)\(5\); 45 CFR 46.115\(a\)\(6\); 21 CFR 56.108\(b\), 21 CFR 56.115\(a\)\(6\)](#)

1. PURPOSE

This policy describes the process for initiating a response to an emergency/disaster situation impacting the HRPP or HRPP operations. Challenges to HRPP operations or the conduct of Human Research may arise, for example, from:

- 1.1.1 Extreme weather events.
- 1.1.2 Natural disasters.
- 1.1.3 Man-made disasters.
- 1.1.4 Infectious disease outbreaks.

The process starts when an emergency/disaster situation impacting the HRPP has occurred, or in preparation for scenarios where a potential emergency situation is imminent (e.g., natural disaster, man-made disaster, infectious disease pandemic, etc.) and HRPP operations and/or the ability of investigators to conduct Human Research is, or is likely to be, adversely impacted.

The process ends when the impact to the HRPP and the conduct of Human Research is assessed, and appropriate guidance is provided to HRPP personnel and the broader Human Research community.

2. POLICY STATEMENT

The University's Mission Continuity Program (MCP) works with Schools and Centers from across Penn to participate in a campus-wide effort to create, maintain and innovate around continuity planning, including emergency preparedness. Annually, offices across Penn engage in exercises to plan and brainstorm responses to various emergency scenarios.

HRPP leadership defers to designated institutional leadership on institution-wide disaster and emergency response planning and limits HRPP-specific disaster and emergency response planning only to those areas of operations or human research protections not otherwise covered by institution-level plans.

The Director for Human Research Protections, or their designee, collaborates with the Senior Vice Provost for Research, Senior Vice Dean for Clinical Research, and other appointed designees as the Incident Response Team.

The Incident Response Team will develop, implement, communicate, and assess emergency preparedness procedures for the HRPP. This includes determining and prioritizing the types of research that may continue and the types that the organization may need to temporarily postpone. The close integration with health system operations allows for rapid assessment of the clinical environment and prompt response and planning.

HRPP leadership evaluates its emergency response plans in accordance with GA 103.

3. SPECIFIC POLICIES

3.1 Existing Plan Assessment

If an emergency/disaster has occurred, or there is an imminent possibility of an upcoming emergency/disaster, HRPP leadership will assess the nature of the event and the appropriate response.

HRPP leadership will consult Mission Continuity Plans to reference existing HRPP specific or institution specific emergency preparedness plans or information already in place.

If a plan is already in place, HRPP leadership will proceed in accordance with those plans and determine whether further contact or notification of the human research community is necessary.

If a plan is not already in place, HRPP leadership will develop and implement a plan as well as communicate the plan to the human research community.

3.2 Impact of HRPP Operations

3.2.1 IRB Meeting Operations

If the current or anticipated emergency/disaster will prevent any upcoming IRB meetings from properly convening in-person, and an in-person meeting was planned, IRB staff will determine whether the meeting can be conducted via phone or videoconference.

If a phone or videoconference meeting is feasible, IRB staff will work with IRB members to arrange for a virtual meeting. SOPs FO 302 and 303 will be followed.

If a phone or videoconference meeting is not feasible under the circumstances caused by the emergency/disaster, IRB leadership will determine whether to cancel or reschedule the meeting(s).

If currently approved Human Research has or will expire prior to IRB review due to the IRB meeting cancellation/rescheduling, the IRB Policy on Expired research will be followed.

3.2.2 IRB Staff Operations

If IRB staff will be unable to complete their protocol processing and review responsibilities during the emergency/disaster, or if capacity will be limited for a period of time:

1. HRPP leadership will work with the IRB staff to use any available capacity to re-prioritize protocol processing.
2. HRPP leadership will work with the IRB staff to assess any continuing review submissions that may be expiring. If currently approved Human Research has or will expire prior to IRB review due to IRB office capacity limitations, the IRB Policy on Expired research will be followed.
3. HRPP leadership will notify the research community of the IRB Office's limited capacity to process and review submissions.

When the emergency/disaster no longer presents a limitation to IRB Office functions, HRPP leadership will notify the IRB members, staff, and research community that normal business operations have resumed.

3.2.3 Long-term impact on HRPP operations

If impact to local HRPP operations will be extensive or long-lasting, determine whether reliance on an external IRB(s) is required.

The Penn IRB has master reliance agreements in place with WCG IRB and Advarra IRB. The Penn IRB also participates in the SMART IRB Agreement. These master reliance agreements will be utilized.

If reliance on one or more external IRBs is required and necessary reliance agreements are not currently in place, HRPP leadership will identify appropriate candidates for external IRB reliance and RR 403 Section 3.4 will be followed.

3.2.4 Data and Records

If data or records (paper or electronic) are unavailable during the current or anticipated emergency/ disaster, HRPP leadership will consult with HireIT and electronic system vendors to implement alternative procedures to access data/backup data.

3.3 Flexibility in IRB Review Processes

HRPP leadership will assess whether the emergency/disaster could necessitate additional flexibility in IRB review processes. If applicable, the Director of Human Research Protections will work with the IRB staff to share the Additional Emergency-Disaster Review Considerations guidance document with IRB members.

IRB staff (under the direction of HRPP leadership) will communicate to IRB Members (including Designated Reviewers performing non-committee reviews) that the additional considerations in the worksheet may be incorporated into IRB reviews where appropriate to maximize regulatory flexibility while continuing to assure research participant safety during the emergency/disaster.

HRPP leadership will determine whether additional communications to the research community are necessary to inform investigators of any additional measures the IRB will take to maximize regulatory flexibility during the emergency/disaster and notify the community as appropriate.

3.4 Impact on Investigators Ability to Conduct Human Research

HRPP leadership will assess whether the emergency/disaster could impact some or all investigators' ability to conduct Human Research. If applicable, HRPP leadership will notify the research community of the need for protocol-specific emergency/disaster risk mitigation planning. The guidance Protocol-Specific Emergency-Disaster Risk Mitigation Planning will be shared with investigators.

If the emergency/disaster could impact clinical care standards which could in turn impact research, HRPP leadership will develop guidance for researchers that clarify what does and does not require IRB review (e.g., screening procedures mandated by the health care system in which a clinical trial is being conducted).

When the emergency/disaster no longer presents a limitation to Human Research activities, HRPP leadership will notify the research community that normal business operations have resumed.

3.5 Additional threats or risk to research activities or facilities

HRPP leadership will evaluate whether the nature of the emergency/disaster may pose additional threats or risk to specific aspects of the institution's research activities or facilities. (For example, man-made disasters, industrial accidents, or terrorist threats could potentially impact some chemical, biological, or radiologic facilities to a greater extent than other facilities.)

If there are additional threats or risks to the research or facilities, and if broader institution-level emergency/disaster preparedness measures do not already address these specific activities or facilities, HRPP leadership will work with appropriate institutional leadership to escalate and address any additional threats or risks.

4. REFERENCES

AAHRPP Element I.1.H

[IRB Policy RE: Expired research or research received close to the day of expiration](#)

OP 200 IRB ORGANIZATION

OP 200	IRB ORGANIZATION
201	COMPOSITION OF THE BOARD
202	MANAGEMENT OF THE BOARD
203	DUTIES OF IRB MEMBERS

1. PURPOSE

This section states the requirements for the composition of the IRBs responsible for reviewing research conducted in the University of Pennsylvania system.

2. POLICY STATEMENT

The role of the IRB is to assess the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

Therefore, each IRB will consist of at least five regular, voting members. Qualified persons from multiple professions will be considered for membership. IRB membership will not consist solely of one gender.

The institution will make every effort to have a diverse, equitable, and inclusive membership appointed to the IRB, within the scope of available expertise needed to conduct its functions.

3. SPECIFIC POLICIES

3.1 IRB Member Selection Criteria

The members of the IRB will be sufficiently qualified through experience and expertise, of reviewing research proposals in terms of regulations, applicable law and standards of professional conduct and practice and institutional commitments, therefore the IRB will include persons knowledgeable in these areas.

The membership will be diverse, so selection will include consideration of race, gender, cultural backgrounds, research, healthcare or professional experience and sensitivity to such issues as community attitudes to assess the research submitted for review.

There will be at least 1 member whose primary concerns are in scientific areas and at least 1 member whose primary concerns are in nonscientific areas.

There will be at least 1 member who has no affiliation with this institution.

3.2 Composition of the Board

3.2.1 Knowledge, Skills and Abilities

Regular Members: The backgrounds of the regular members will be varied in order to promote complete and adequate reviews of the types of research activities commonly reviewed by the IRB. Regular members must include:

Nonaffiliated member(s): The nonaffiliated member(s), who can be either scientific or nonscientific reviewers, should be knowledgeable about the local community and be willing to discuss issues and research from that perspective. Consideration should be given to recruiting individuals who speak for the communities from which the University will draw its research participants. The nonaffiliated member(s) should not be vulnerable to intimidation by the professionals on the IRB.

Scientific members: IRBs will include members whose primary interests are scientific. Such members satisfy the requirement for at least one scientist.

When an IRB encounters studies involving science beyond the expertise of the members, the IRB may use a consultant to assist in the review, as provided by 21 CFR 56.107(f) and 45 CFR 46.107(f). At least 1 member of each board, excluding the Social/Behavioral Board (IRB 8), must be a physician licensed to practice medicine in the Commonwealth of Pennsylvania.

Nonscientific member: The intent of the requirement for diversity of disciplines is to include members whose main concerns are not in scientific areas. Therefore, nonscientific members are individuals whose education, work, or interests are not solely in medical, behavioral, or social science areas. Each IRB has at least one member who represents the perspective of research participants.

Representatives of special groups of participants: When certain types of research are reviewed, members or consultants who are knowledgeable about the concerns of certain groups or local context may be required. For example, if an IRB reviews research involving incarcerated persons, a member who can represent this group, either an ex-incarcerated person or an individual with specialized knowledge about this group must be included on the IRB.

Chairs: Chairs will be faculty or senior staff members of the University; be proficient in human research; and be of sound and ethical character and reputation, without conflicts of interest that would curtail their ability to serve objectively and according to the mission of the IRB as defined in applicable laws, regulations, and policies. Chairs are appointed after agreement by the Director, Human Research Protections. In addition, the Director, Human Research Protections and the Associate Director, IRB, may fulfill the role of Chair as needed for coverage for certain meetings.

IRB Executive Chair: The Executive Chair will be a currently serving IRB Chair at Penn and will be a faculty member of the University with demonstrated knowledge, skills, and abilities in the conduct of human research and in applicable laws, regulations, and policies regarding human research protections.

4. REFERENCES

[45 CFR 46.107](#); [21 CFR 56.107](#); [FDA Information Sheets, FAQ Section II, Questions 14 & 15](#)

1. PURPOSE

To describe staff administration and oversight of the IRBs to ensure continuity of membership that has the expertise and commitment to meet its regulatory and institutional mandates.

2. POLICY STATEMENT

The management of the membership of the IRBs and oversight of member appointments, IRB related activities, communications, and other administrative details are the responsibility of the Director.

3. SPECIFIC POLICIES

3.1 Term of Appointment

The initial term of appointment is one to three years. Reappointment for additional terms may occur by mutual agreement of the IRB member, the Director, and IRB Chair.

3.2 Appointments

The Director of Human Research Protections has the authority to appoint members to the IRB and will consult with the Vice Provost for Research and Senior Associate Vice Provost for Human Research, as needed. Members will be solicited from the University and the greater Philadelphia communities.

3.2.1 IRB Members Including Alternates

IRB members are nominated from a variety of sources, including previous and current IRB members, division chiefs, department chairs, compliance administrators, and various public groups.

When an individual is nominated or when an individual expresses interest in serving on the IRB a copy of the individual's *curriculum vitae* (CV) or resume will be requested, and the nominee will be invited to observe an IRB meeting. The nominee's CV/resume and any relevant correspondence are reviewed by Senior IRB Administrative staff and recommendations are made to the Director of Human Research Protections. Nominees appointed to serve on the IRB receive a letter of appointment signed by the Director of Human Research Protections. Terms of appointments may be for one, two, or three years.

3.2.2 IRB Chairs

The Director of Human Research Protections reviews candidates for IRB Chair and determines appointment based on previously noted criteria. The Senior Associate Vice Provost for Human Research may consult on these appointments as needed. During any period of temporary vacancy, the Director of Human Research Protections may appoint an interim or acting Chair.

3.2.3 Consultants

The determination that a consultant is required may be made under certain circumstances during the review process. Such circumstances are as follows: senior IRB administrative staff, or IRB Chairs determine, upon pre-review, that a consultant is required; or members of the IRB may request at any time during the review process a consultant's review. This determination will be based on the topic of the protocol and the expertise of the voting members.

The consultant will be selected by the IRB Chair, Director for Human Research Protections, or Senior IRB staff. The Chair may consult with the principal investigator, Department Chair, Division Chief, or any other individual deemed appropriate to determine a suitable consultant. A consultant may be an individual who is either internal or external to

Penn. A consultant may be asked to review a protocol or provide education on a topic of specific concern to the IRB; to provide information to the IRB by written report, attending a meeting(s), or both. A consultant may participate in all discussions, however, is not authorized to participate in the deliberations and may not vote.

All individuals who are asked to serve as consultants will be queried to determine whether any conflict of interest exists prior to their work with the IRB. If there is any conflict of interest they will not be allowed to consult, and another consultant will be selected.

The IRB administrative staff, Director or designee will contact the consultant and will determine how the information will be conveyed to the IRB: i.e., attendance at the meeting or written report.

Key information provided by consultant will be documented in the minutes. All written reports or other documentation of consultant reviews will be maintained in the protocol file.

Use of consultants will be documented in the minutes, as this will be presented to the convened IRB during the discussion of the protocol. For submissions reviewed via the expedited mechanism, use of a consultant will be documented in the protocol file.

3.2.4 IRB Executive Chair.

The IRB Executive Chair role is filled by an IRB Chair selected by the Director of Human Research Protections and approved by the Vice Provost for Research.

3.3 Resignations and Removals

A member may resign before the conclusion of his/her/their term. The vacancy will be filled as quickly as possible. The Director of Human Research Protections may remove a member at any time.

3.4 Compensation

Participation by University faculty or staff as an IRB member is considered to either be voluntary or a component of their job responsibilities as established by their supervisors. Regular members who are not affiliated with the University shall receive reimbursement for parking and other miscellaneous expenses. IRB Chairs receive salary compensation for their respective roles as permitted by the Vice Provost for Research.

3.5 Liability Insurance

Regular and alternate members have liability insurance coverage as part of their IRB membership in their capacity as agents of the University.

3.6 IRB Rosters

IRB rosters will be maintained by the IRB Administrators and will include:

- Names of IRB members
- Earned degrees
- The representative capacity of IRB members
- Scientist and nonscientist
- Affiliated or nonaffiliated member including employment or other relationships between the IRB member and the organization.
- Knowledge of vulnerable populations, if the member is representing a vulnerable population
- Indications of IRB members' experience sufficient to describe each IRB member's chief contribution.
- Alternate members

- The regular members or class of regular members from whom each alternate may substitute.

4. REFERENCES

[45 CFR 46.103\(b\)\(3\)](#); [21 CFR 56.115\(a\)\(5\)](#)

1. PURPOSE

This policy defines the duties required of IRB members.

2. POLICY STATEMENT

Each IRB member's primary duty is the protection of the rights and welfare of the individual human beings that are serving as the participants of that research. The reviewer must understand that he/she/they is not serving on the Board to expedite the approval of research, but to serve as a link between the investigator and the research participants. In order to fulfill his/her/their duties, IRB members are expected to be knowledgeable of the regulations governing human participant protection, biomedical and behavioral research ethics, and the policies of the University of Pennsylvania germane to human participant protection. The IRB must be perceived to be fair and impartial, immune from pressure either by the institution's administration, the investigators whose protocols are brought before it, or other professional and nonprofessional sources.

3. SPECIFIC POLICIES

3.1 University Service

The IRBs are appointed as University Committees. As such, the IRB members serve the University of Pennsylvania as a whole, rather than a particular school or department. Therefore, members must not allow their own interests or that of their departments or schools to supersede their duty to protect the rights and welfare of research participants.

3.2 Term of Duty

Regular IRB members and chairpersons are expected to commit to at least a 1-year term and during that time, fulfill certain duties. These duties will be described prior to appointment and each IRB member is expected to fully understand the duties of IRB members prior to accepting appointment as an IRB member.

Students of the Masters of Translations Research (MTR) Program or comparable educational programs are not IRB members during their program required service but may join the IRB after their program requirements are fulfilled.

3.3 Specific Duties

3.3.1 Regular Members: All members are expected to review all actions scheduled for convened review, be familiar with them, and prepared to discuss the materials at the convened IRB meeting.

Non-affiliated member(s): Nonaffiliated members are expected to provide input regarding their knowledge about the local community and be willing to discuss issues and research from that perspective.

Non-scientific members: Nonscientific members are expected to provide input on areas germane to their knowledge, expertise and experience, professional and otherwise. For example, members who are lawyers should present the legal views of specific areas that may be discussed, such as exculpatory language or state requirements regarding consent. Non-scientific members should advise the Board if additional expertise in a non-scientific area is required to assess if the protocol adequately protects the rights and welfare of participants and to comment on the comprehension of the consent document.

Scientific members: Scientific members are expected to contribute to the evaluation of a study on its scientific and statistical merits and standards of practice. These members should also be able to advise the Board if additional expertise in a scientific or non-scientific area is required to assess if the protocol adequately protects the rights and welfare of participants.

Chair: In addition to the above responsibilities (germane to the member's capacity) the chair leads convened meetings of the IRB and is expected to review the protocol(s), informed consent form(s), and all supporting documents that will be reviewed by the convened IRB. The Chair is expected to review this information prior to the meeting and participate in the review and facilitate the ensuing discussion. The Chair is expected to be broadly familiar with all protocols being reviewed by the convened IRB. The Chair is empowered to recommend suspending the conduct of a research project deemed to place individuals at unacceptable risk.

The Chair is expected to provide oversight of the IRB, determine eligibility for and, where appropriate, conduct expedited reviews.

The Executive Chair may appoint a Co-chair to assist or act on behalf of the chair in particular IRB matters and at IRB meetings, either as a general procedure, or on a case-by-case basis.

3.3.2 Primary Reviewers: In addition to the duties described in section 3.3.1 each regular member will be expected to act as a primary reviewer for assigned studies at convened meetings. The primary reviewer presents his/her/their findings resulting from review of the application materials and provides an assessment of the regulatory criteria and recommends specific actions to the Board. He/she/they leads the discussion of the study by the convened IRB. The primary reviewer is required to read the entire submission, be familiar with it, and be prepared to conduct an in-depth review of all materials. The primary reviewer is expected to contact the investigator, IRB Chair, or Administrator in advance of the convened meeting for clarification of unresolved issues related to the submission.

3.3.3 Alternate members. The appointment and function of alternate members is the same as that for regular IRB members, and the alternate's expertise and perspective are comparable to those of the Principal member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a regular member, the alternate member will receive and review the same materials prior to the IRB meeting that the Principal member received or would have received.

The IRB roster identifies the regular member(s) for whom each alternate member may substitute. The alternate member will not be counted as a voting member unless the regular member is absent. The IRB minutes will document when an alternate member replaces a regular member.

3.4 Evaluation of IRB Members and Chairs Performance

3.4.1 IRB members and Chairs will be asked to complete Self Evaluation Forms on an annual basis and submit the forms to the appropriate members of the IRB staff.

3.4.2. The Director for Human Research Protections and Associate Director, in conjunction with appropriate staff members, will review the IRB Member and Chair self-assessments periodically to determine education and training needs and to make decisions regarding continuation of IRB membership. This process is outlined in the Guide to Daily Operations.

3.5 Periodic Review and Adjustment of the Membership and Composition of the IRBs

The Director of Human Research Protections and Associate Director will regularly assess and adjust membership and composition of the IRB to meet regulatory and organizational requirements.

3.6 Allegations of Undue Influence

The Provost and the Vice Provost for Research prohibit attempts by investigators, employees, and sponsors contracting with institutional officials to use undue influence with the IRB, any of its members or staff, an investigator or any other member of the research team to obtain a particular result, decision or action.

“Undue influence” means attempting to interfere with the normal functioning and decision-making of the IRB or to influence an IRB member or staff, an investigator or any other member of the research team outside of established processes or normal and accepted methods, in order to obtain a particular result, decision or action by the IRB or one of its members or staff.

IRB members and IRB staff should report undue influence to the Director of Human Research Protections. The Director is responsible for the initial investigation. The following institutional officials will be notified, as appropriate, of allegations of undue influence and may be asked to review and endorse a corrective action plan. Institutional officials may include the following:

- Provost
- Vice Provost for Research
- Dean of applicable School
- Department Chair
- Office of General Counsel
- Other compliance offices

Individuals who are responsible for business development are prohibited from:

- Serving as members or ex-officio members on the IRB.
- Carrying out day-to-day operations of the review process.

4. REFERENCES

[45 CFR 46.107](#); [21 CFR 56.107](#); [45 CFR 46.110\(b\)\(2\)](#); [21 CFR 56.110\(b\)\(2\)](#); [OHRP: IRB Guidebook](#); [FDA Information Sheets: FAQ, Section II, Question 17](#)

FO 300 FUNCTIONS AND OPERATIONS

FO 300	FUNCTIONS AND OPERATIONS
301	RESEARCH SUBMISSION REQUIREMENTS
302	IRB MEETING ADMINISTRATION
303	ADMINISTRATIVE REVIEW AND DISTRIBUTION OF MATERIALS
304	DOCUMENTS AND DOCUMENT MANAGEMENT

1. PURPOSE

This policy outlines the required documents and supporting information required from investigators for IRB assessment.

2. POLICY STATEMENT

IRB members often rely solely on the documentation submitted by investigators, or other parties for initial and continuing review. Therefore, this material must provide IRB members with enough information about a study to assess if it adequately meets the IRB's criteria for approval. A submitted protocol will be scheduled for IRB review only when the IRB staff determines that the information and materials submitted present an adequate description of the proposed research.

3. SPECIFIC POLICIES

3.1 Submission Requirements for Initial Review

Electronic submission requirements for initial review are outlined in the IRB Application and supplemental guidance available on the HS-ERA website. Investigators applying for initial approval of proposed research must follow the guidance.

3.2 Submission Requirements for Ongoing Review

3.2.1 During the approval period, investigators must submit documentation to inform the IRB about changes in the status of the study. Ongoing review includes but may not be limited to the following activities: Site Visits and Third-Party Verification, Continuing Reviews, Deviations, Reportable Events, Significant New Findings, and Modifications. For electronic submissions, all ongoing review submissions must be submitted via HS-ERA.

3.2.2 Study Expiration Tracking and Reminders

Investigators are responsible for tracking the expiration dates of their studies. As a courtesy, the IRB may send notification reminders regarding study expiration. For convened review protocols, 90 days prior to IRB approval expiration date, investigators receive a notification that their continuing review application will be required. A notification is also received 45 days from and the day of expiration. The notification reports to the Investigator the process for seeking continuing approval for the protocol. For expedited review protocols, the notifications are sent 45 days from and the day of expiration.

3.3 Action Taken If Documentation is not adequate or Additional Information is Required

If the IRB or IRB staff determines that the submitted documents are not adequate, investigators may be required to submit additional information, or their presence may be requested to answer questions or explain the details of the study. Incomplete submissions will not be reviewed by the IRB.

4. REFERENCES

[45 CFR 46.115; 21 CFR 56.108\(a\)\(4\); OHRP Guidance on Continuing Review, January 15, 2007](#)

1. PURPOSE

The policies in this section provide the framework to ensure that IRB meetings are conducted and documented in a consistent manner in order to meet federal and institutional requirements.

2. POLICY STATEMENT

Except when an expedited or exempt review procedure is used, the IRB will review proposed research at convened meetings at which a quorum is present. Each IRB will meet monthly, or at some other frequency determined by the Chairperson and the Director of Human Research Protections.

3. SPECIFIC POLICIES

3.1 Quorum

3.1.1 A majority of members must be present. Majority is defined as first whole number that exceeds 50%.

3.1.2 A quorum consists of regular and/or alternate members and includes at least one member whose primary concerns are in scientific areas, and one member whose primary concerns is in a nonscientific areas.

- 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 are present.
- If required members (i.e. non-scientific) leave the room and quorum is lost, votes cannot be taken until the quorum is restored, even if half of the members are still present.

3.1.3 An alternate member may attend in the place of a regular member in order to meet the quorum requirements outlined above.

3.1.4 Special consultant(s) will not be used to establish a quorum.

3.1.5 If a member identifies a conflict with an agenda item, that member will leave the room during the discussion and vote of the protocol and will only return to the discussion to answer directive questions raised by the Committee during the review and the member will not count towards the quorum.

3.1.6 If a member has not reviewed an agenda item or items, they will be expected to abstain from the discussion and vote for those items, but the member will still count towards the quorum.

3.2 Primary Reviewers, Secondary Reviewers, and Regulatory Representatives

Prior to the meeting, the IRB administrator will designate primary and secondary reviewers for each research protocol. For protocols requiring review by a convened meeting of the IRB, the primary reviewer will conduct an in-depth review of all materials and will be prepared to lead the discussion at the convened meeting of the IRB. All other members will review materials provided prior to the meeting and will be prepared to participate in the discussion at the convened meeting.

The Secondary Reviewer is responsible for review specifically related to the content of the informed consent form and a review of the informed consent process. They will also review all materials provided in support of the application to the IRB.

If a member is determined to require specific support to complete the review of a submission for convened review, the Chair will be a co-reviewer and will be listed as such for documentation purposes.

The Regulatory Representative is a member of the Senior IRB staff. These individuals will be in a position to provide additional guidance on currently established research regulations and any additional policies related to protections of human participants in research conducted at Penn or other sites covered by Penn.

Each IRB has at least one unaffiliated member, who is requested to attend at least 8 of 12 meetings per year.

At least one member of the board present at convened meetings represents the general perspective of participants. The unaffiliated member and/or the non-scientist member may be the same person representing the perspective of participants.

3.3 Meeting Materials Sent Prior to IRB Meetings

All IRB members will be sent study documentation required for review in sufficient time prior to the meeting to allow for adequate review. IRB members are sent study documentation 5 to 8 business days before the meeting except in circumstances requiring a rush review from the investigators (i.e. patient safety notification, funding contingencies). This study documentation includes:

3.3.1 Agenda: A meeting agenda will be prepared by an IRB administrator or designee and distributed to IRB members prior to each meeting. A copy of the agenda and attached materials will be maintained on file with the meeting minutes.

The meeting agenda will remind members to contact the IRB Administrator or Chair as soon as possible to declare any potential COI they may have with research that will be reviewed by the convened IRB.

3.3.2 Reviewer materials: The materials necessary to successfully review the submissions to verify that the approval criteria are met will be provided to the IRB members, including copies of the completed Pre-Review Forms and all appropriate IRB Reviewer Checklists.

3.4 Minutes

3.4.1 Recording: The IRB administrator or designee will prepare IRB minutes according to the outlined template for organizing content of the minutes.

3.4.2 Draft minutes will be distributed to members at the next IRB meeting following completion by staff for review. Any corrections requested by the IRB will be made by the administrator or designee and the minutes will be included on the agenda of the next IRB meeting. The minutes will be forwarded for acceptance at the next possible convened meeting of the specific board.

IRB administrators will maintain copies of the agendas and minutes on the IRB shared drive. All IRB minutes shall be available to the Institutional Official if they are requested. IRB Minutes shall be available to the Senior Associate Vice Provost for Human Research by way of the Office of Clinical Research Compliance Unit as well as the Research Compliance Officer as the Vice Provost for Research has delegated this responsibility to the Senior Associate Vice Provost for Human Research and the Research Compliance Officer.

3.5 Telephone or Videoconference Use

3.5.1 Convened Meeting Using a Speaker Phone or Videoconference

Should a member not be able to be physically present during a convened meeting, but is available by telephone or videoconference, the meeting can be convened using a speakerphone or videoconference software. The member who is not physically present will be connected to the rest of the members via speakerphone or videoconference. In this manner, all members will be able to discuss the protocol even though one member is not physically present. Members participating by such speakerphone call or videoconference may vote provided they have had an opportunity to review all the material the other members have reviewed. The minutes will document which members, if any, participated in the convened meeting via telephone or videoconference.

3.5.2 Meetings Conducted Via Telephone Conference Calls

Meetings may be convened via a telephone or video conference call. A quorum (as defined above) must participate for the conference call meeting to be convened.

To allow for appropriate discussion to take place, all members must be connected simultaneously for a conference call to take place. "Telephone polling" (where members are contacted individually) will not be accepted as a conference call. Members who are not present at the convened meeting or participating in the conference call may not vote on an issue discussed during such a telephone conference convened meeting (i.e., voting by proxy is not permitted).

3.6 Voting

Members of the IRB vote upon the recommendations made by the primary reviewers according to the criteria for approval (See SOP RR 403 and RR 405). If quorum is lost during a meeting, the IRB cannot take votes until it is restored.

Votes are taken in the convened meeting and documented in the minutes by the IRB staff member serving in the administrative function.

The IRB may make the range of decisions described in RR 407. Members also will determine level of risk and the frequency of review for each protocol.

If an IRB staff member is serving on the Board as a regular or alternate member that staff member will not be responsible for any administrative functions during that meeting, specifically, he/she/they is expected to contribute to the discussion as a substantive participant.

3.7 Non-members and Guests

If the IRB permits non-members and guests to attend a convened meeting, the minutes will record the names(s) of all such attendees. The minutes will be clear that the non-member or guest did not participate in the deliberation and voting. Non-members and guests do not count towards the quorum.

4. REFERENCES

[45 CFR 46.103\(b\)\(4\)](#); [45 CFR 46.107\(f\)](#); [21 CFR 56.107\(f\)](#); [45 CFR 46.108](#); [21 CFR 56.108\(c\)](#); [45 CFR 46.109\(a\)](#); [21 CFR 56.109\(a\)](#); [45 CFR 46.115\(a\)\(2\)](#); [21 CFR 56.115\(a\)\(2\)](#); [FDA Information Sheets](#)

1. PURPOSE

The policies in this section describe the requirements to document pre-review and distribution prior to IRB review.

2. POLICY STATEMENT

The efficiency and effectiveness of the IRBs are supported by administrative procedures that assure that IRB members not only have adequate time for thorough assessment of each proposed study, but that the documentation they receive is complete and clear enough to allow for an adequate assessment of study design, procedures, and conditions.

3. SPECIFIC POLICIES

3.1 Incomplete Submissions

Incomplete applications will be logged into the database and assigned an IRB protocol number for tracking. The IRB Administrative staff will contact the investigator and request all necessary materials or will return the submission to the investigator, if necessary, to provide the materials needed for a complete application.

3.2 Scheduling for Review

If a complete submission meets expedited or exempt review requirements, the review will be performed as described in SOP 402. All other applications requiring review by a convened IRB will be placed on an appropriate agenda for review.

3.3 Distribution Prior to IRB Meetings

Primary reviewers, regular members and alternates attending the meeting receive and review the materials uploaded in the electronic submission system. At least one member is assigned as the primary reviewer. The materials provided for review include, but are not limited to, the consent document and standalone protocol, as applicable.

Alternates are required to receive and review the same materials as any other IRB member. Consultants will only receive copies of material that pertain to their requested input as determined by the Director, Associate Director, or Chair.

Electronic submission(s) are made available to the IRB members via HS-ERA and the agendas provided include a confirmation code and protocol number for members to access the submission(s).

Copies of application materials described in Policy 302.3.3 will be distributed to all IRB members attending, prior to the IRB meeting, either via paper or electronically by email. Late submission add-ons will be approved for addition to the agenda by the Director or Associate Director and will be submitted to members via e-mail prior to the IRB meeting. Original submission materials will be retained by IRB administrative staff and will be available for the IRB meeting.

3.4 Confidentiality

All material received by the IRB will be considered confidential and will be distributed only to meeting participants (regular members, alternate members and special consultants) for the purpose of review. All application materials will be stored in an IRB study file with access granted to appropriate IRB personnel, IRB members, HS-ERA reviewers, and ancillary Committee members that support human research at Penn.

3.5 Destruction of Copies

All material received by the IRB considered to be confidential and in excess of the required original documentation and appropriate uncontrolled forms will be collected at the end of the meeting and destroyed by a method deemed appropriate by the Director.

4. REFERENCES

[45 CFR 45.108\(a\)](#); [21 CFR 56.108\(a\)](#)

1. PURPOSE

The policies in this section describe the requirements for document management, including:

- Document Retention
- Administrative Documents
- Archiving

2. POLICY

Institutional Review Board files must be maintained in a manner that contains a complete history of all IRB actions related to review and approval of a protocol, including scientific reviews, if any, continuing reviews, modifications, reports of unanticipated problem increasing risks to participants or others, participant complaints (which will be kept independent of the file), and reports of serious or continuing noncompliance. All records regarding a submitted study (regardless of whether it is approved) must be retained in an appropriate manner as required by regulatory requirements and/or institutional policy.

Records must be accessible for inspection and copying by authorized representatives of the sponsor, funding department or agency and institutional auditors at reasonable times and in a reasonable manner.

Required documents must be submitted to the appropriate funding entity as required.

If an external site has agreed to rely on the IRB through an IRB authorization agreement, relevant records, including but not limited to minutes, approved protocols, consent documents, and other records may be made available to the relying organization upon request.

3. SPECIFIC POLICIES

3.1 Document Retention.

In alignment with federal regulatory requirements, the IRB must retain all records regarding a project or protocol application (regardless of whether it is approved) for at least three (3) years. For all applications that are approved, and the research initiated, the IRB must retain all records regarding that research for at least three (3) years after completion of the research or termination of IRB approval. If a protocol is cancelled without participant enrollment, IRB records are still maintained for at least three years after cancellation. In accordance with institutional policy, such records may be confidentiality destroyed after this length of time, but within 7 years after completion of the research, cancellation, or termination of IRB approval.

3.1.1 Adequate documentation of each IRB's activities will be prepared, maintained and retained, including:

Submissions: Copies of all original research protocols or project descriptions reviewed, scientific evaluations, if any, that accompany the proposals, approved consent documents, progress reports submitted by investigators, and reports of unanticipated problems occurring to participants and reported protocol deviations as submitted.

Regulatory Documents/documentation:

- Correspondence between the IRB and investigator
- Statements of significant new findings provided to participants
- For the initial & continuing review of research by expedited procedure

- The specific permissible category
- Description of action taken by reviewer
- Any findings under the regulations
- For exemption determinations, the specific category of exemption
- Unless documented in the minutes, determinations required by the regulations and protocol specific findings for:
 - Waiver or alteration of the consent process
 - Research involving pregnant individuals, fetuses, and neonates
 - Research involving incarcerated persons
 - Research involving children
- For each protocol's initial and continuing review, the frequency for the next continuing review.

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

Reports of any complaints received from participants, regulatory agencies and their resolution (as noted above, which will be kept separate from the file for confidentiality purposes).

Agendas and Minutes of all IRB meetings.

In order to allow a reconstruction of a complete history of IRB actions related to the review and approval of the protocol, the IRB records include copies of all materials reviewed by the IRB.

3.2 IRB Administration Documents

In alignment with federal regulatory requirements, the IRB must maintain and retain all records regarding IRB administrative activities that affect review activities for at least three (3) years. The IRB must retain all records regarding protocols that are approved, and the research initiated for at least three (3) years after completion of the research, cancellation, or termination of IRB approval. In accordance with institutional policy, such records may be confidentiality destroyed after this length of time, but within 7 years after completion of the research, cancellation, or termination of IRB approval.

3.2.1 IRB Rosters. Rosters of regular and alternate IRB members identified by name, earned degrees, representative capacity, and indications of experience sufficient to describe each regular and alternate member's chief anticipated contribution 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 governing panel or board, stockholder, paid or unpaid consultant).

Alternate members will be included on the roster. In addition to the above information, the roster shall indicate the regular member for whom the alternate may substitute

Current and previous membership rosters will remain in the IRB office for review as needed.

The roster of IRB members must be submitted to Office for Human Research Protections (OHRP). Any changes in IRB membership must be reported to the head of the department or agency supporting or conducting the research, unless the department or agency has accepted the existence of an FWA. In the latter case, changes in membership are to be reported to OHRP.

3.2.2 Current and obsolete copies of the Standard Operating Policies

3.3 Archiving

All documents and materials germane to IRB determinations will be archived according to institutional policy 3 years after completion of the research, cancellation, or termination of IRB approval.

The IRB may archive materials for active research studies that are more than 3 years old. These archived materials will be available for retrieval if required for an audit or inspection.

4. REFERENCES

[45 CFR 46.103](#); [45 CFR 46.115](#); [21 CFR 56.115](#); [University Policy](#)

RR 400 REVIEW OF RESEARCH

RR 400	REVIEW OF RESEARCH
401 A	NON-RESEARCH ACTIVITIES AND RESEARCH NOT INVOLVING HUMAN PARTICIPANTS
401 B	EXEMPT AND RESEARCH UNDERGOING LIMITED REVIEW PROCEDURES
402	EXPEDITED REVIEW
403	INITIAL REVIEW - CRITERIA FOR IRB APPROVAL
404	ONGOING REVIEW
405	CONTINUING REVIEW - CRITERIA FOR RENEWAL
406	STUDY COMPLETION
407	CATEGORIES OF ACTION
408	RESPONDING TO REPORTS OF NONCOMPLIANCE
409	ADMINISTRATIVE HOLDS AND SUSPENSIONS, TERMINATION OF IRB APPROVAL

RR 401 A NON-RESEARCH ACTIVITIES AND RESEARCH NOT INVOLVING HUMAN PARTICIPANTS

1. PURPOSE

This policy describes the activities that do not require IRB review because the activity does not involve research with human participants.

2. POLICY STATEMENT

Human research is any activity that either 1) meets the HHS definition of “research” and involves “human participants” as defined by the HHS regulations or 2) meets the FDA definition of “clinical investigation” and involves “human participants as defined by the FDA regulation.

Unless otherwise required pursuant to institutional policy, activities that do not meet the definition of human research do not require submission to the IRB.

The IRB Guidance: “Is IRB Review Required?” provides direction on making human research determinations.

3. SPECIFIC POLICIES

3.1 Activities that do not require IRB Review

In addition to the Director and designated IRB members, the Senior IRB Staff may determine that an activity does not meet the regulatory definition of human research. Analysts may determine that an activity does not meet the regulatory definition of human research in consultation with Senior IRB Staff. Investigators who elect to obtain an official determination may submit the Human Research Determination Form or the Quality Improvement Form for review.

Staff will review the form and supporting documents. Formal submissions will be logged into the database and filed. Investigators will be notified in writing regarding whether the proposed activities do or do not meet the regulatory definition of human research.

4. REFERENCES

[21 CFR 50.3](#); [45 CFR 46.102](#); [21 CFR 812.3\(p\)](#)

1. PURPOSE

This policy describes the process for determining whether human research qualifies for review under exempt and limited review categories.

2. POLICY

Research activities in which the only involvement of human participants will be in one or more specific categories may be exempt from IRB review. Determination of exemption must be based on regulatory and institutional criteria and documented. Exempt status may be determined by authorized designees of the Director of Human Research Protections.

3. SPECIFIC POLICIES

3.1 Exempt Research Activities

The IRB will exempt from ongoing IRB review only those research activities that involve human participants that fall within one or more of the specified exempt categories.

3.2 Review of Exempt Research

When granting exemptions, the IRB will determine that the following criteria are met where applicable:

- The research presents no more than minimal risk to participants.
- Selection of participants is equitable.
- If the research involves interactions with participants, the circumstances of consent minimize coercion and undue influence.
- Participants will be informed about:
 - The study involves research,
 - The study procedures
 - That the research is voluntary, and
 - Whom to contact with questions.
- Provisions for protecting the privacy interests of participants are adequate.
- If private identifying data are recorded, provisions for maintaining the confidentiality of data are adequate.

3.3 Execution of Exempt Research

3.3.1 Continuing Review. Annual continuing review is **not** required for research granted exemption. Investigators may submit a request to close the research protocol when research is completed.

3.3.1. Modifications. Investigators are required to report modifications that may change the eligibility of the protocol's exempt status, or any applicable HIPAA waiver determination changes.

It is the investigator's responsibility to notify the IRB of any changes or modifications that are made to the study's design, procedures, and so on, that do not fall within one of the categories exempted from the regulations.

3.4 Limited IRB Review

For exempt research subject to limited IRB review, the IRB shall apply the criteria set forth in 45 CFR 46.111(a)(8). IRB Members conducting limited IRB review may not disapprove research. However, the IRB retains the authority to suspend or terminate IRB approval of research approved with limited IRB review.

- Research eligible for limited IRB review meets one or more exempt categories 2(iii), 3(C), 7, or 8.
- If an IRB member reviewing the research finds that research is greater than minimal risk, the reviewer must document the rationale for this determination and the rationale for review by the convened IRB.
- The following information must be submitted by researchers for a limited IRB review determination as applicable to the research, including:
 - The full protocol, application, or a protocol summary containing the relevant information to determine whether the proposed research fulfills the criteria for approval;
 - Proposed consent document; and
 - Recruitment materials
- The following determinations must be documented when conducting limited IRB review:
 - For exemption Categories 2(iii) and 3(C): there are adequate protections for the privacy interests of participants and the confidentiality of identifiable data.
 - For exemption Category 7:
 - Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained;
 - Broad consent is appropriately documented, or documentation is waived; and
 - There are adequate protections for privacy interests of participants and the confidentiality of identifiable data
 - For exemption Category 8:
 - Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained;
 - Broad consent was appropriately documented, or documentation is waived;
 - The research to be conducted is within the scope of the broad consent referenced; and
 - There are adequate protections for privacy interests of participants and the confidentiality of identifiable data.

4. REFERENCES [45 CFR 46.101\(b\)](#); [45 CFR 46.102](#); [21 CFR 56.104](#)

1. PURPOSE

This policy describes the research that can be reviewed by the Director of Human Research Protections or designee and outlines the process to determination if the research meets criteria for expedited review.

2. POLICY

An expedited review procedure consists of a review of research involving human participants by an appropriately trained IRB Analyst/Administrator, who is trained in the application of these particular regulations. The IRB Analyst/Administrator places submissions determined to meet these approval criteria for approval by the Director, Associate Directors, or other designated IRB members.

The categories of research that may be reviewed by the IRB through an expedited review procedure include research activities that (1) present no more than minimal risk to human participants, and (2) involve only procedures listed in one or more of the specific categories listed in the regulations at 45 CFR 46.110 and 21 CFR 56.110. This policy pertains to both initial and continuing IRB review of the items included in this policy.

The expedited review process may not be used by the IRB of record for classified research involving direct interactions with human participants. Expedited review of an initial submission that requests direct interaction with incarcerated persons will also not apply.

3. SPECIFIC POLICIES

3.1 Authority of the Expedited Reviewer

The Chair, Co-Chair or other experienced IRB member reviewers, designated in writing, by the Director, or by the IRB members voting in a convened meeting may exercise all of the authorities of the IRB, except that he/she/they may not disapprove the research. A research proposal may be disapproved only after review by the convened IRB.

Consultants may assist the IRB in the review of issues that require expertise beyond that available on the committee; but may not carry out the expedited review. Individuals conducting expedited review will contact the Director to request a consultant's review.

3.2 Notification of the Board

When the expedited review procedure is used, all regular members will be informed via the IRB minutes of actions taken by the designated IRB reviewer. The IRB minutes include a report of expedited actions that the members review and accept at the convened meeting. The IRB members are given an opportunity to ask questions or raise concerns with any expedited actions and those concerns are summarized in the following month's meeting minutes.

3.3 Documentation

The information received by the Primary Reviewer for expedited review is the same information provided to the Primary reviewer for review at a convened IRB meeting.

If the study qualifies for review via expedited review, the designated IRB reviewer will document his/her/their determination of the applicable expedited review category. Consistent with review by a convened IRB, expedited reviewer will consider:

- All the criteria for review found at 45 CFR 46.111 and 21 CFR 56.111

- All requirements found at Subparts B, C, and D, when applicable
- The requirements for informed consent including altering or waiving the requirement for consent
- Other applicable requirements (including but not limited to: FDA exemption, DOD requirements, HIPAA requirements, etc.)

When research is FDA regulated (clinical investigations), the IRB requires the submission of product information, such as a package insert, investigator's brochure, or device manual to consider the nature of and any risks posed by the clinical investigation, the degree of uncertainty regarding the risks involved, and whether the study involves novel therapies.

The IRB verifies the projected rate of enrollment for clinical investigations led by industry sponsors or other sites from the clinical protocol, DSMB charter, and Data and Safety Monitoring Plan.

The IRB's minutes will include documentation of the studies that were reviewed via expedited review including a brief description of the purpose of the research, the designated IRB reviewer who approved the research and the approval date.

3.4 Additional Items that May be Reviewed by the Chair or Designee

3.4.1 Withheld Approval Pending Minor Revisions or Conditional Re-approvals

Minor revisions to consent documents and documentation submitted as a result of convened IRB review and as a condition to final approval may be reviewed by the Director, Associate Directors, IRB Chair or other designated IRB members.

However, when the response submission contains substantive clarifications or modifications that are directly relevant to the criteria for approval, the protocol will go back to a convened IRB and not be approved by the IRB Chair or other personnel noted above.

3.4.2 Ongoing Review

The Director, Associate Directors or other designated IRB members may use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Any protocol revision that entails more than a minimal risk to the participant as determined by the Director or his/her/their designee must be reviewed by the convened IRB at a convened meeting.

Revisions to Informed Consent Documents: Minor changes to informed consent documents that do not affect the rights and welfare of study participants, or do not involve increased risk or significant changes in study procedures may be reviewed and approved by the Director, Associate Directors, or other designated IRB members.

Advertisements/Other supplemental documentation: The Director, Associate Directors, or other designated IRB members may approve new or revised recruitment advertisements, recruitment flyers, and audio or video recruitment materials.

3.4.3 Approval of Participating Sites

The Director, Associate Directors, or other designated IRB members may use the expedited review procedures to review external site requests to rely on the Penn IRB's approval. These requests to add external sites may be submitted as modifications to previously approved research. Review of these requests is necessary if the external organization has agreed to rely on the Penn IRB through an IRB authorization agreement or under the conditions of an approved cooperative agreement. The Penn IRB, as the IRB of Record, will review the participating site's application, which shall include information regarding the participating site's research team, the nature of their participation in the multi-site protocol, and the results of any local context review conducted by the external organization's IRB or Human Research Protections Program. This may include revisions to the IRB approved consent form.

Minor changes to the informed consent documents or the conduct of the multi-site protocol may be reviewed and approved using the expedited mechanism. Any protocol revision that entails more than a minimal risk to the participant as determined by the Director or his/her/their designee must be reviewed by the convened IRB at a convened meeting.

4. REFERENCES

[45 CFR 46.102\(i\)](#); [21 CFR 56.102\(i\)](#); [45 CFR 46.110](#); [21 CFR 56.110](#); [Federal Register Vol. 63, No. 216, 11/9/98, pp. 60353-60356](#); [45 CFR 46.111](#); [21 CFR 56.111](#)

1. PURPOSE

This policy elucidates the minimal requirements that all research proposals that involve human participant participation must meet in order to be approved for conduct at the University of Pennsylvania.

2. POLICY

All research proposals that intend to enroll human participants must meet certain criteria before study related procedures can be initiated. The criteria are based on the principles of justice, beneficence and autonomy as discussed in the Belmont Report and are specified below. In addition, certain other criteria that are unique to the University of Pennsylvania may apply and must be met as well before any involvement of human participants may begin.

3. SPECIFIC POLICIES

3.1 Minimal Criteria for Approval of Research

In order for a research project to be approved, the IRB must find that:

- 3.1.1 Risks to participants are minimized: By using procedures which are consistent with sound research design, and which do not unnecessarily expose participants to risk, and, whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.
- 3.1.2. Risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may be expected to result. In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies those participants 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.
- 3.1.3 Selection of participants 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, incarcerated persons, pregnant individuals, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.
- 3.1.4 Informed consent will be sought from each prospective participant or the participant's legally authorized representative, in accordance with and to the extent required by appropriate local, state and federal regulations.
- 3.1.5 Informed consent will be appropriately documented as required by local, state and federal regulations.
- 3.1.6 Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants.
- 3.1.7 Where appropriate, there is adequate provision to protect the privacy of participants and to maintain the confidentiality of data.
- 3.1.8 When some or all of the participants, such as children, incarcerated persons, pregnant individuals, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to

coercion or undue influence or international sites are used, additional safeguards have been included in the study, and in the IRB review process to protect the rights and welfare of these participants.

3.1.9 The IRB determines that the provisions are adequate to protect the privacy interests of participants.

3.1.10 The IRB determines that the provisions are adequate to protect the confidentiality of data.

3.1.11 For repository activities, the IRB may make determinations concerning the regulatory status and appropriate use of stored data and biologic samples.

3.1.12 The IRB determines that the research studies 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.

3.1.13 Where appropriate (i.e. greater than minimal risk research), the IRB considers provisions for monitoring data to ensure the safety of participants to be appropriate.

3.2 Additional Criteria for Studies Involving Protected Health Information

Studies proposing access to or collection of protected health information within the covered entities of the University of Pennsylvania require consideration of additional items to protect the privacy of the protected health information. Therefore, the IRB must find that one of the following applies:

3.2.1 Appropriate authorization is obtained from human participants or their effective representative for the use or disclosure of their protected health information;

3.2.2 The IRB has approved a waiver of such authorization;

3.2.3 The protected health information will be contained in a limited data set with appropriate safeguards to maintain privacy; or,

3.2.4 The protected health information will be de-identified.

3.3 Other Criteria

The IRB may require verification of information submitted by an investigator. The purpose of the verification will be to provide necessary protection to participants when deemed appropriate by the IRB.

3.4 Reliance on Other IRBs for Review and Approval of Research Conducted at the University of Pennsylvania

The IRB may enter into joint review arrangements, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. The reliance on another IRB will be outlined in an approved IRB authorization agreement or under the conditions of an approved cooperative agreement.

The Director of Human Research Protections will be responsible for determining whether another IRB is appropriately qualified to serve as the IRB of Record for the University of Pennsylvania. If the Director of Human Research Protections agrees to rely upon a non-accredited IRB or EC for a portion of the research, the Director of Human Research Protections

will determine if additional steps are necessary, based on the risks posed by the research, to ensure participants in the research are adequately protected.

When the Penn IRB agrees to rely upon the review of another qualified IRB, that other IRB, as the IRB of Record, will conduct the ethical review and determination that the criteria for IRB approval have been met. The Penn IRB as the relying IRB will be responsible for conducting a local context review.

The local context review is an administrative review performed by IRB staff. The review is to ensure that the protocol meets any applicable requirements from state or local laws, regulations, institutional policies, standard, or other local factors, that would affect the conduct or approval of the research at Penn. It will also include a review of any applicable consent forms to ensure that all approved Penn required language is incorporated into the forms that will be used to enroll participants at Penn. The results of this local context review will be communicated to the research team so that they can be submitted to the IRB of Record for their review and approval.

Local context review also includes review by any applicable ancillary review committees that are required to review the research according to Penn institutional policies. Ancillary committee reviews are not conducted by IRB staff; however, research may not begin at Penn until they have been completed. If the IRB of Record requests additional information about local requirements or local research context issues relevant to their determinations, the Penn IRB will respond to the requests or assist the research team in responding to the request.

3.5 Additional Considerations for Initial Review of Community Based Participatory Research

Community-based participatory research (CBPR) is a form of community-engaged research, involving a collaborative approach for participation, shared decision-making, and mutual ownership in all aspects of the research process by communities affected.

Review of studies that involve community participation may require special considerations and expertise when initially reviewed. While participatory studies need to meet all requirements for initial approval, the IRB recognizes that community engaged research often requires additional thought to both protect participants and facilitate conduct of the research. The IRB has experience reviewing community-engaged research.

The IRB recognizes that there is not a “one size fits all” approach to the review of CBPR and will therefore consider the following tools when appropriate:

3.5.1 Periodic IRB member / staff trainings about review of participatory projects, with emphases on equitability and justice within the review process for community engaged research. Trainings may be conducted by the IRB, investigators, or community members who are or have been engaged in participatory research.

3.5.2 Recruitment of board members with experience conducting participatory projects in both biomedical and social-behavioral settings, including within the clinical investigation milieu.

3.5.3 Distribution of guidance regarding the review and conduct of participatory research.

3.5.4 Recruitment and utilization of board members consultants with lived experiences to advise on the review of the project. Consultants should ideally be members of the community or communities involved in the research.

3.5.5 IRB application requirements related to participatory methods. Minimum requirements include a completed Community Based Research form, a letter of study support from representatives of the community or communities who are actively involved in the research, and a clear and detailed plan for disseminating results to community members throughout and at the conclusion of the study. Other requirements may vary based on specifics of each project and

engaged population. They could include assurances of human research ethics training from community members who are actively engaged in the research and confirmation of additional support from relevant associated community organizations.

4. REFERENCES

[45 CFR 46.111; 21 CFR 56.111; OHRP Guidance on Engagement of Institutions in Human Subjects Research, October 16, 2008; OHRP Frequently Asked Questions: Assurance Process; OHRP Correspondence: Determining when institutions are engaged in research, January 13, 2009](#)

1. PURPOSE

This section elucidates the policy for the ongoing review that occurs after approval.

2. POLICY

IRB approval may be withdrawn at any time if warranted by the conduct of the research. The regulations authorize the IRB to establish procedures for the concurrent monitoring of research activities involving human participants. Periodic review of research activities is necessary to determine whether approval should be continued or withdrawn. Research not qualifying for exemption or expedited approval involving human participants must be reviewed (renewed) not less than once per year.

No research related activities, including new participant enrollment, may occur after the protocol expiration date unless the PI contacts the IRB, and it is determined that it is in the best interest of participants to continue during the lapse in IRB approval.

IRB approval for the conduct of a study may be withdrawn at any time if the risks to the participants are determined to be unreasonably high; for example, more than an expected number of adverse events, unexpected serious adverse events; or evidence that the investigator is not conducting the investigation in compliance with IRB or University guidelines. Such findings may result in more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken, or the study terminated.

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

- 3.1 Ongoing Review for Minimal Risk Research
- 3.2 Site Visits and Third-Party Verification
- 3.3 Review of Unanticipated Problems Posing Risks to Participants or Others or any Other Reportable Events
- 3.4 Modifications
- 3.5 Review of Significant New Findings
- 3.6 Review Of Oversight And Monitoring Reports/Findings
- 3.7 Reports from Employees, Staff and Faculty
- 3.8 Reports of Serious or Continuing Noncompliance
- 3.9 Suspension or Termination of IRB Approval

3. SPECIFIC POLICIES

3.1 Ongoing Review for Minimal Risk Research

Research that qualifies for exemption or limited review does not require annual continuing review. Research that qualifies for expedited approval does not require annual continuing review unless otherwise determined by the IRB.

Generally, the following should not require annual continuing review by an IRB member:

1. Research eligible for expedited review in accordance with §46.110;
2. 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 procedures that participants would undergo as part of clinical care.

However, ongoing review (for example: modifications, exceptions, deviations or reportable events) is still required for research eligible for expedited approval. In addition to communications to remind research personnel that the protocol is still open, the IRB utilizes these ongoing review submissions to maintain oversight of all open studies where laws, codes, and regulations do not require the IRB/EC to conduct continuing review.

Likewise, the IRB may determine that continuing review is required for any research protocol that falls within the above criteria. For example, the IRB may determine that continuing review is required when:

1. The study is FDA regulated, meaning it meets the FDA definition of a clinical investigation (regardless of whether the study is IND or IDE exempt);
2. Required by other applicable regulations (e.g., study is funded by a regulatory agency that has not harmonized with the revised 2018 Common Rule, etc.);
3. The study was reviewed under the pre-2018 Common Rule and changes have not been made to the informed consent to align with the 2018 Common Rule requirements;
4. The research involves topics, procedures, or data that may be considered sensitive or controversial;
5. The research involves particularly vulnerable participants or circumstances that increase participants' vulnerability;
6. An investigator has minimal experience in research or the research type, topic, or procedures; and/or
7. An investigator has a history of noncompliance

3.2 Site Visits/Audits and Third-Party Verification

The IRB has the authority to observe, or have a third party observe, the consent process of research it has approved, and to verify that the study is being conducted as required by the IRB and within the University Policies and Procedures and site-specific procedures as appropriate. Under the direction of the Director, IRB personnel or members may perform site visits or use another party either affiliated with the institution or not, to verify information in the study application, or in any interim, continuing review or renewal submissions.

The IRB will consider the following criteria to determine if a site visit or third-party verification process is required:

- The research involves vulnerable populations or high-risk procedures.
- The investigator has a history of serious or continuing non-compliance related to continuing review in the past three years.
- The IRB has reason to doubt the veracity of the information provided by the investigator.
- The information provided by the investigator is inconsistent with other information known to the IRB and the inconsistency cannot be resolved through communication with the investigator.
- Any other reason where the IRB believes verification should be required.

Other means of verification; sponsors may be asked to submit copies of monitoring reports. The IRB may conduct interviews with screened and/or enrolled participants as deemed necessary.

3.3 Reportable Events, including Potential Unanticipated Problems Increasing Risks to Participants or Others

Consistent with federal regulations, the University of Pennsylvania requires reporting to the IRB of potential unanticipated problems posing risks to participants or others. Unanticipated problems are: (1) unforeseen; (2) possibly, probably, or definitely related to the research, and (3) indicate that participants or others are at increased risk of harm than was previously known or recognized.

The IRB requires researchers to submit reports of the following types of reportable events within 10 business days of the time the event becomes known to the study team with one exception. The one exception for prompt reporting within 10 business days applies to death of a research participant as noted below.

3.3.1 Adverse Event (regardless of whether the event is serious or non-serious, on-site or off-site) that occurs any time during or after the research study, which in the opinion of the principal investigator is both unexpected and related to research procedures.

An event is “unexpected” when its specificity and severity are not accurately reflected in the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts);

An event is “related to the research procedures” if the event is deemed probably or definitely related.

If the adverse event involved an unforeseen death and indicates participants or others may be at increased risk of harm, the study team should report the event to the IRB within three (3) calendar days.

3.3.2 Unanticipated adverse device effect. Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants.

3.3.3 Information that indicates a change to the risks or potential benefits of the research, in terms of severity or frequency. For example:

- An interim analysis indicates that participants have a lower rate of response to treatment than initially expected.
- Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected.
- A paper is published from another study that shows that an arm of the research study is of no therapeutic value.

3.3.4 Any adverse event that represents a serious unexpected problem that is rare in absence of product exposure (e.g. agranulocytosis, hepatic necrosis, or Stevens-Johnson syndrome).

3.3.5 Adverse event that would cause the sponsor to modify the investigator’s brochure / product manual, protocol, or informed consent to assure the protection of human participants.

3.3.6 Withdrawal from marketing for safety concerns of a drug, device, or biologic used in a research protocol.

3.3.7 Change to the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant.

Other Reportable Events

Other events that may be evaluated by the IRB as an unanticipated problem include but are not limited to:

3.3.8 Complaint of a participant when the complaint indicates unexpected risks, or the complaint cannot be resolved by the research team.

3.3.9 Deviations, meaning an accidental or unintentional change to the IRB approved protocol) that placed one or more participants at increased risk, has the potential to occur again, or has the potential to qualify as serious or continuing noncompliance. This also includes deviations from the approved confidentiality plan, i.e., a breach of confidentiality.

3.3.10 Incarceration of a participant when the research was not previously approved under Subpart C and the investigator believes it is in the best interest of the participant to remain on the study.

3.3.11 Premature completion of a study.

When ICH-GCP (E6) applies:

Problems researchers have to report to the IRB include:

- New information that might affect adversely the safety of the participants or the conduct of the clinical trial.
- Any changes significantly affecting the conduct of the clinical trial or increasing risks to participants.

The IRB will accept other reports when the investigator is unsure whether the event should be reported, and the IRB will review such reports to determine whether the event qualifies as a reportable event requiring further review and whether review by the convened board is necessary

Principal investigators will submit a written report of the above events. Initial reports may be accepted by other means such as e-mail, or phone when necessary to ensure prompt reporting with a follow up written report.

For a reportable event requiring convened review to determine if the event is an unanticipated problem, the IRB Administrator selects the primary reviewer. When possible, the IRB member assigned to the initial primary review will review the event. Otherwise, reviewers will be selected based on their education, experience, and areas of expertise.

All reportable events meeting reporting criteria should be summarized at the time of continuing review and IRB members/reviewers will review these events in aggregate and comment, if necessary.

Primary reviewers will have access to, as applicable, the sponsor protocol, investigator brochure, original IRB application form, consent document, event summary, and any other supplemental information required to complete the review.

All other IRB members will have access to the original application form; consent document, event summary, and any other supplemental information require completing the review.

The IRB may request a consultant opinion or engage the division or department chair to collect additional information on the event.

The IRB considers the following actions:

- Accept report or with no additional requirements
- Approve investigator's proposed changes
- Administrative hold on the study pending IRB receipt of further information
- Modification of the protocol
- Modification of the information disclosed during the consent process
- Providing additional information to current participant the information may relate to the participant's willingness to continue participation
- Arrange for clinical care outside the research or additional follow-up for participants
- Providing additional information to past participants
- Requiring current participants to re-consent to participation
- Observation of the research or the consent process
- Requiring additional training of the investigator
- Notification of investigators at other sites
- Obtaining additional information
- Termination or suspension of the research

When determining if the event qualifies as an unanticipated problem requiring external reporting, the following three criteria are applied for DHHS regulated research:

1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
2. related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); AND
3. Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

3.4 Modifications

Federal regulations require that all modifications for nonexempt research, during the period for which approval has already been given, may not be initiated without prior IRB review and approval except where necessary to eliminate apparent immediate hazards to human participants. Sometimes modifications are noted or recognized after they occur. These changes will be reviewed by the IRB as events that may qualify as noncompliance and to determine whether the change was consistent with ensuring the participants' continued welfare.

3.4.1 The IRB categorizes modifications into 3 types: Amendments, Exceptions, and Deviations that require reporting to the IRB.

Amendments

An amendment is a permanent, intentional action or process that revises/amends/modifies a previously approved research protocol. Information relating to protocol amendments will be provided to research participants when the information may relate to their willingness to continue to be a part of the research. Investigators or sponsors must submit requests for changes to the IRB. Upon receipt of the protocol amendment, an IRB Administrator with the assistance of the Director, Associate Directors, or Senior IRB Administrative staff determines the appropriate level of review.

Electronic protocols will have any revisions submitted via HS-ERA.

The IRB Modification Review Guidance provides direction that the IRB staff may utilize when preparing modifications for convened IRB review.

Minor modifications are defined as those that A) do not materially affect an assessment of the risks and benefits of the study, B) would not potentially affect a participant's willingness to participate, and C) do not substantially change the specific aims/design of the study. Likewise, they would not include the addition of procedures involving more than minimal risk to participants or changes that do not fall in categories (1)-(7) of research that could be reviewed using the expedited procedure. Representative minor modifications include but are not limited to:

- The addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol;
- A minor increase or decrease in the number of participants;
- Minor changes to the selection criteria;
- Changes to the dosage form (e.g. tablet to capsule or oral liquid) of an administered drug (when the dose and route of administration remain constant);
- Decreasing the number of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations;
- An increase in the number of study visits for the purpose of increased 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 to improve the clarity of statements or to correct typographical errors, provided that such a change does not 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.

Exceptions (Prospective Deviations)

An exception is a prospective, one-time deviation (intentional action or process that departs from the IRB approved study protocol). Exceptions are usually limited to single isolated events. If the same exception is requested multiple times, the IRB may request that the PI submit an amendment to the protocol.

Exception requests shall be submitted through HS-ERA for electronic protocols. Time sensitive exception requests requiring approval within 24 hours should be submitted via email and must include the IRB exception request form.

The IRB Exception Request Guidance provides direction for submitters when preparing exception requests for IRB review.

Upon receipt of an exception request, an IRB Administrator with the assistance of the Director, Associate Directors, or Senior IRB Administrative staff determines the appropriate level of review. An IRB Chair will be consulted as needed.

The level of review required for exception requests (expedited or convened) is dependent upon the following factors:

- The time sensitivity of the request
- The level of risk involved in both the study itself and the planned alteration.
- Whether the exception request is thought to be in the best interest of the participant
- Whether the exception request holds out the prospect of direct benefit to the participant
- Whether the risk/benefit ratio specifically related to the exception request is favorable

The following exception requests are eligible for expedited review:

- Exception requests where the planned exception poses no more than minimal risk to the participant
- Exception requests where the planned exception may pose greater than minimal risk to the participant, but the request is time sensitive and
 - The exception is in the best interest of the participant and/or the prospect of direct benefit exists
 - The risk/benefit ratio for the proposed exception request is favorable

The following exception requests will require convened IRB review:

- Exception requests where the planned exception may pose greater than minimal risk to the participant and any of the following apply:
 - It is unclear whether the exception is in the participant's best interest or whether there is the prospect of direct benefit to the participant
 - It is unclear whether the risk/benefit ratio is favorable
 - The request is not time sensitive and there is sufficient time to allow convened IRB review to occur

Deviation

A deviation is an unintentional action or process that departs from IRB approval and is identified retrospectively. The deviation is reportable to the IRB within 10 business days from the time the event becomes known to the study team only when: one or more participants were placed at increased risk of harm, the event has the potential to occur again, or the event has the potential to qualify as serious or continuing noncompliance.

When the IRB reviews the exceptions and deviations, a determination will be made as to whether information related to protocol changes should be provided to participants when such information might relate to their willingness to continue to take part in the research Supplemental materials, e.g. an addendum consent form, telephone script or participant letter may be required by the IRB.

3.5 Significant New Findings

During the course of a study, the IRB may review reports generated from the DSMB, adverse events, current literature, and other sources to ascertain the status of the study and assess whether or not the risk/benefit balance is still acceptable, whether or not new information needs to be conveyed to participants, or if a segment of the population may be bearing an

undue burden of research risk or being denied access to promising therapy. Such significant new findings will be reviewed by the IRB chair, Director or other designated IRB members who shall decide whether such new information merits further review by the convened board.

3.6 Review Of Oversight And Monitoring Reports/Findings

For studies that operate with a safety monitoring plan that includes oversight by a DSMB or equivalent (DMC, DRC, DSMC, etc..) the IRB requires copies of reports to be submitted in real time after receipt from that entity. Submission of these reports may result in follow up correspondence or official submissions to ensure compliance with DSMB recommendations. Additionally, at the time of Continuing Review, the following processes are implemented:

For greater than minimal risk research currently enrolling participants, study teams are required to confirm that all reports from safety monitoring committees (that issue such reports) have been submitted to the IRB. In terms of quality control monitoring, for clinical research studies with no regulatory sponsor conducting quality control monitoring, study teams are required to self-monitor.

3.7 Reports from Employees, Staff and Faculty

It is the responsibility of the investigative team, medical staff, nursing staff, or any other employee of this institution to promptly report to the IRB any findings, results, occurrence, or new information about a study being conducted at any facility under the jurisdiction of the IRB that could affect the rights and welfare of research participants. It is the responsibility of the IRB staff and members to act on any such information in order to protect research participants.

3.8 Reports of Serious or Continuing Noncompliance Federal Regulation; or the Requirements or Determinations of the IRB

Reports of serious or continuing noncompliance or the requirements or determinations of the IRB will be handled in accordance with SOPs 408 and 409.

3.9 Suspension or Termination of IRB Approval

A decision to suspend or terminate a protocol must include an explicit consideration for the rights and welfare of participants already enrolled in the study. If the suspension or termination is imposed on the investigator, an IRB Chair may be consulted about whether and how to continue the care of enrolled participants. The matter will be discussed at the next convened meeting of the IRB.

Any suspensions or terminations of approval shall include a statement of the reasons for the IRB's action and shall be promptly reported by the IRB to the investigator, any appropriate compliance offices, and Institutional Official. The timeframe for notification to the institutional official, sponsors, and regulatory agencies will depend on the urgency of the matter. Situations presenting immediate, unforeseen risk to participants will be reported immediately to the institutional official and sponsors. When the research is sponsored or supported by the Department of Health and Human Services, the Institutional Official, or authorized designee, will notify OHRP. For FDA regulated research, the Institutional Official, or designee, will notify FDA in writing after the IRB has made a final determination.

Enrolled participants will be notified if a protocol in which they are enrolled is suspended or terminated. The IRB will determine at a convened meeting how and when the notification will take place. The IRB will consider whether to notify former participants.

If the Penn IRB is serving as the IRB of Record for external organizations or Universities through an IRB authorization agreement, the IRBs at the relying organizations or Universities will be promptly notified of any decision to suspend or terminate the protocol.

REFERENCES

[45 CFR 46.103](#); [21 CFR 56.108](#); [45 CFR 46.109](#); [21 CFR 56.109](#); [45 CFR 45.115](#);
[21 CFR 56.115](#); [OHRP Guidance on Continuing Review, January 15, 2007](#); [FDA Information Sheets, Continuing Review after Study Approval](#); [OHRP Guidance on Reporting and Reviewing Adverse Events and Unanticipated Problems Involving Risks to Participants or Others, January 15, 2007](#); [FDA Final Guidance on Adverse Event Reporting to IRBs, January 2009](#)

1. PURPOSE

This section elucidates the policy for the continuing review (for research not qualifying for exemption or expedited approval or where the IRB determined continuing review is required per RR 404) prior to the expiration of the IRB approval period.

2. POLICY

The IRB conducts continuing review of research taking place within its jurisdiction at intervals appropriate to the degree of risk, but not less than once per year, and has the authority to observe or have a third party observe the consent process and the research.

3. SPECIFIC POLICIES

3.1 Interval for Review for Purpose of Renewal

The IRBs must conduct continuing review of protocols for purposes of renewal of the IRB approval period at intervals appropriate to the degree of risk, which is determined at the time of initial review. For research determined to pose greater than minimal risk, requiring continuing review by the convened Committee (IRB Board), the expiration date will be set to align with the following year's Convened Committee date. The expiration date will ensure continuing review of the research at least once per year. The IRB will inform investigators of the expiration date in a letter following the meeting. The annual progress report must be reviewed on or before the expiration date, even if the research activity may not begin until sometime after the IRB has given approval.

The IRB may also eliminate the requirement for continuing review of a minimal risk research study reviewed under the pre-2018 Common Rule. For such approved research not requiring continuing review, the rationale for this assessment is documented in IRB review records and communicated to study teams via IRB determination letters.

Determination letters include specifications for types of IRB submissions that are still required despite the elimination of continuing review under the 2018 Common Rule. In addition to study specific communications regarding IRB determinations, the IRB may also periodically follow up with individual investigators for updates regarding the statuses of all studies in an investigator's research portfolio in order to maintain appropriate oversight.

The IRB may approve a protocol for a shorter period if warranted by the risks presented to participants. For example, the IRB may stipulate IRB review occurs after a defined number of participants have been enrolled (*e.g.*, review after the first three participants receive a Phase I drug that has never been tested in humans).

Investigators or qualified designees are required to submit a Request for Continuing Review, or an electronic application requesting continuing review and other materials as outlined. For protocols requiring convened review, the report should normally be filed about eight weeks before the study approval period ends.

3.2 Extensions of 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. If an investigator fails to provide continuing review information to the IRB, or the IRB has not reviewed and approved a research study before the expiration date specified by the IRB, no research related activities may occur after the protocol expiration date unless the PI contacts the IRB, and the IRB determines that it is in the best interest of individual participants to continue during the lapse in IRB approval.

3.3 Criteria for Renewal

Continuing review must contain the required information needed to determine that the study should be allowed to continue. The IRB must determine that the approval criteria continue to be met.

Because it may be only after research has begun that the real risks can be evaluated and the preliminary results used to compute the actual risk/benefit ratio; the IRB can then determine whether or not the study can be renewed at the same risk/benefit, or if new information has changed that determination.

In order to determine the status of the study, the following will be reviewed:

3.3.1 Currently Approved Consent Document: Each member of the IRB shall review the currently approved consent document and must ensure that the information is still accurate and complete. Any significant new findings that may relate to the participant's willingness to continue participation should be provided to the participant in an updated consent document.

3.3.2 Currently Approved Protocol including any amendments to Protocol since initial review. A copy of the protocol will be available to the primary reviewer of the continuing review. Amendments to a research protocol should be submitted on an ongoing basis during the course of the study. They may be submitted at the time of continuing review, but only for submissions that are paper based. A separate cover letter describing the amendment and all appropriate documentation (revised consent form) must accompany the continuing review application. Electronic submissions do not allow for amendments with a continuing review submission. The electronic submission system requires two independent submissions for continuing review and modifications. Concurrent continuing review and modification submissions are not recommended within the electronic submission due to technical issues that arise.

3.3.3 Progress report. A summary of ongoing activity on the study in the past year will be prepared and submitted by the principal investigator or designee. The report will include a summary of enrollment, participant experiences, and, as applicable, reportable adverse events, and deviations.

3.3.4 Continuing Review of DSMB-Monitored Clinical Trials. When a clinical trial is subject to oversight by a Data Safety Monitoring Board (DSMB), whose responsibilities include review of adverse events, interim findings and relevant literature (e.g. DSMBs operating in accordance with the National Cancer Institute Policy for Data and Safety Monitoring of Clinical Trials), the IRB conducting continuing review may rely on a current statement from the DSMB indicating that it has reviewed study-wide adverse events, interim findings and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

3.3.5 Request for Continuing Review Form: All IRB members shall receive a request for continuing review form or access to the electronic submission for continuing review, for any protocols requiring convened review, which is prepared and submitted by the principal investigator or designee.

3.4 Possible Outcomes of Continuing Review

As an outcome of continuing review, the IRB may authorize continuation of the research, require that the research be modified or halted altogether. The IRB may need to impose special precautions or relax special requirements it had previously imposed on the research protocol such as frequency of monitoring, requirement for interim reports or duration of IRB approval period (so long as the approval period does not exceed one year). Any changes required to obtain continued renewal approval shall be provided to the investigators by the IRB staff.

3.5 How the Continuing Review Date is Determined

When the IRB has determined that continuing review will occur no sooner than within 1 year, the date of continuing review is determined by using the date the protocol was reviewed and approved by the convened IRB.

4. REFERENCES

[45 CFR 46.109\(c\); 21 CFR 56.109\(f\); OHRP Guidance on Continuing Review, January 15, 2007; FDA Information Sheets, Continuing Review after Study Approval](#)

1. PURPOSE

This section elucidates the policy for the closing a research project or protocol.

2. POLICY

The completion of a study previously determined to qualify for expedited or convened review is a change in activity and should be reported to the IRB in order to receive an official completion approval for the study. Although participants will no longer be "at risk" under the study, a final report/notice to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

3. SPECIFIC POLICIES

3.1 Determining When a Project can be Closed

3.1.1 Externally or internally funded protocols: When the project is complete with no participants in follow up and no further contact with participants and all data analysis that requires contact with records or specimens linked to privately identified information is complete.

3.1.2 Multi-site industry supported clinical trials may be closed when data collection and follow-up is complete at the institutional site and the industry monitor has closed the site.

If multiple sites are relying on the Penn IRB through an IRB authorization agreement, the Penn IRB will approve requests to close individual relying sites while not closing the entire protocol. A relying site may be closed when no participants at that site are in follow up and no further contact with participants and all data analysis that requires contact with records or specimens linked to privately identified information is complete.

3.2 Completion Reports

Final Reports should be submitted within 30 days after completion of the study. Final reports may be submitted in any format that provides adequate information about the status of the study, such as emails, letters, etc. Final reports may be submitted by the investigator or his/her/their designee. The IRB Staff will review all reports of study completion and, if needed, request further information from the investigator to clarify any questions that may arise.

Notice of the submission of Final Reports or closures will be reported to the Board via the minutes and copies of the reports and any supplement information will be available for the members.

4. REFERENCES

[21 CFR 56.108 \(a\)\(3\); 45 CFR 46.103\(b\)\(5\)](#)

1. PURPOSE

This section elucidates the actions the IRB may take as resulting from its review of research.

2. POLICY

As a result of its review, the IRBs may determine to approve or disapprove the proposed research activity, or to require modifications to the project/protocol/documents in order to secure IRB approval of the research activity. Except when the expedited review procedure is used, these actions will be taken by a vote of a majority of the regular and alternate members present, except for those members present but unable to vote in accordance with IRB's conflict of interest policies. When reviewed via expedited review, the Director or his/her/their designee can take any of the following actions except to disapprove a study.

3. SPECIFIC POLICIES

3.1 Determinations: Initial Review

Initial Review: The IRB may make one of the following determinations as a result of its review of research submitted to the convened IRB for initial review:

3.1.1 Approval - When an acceptable risk/benefit ratio exists, and the approval criteria found in the regulations at 45 CFR 46.111 and 21 CFR 56.111 are determined to be met, the protocol is approved as submitted, with the following exceptions:

- Administratively Finalized: When additional documentation is needed before research activity may begin (i.e. approval from other sites, etc.)
- Approved Pending Contract: Applies for studies with industry funding, where a contract is not yet executed, and enrollment should not commence

3.1.2 Withheld Approval Pending Changes - The IRB determines that the protocol will meet the approval criteria found in the regulations at 45 CFR 46.111 and 21 CFR 56.111 provided the investigator agrees to make changes to the IRB application including the informed consent document, as applicable.

The IRB Chair, Director or another designated IRB member may subsequently approve the revised research protocol on behalf of the IRB if the conditions for approval are determined to be met. Research may not be initiated until a letter of IRB approval is received and other applicable committee reviews are satisfied.

When the IRB requires substantive changes that are directly relevant to the determinations required by the IRB under federal regulations, the IRB may not grant withheld approval of the protocol.

3.1.3 Tabled - The IRB requires substantive changes that are directly relevant to the determinations required by the IRB under the approval criteria found in the regulations at 45 CFR 46.111 and 21 CFR 56.111; the IRB will table the approval of the protocol pending subsequent review by the convened IRB of the responsive material.

3.1.4 Disapproved - The IRB determines that the research does not meet the regulatory criteria for approval and cannot provide modifications that may allow the protocol to be approved. The IRB will notify the investigator in writing of the reasons for the decision and will give the investigator an opportunity to respond in person or in writing.

3.2 Determinations: Ongoing Review (including modifications submitted)

3.2.1 Approval - When an acceptable risk/benefit ratio exists and the approval criteria found in the regulations at 45 CFR 46.111 and 21 CFR 56.111 are deemed acceptable, protocol is approved as submitted.

3.2.2 Conditional Re-approval - When the IRB has determined that the approval criteria found in the regulations at 45 CFR 46.111 and 21 CFR 56.111 continue to be met but additional information is needed to approve a continuing reviewing request.

3.2.3 Withheld Approval - When the IRB has determined it requires minor revisions to a modification submission in order to meet the approval criteria found in the regulations at 45 CFR 46.111 and 21 CFR 56.111.

3.2.4 Suspension - Study is suspended pending further clarification of substantive issues related to the approval criteria found in the regulations at 45 CFR 46.111 and 21 CFR 56.111.

4. REFERENCES

[45 CFR 46.109\(a\)](#); [21 CFR 56.109\(a\)](#); [45 CFR 46.111](#); [21 CFR 56.111](#)

RR 408 NONCOMPLIANCE

1. PURPOSE

This policy affirms the standards of conduct, elucidates the policy for responding to reports of noncompliance and defines the actions the IRB may take as a result of its review of the reports.

2. POLICY

Penn pledges to promote and uphold the highest ethical standards in the conduct of human research. Employees and agents of the organization are required to comply with federal regulations, institutional policies, and the requirements and determinations of the IRB. If Penn is relying on another IRB to serve as the IRB of Record according to an IRB authorization agreement, employees and agents of the organization are required to comply with the requirements and determinations of the IRB of Record.

All employees and agents of the University of Pennsylvania share the responsibility for reporting incidences of noncompliance with the regulations or the requirements or determinations of the IRB.

The IRB may use its discretion in determining whether an event meets the definition of noncompliance, serious noncompliance, or continuing noncompliance. Likewise, the IRB may use its discretion in determining whether noncompliance is reportable to internal or external entities.

3. SPECIFIC POLICIES

3.1 Definitions

3.1.1 Noncompliance is defined as a failure to follow applicable regulations or policies, the IRB approved protocol, or requirements and determinations made by the IRB. This applies to: research staff, research support entities, University / Hospital employees or agents, and any member of the human research protection program.

3.1.2. Serious noncompliance is noncompliance that:

- adversely affects the rights* of participants, OR
- may adversely affect the welfare** of participants, including actual or potential substantive harm, OR
- adversely affects the scientific integrity*** of the study

Note:

*Rights include a participant's willingness to participate

**Welfare may be defined as safety, physical integrity, or mental integrity

***Scientific integrity may include the overall scientific value of the trial and/or the reliability of the trial results

3.1.3 Continuing noncompliance is a pattern of repeated serious noncompliance including inadequate efforts to take corrective actions within a reasonable timeframe.

The frequency of noncompliance is assessed mainly by the number of incidents occurring during the course of a protocol and would also take account of whether the same noncompliant action was repeated, or many different noncompliant events occurred.

3.1.4 Allegation of noncompliance: A report of noncompliance that represents an unproven assertion.

3.1.5 Finding of noncompliance: A report of noncompliance that is true or an allegation of noncompliance that is determined to be true.

3.2 Reporting Concerns

3.2.1 Reports of noncompliance in human research may come from many sources including, but not limited to, an investigator (as a self-report); a study monitor; university or school based compliance and audit offices; a sponsor; a research participant; a department chair; a member of the research team; or a person not directly involved with the research.

3.2.2 Persons raising such concerns are encouraged to express them in writing. However, verbal concerns will be received and should be documented accordingly.

3.2.3 Reports of suspected noncompliance .

Within the Perelman School of Medicine, the Vice Provost has delegated to the Office of Clinical Research (OCR) the responsibility for conducting routine and directed compliance audits within the School. OCR audit findings related to human participants' protections are submitted to the IRB for consideration and recommendations are made to investigators regarding what findings may require submission to the IRB for assessments of noncompliance or unanticipated problems. The management plan is developed by the investigator.

Reports of noncompliance from any other school-based audit programs will be communicated in writing to the IRB for consideration.

3.3 Audits and Compliance Reviews within the Perelman School of Medicine

Audits and compliance reviews are conducted in the form of directed audits and periodic compliance reviews. These audits and reviews are designed to assess compliance with local, State, and Federal laws, research participant safety, and IRB policies and procedures.

3.3.1 Directed Audits. Directed audits are conducted to assess the Investigator's compliance with Federal, State, and local law, university and IRB policies and to identify areas for improvement. Triggers for audit activities may include:

- Any IRB committee directives or concerns;
- A response to an externally initiated complaint (OHRP, FDA or Sponsor) of potential protocol violations or regulatory noncompliance;
- A response to an internally initiated complaint or concern (a participant, a family member, Institutional personnel); or
- An Investigator with a history of poor adherence to Penn policies and procedures.

3.3.2 Periodic Compliance Reviews. Periodic compliance reviews are conducted using a systematic method to review IRB-approved research or IRB records/activities on a regular basis. Periodic compliance review activities may include but are not limited to the following:

- Requesting progress reports from Investigators, including a self-assessment of execution of the research and verification that the research is executed within the parameters outlined in the approved protocol;
- Examining the entire research project;

- Contacting research participants
- Assigning observers to the sites where research involving human research participants and/or the informed consent process is being conducted;
- Auditing advertisements and other recruiting materials;
- Reviewing projects to verify that the Investigator has not initiated unapproved changes since previous review;
- Monitor conflict of interest concerns to assure the consent documents include the appropriate information and disclosures;
- Examining HIPAA authorizations.

3.4 Evaluation

3.4.1 The Director/ Associate Directors/ appointed Senior IRB Staff is responsible for the initial review of allegations of noncompliance, review of employee, staff, and faculty reports and complaints and review of audit findings that indicate potential serious or continuing noncompliance.

3.4.2 Allegations of noncompliance

When an allegation of noncompliance is referred to the IRB, the Director/ Associate Directors/ appointed Senior IRB Staff conducts the initial review to verify the veracity of the allegation.

The Staff member assessing the report may choose any of the following methods to gather the required information:

- Conduct the initial review alone
- Conduct the initial review in coordination with the IRB Chair, or Director of Human Research Protections
- Request an audit of the specific protocol, or Investigator, by the Office of Clinical Research (OCR) or another appropriate auditing entity if study site is external to Penn
- Request advice from the Office of General Counsel, University or School Offices of Audit and Compliance, or outside consultants

The individual(s) or subcommittee conducting the investigative process may take any of the following actions as they deem necessary to verify the veracity of any allegations and the seriousness or number of occurrences of the actions:

- Review any written materials
- Interview knowledgeable sources
- Collect relevant documentation

A written record of findings and evidence will be made by the staff member processing the report. The report will include an assessment of whether the preponderance of evidence shows that any of the allegations of noncompliance are potential findings of noncompliance.

If the investigation results in potential findings of noncompliance, the process for assessing if the noncompliance is serious and continuing noncompliance will be followed.

3.4.3 Noncompliance that does not have the potential to qualify as serious or continuing.

If it is determined by the investigative team that (1) the noncompliance was clearly not serious and not continuing, (2) the research staff recognized the noncompliance, and (3) the research staff took appropriate corrective actions, then the report will be forwarded to the appropriate IRB Chair, the Director, Human Research Protections, or an appropriate designee for acknowledgement. No further action is required.

If it is determined that additional corrective actions are required, these will be communicated to the PI/study team.

3.4.4 Noncompliance that has the potential to qualify as serious and/or continuing.

The Staff member assessing the report is responsible for obtaining as much information as possible from the individual who initially reports the incident and for the initial fact finding process to help assess whether each incident of noncompliance has the potential to qualify as serious or continuing noncompliance.

If the incident is considered to potentially qualify as serious or continuing noncompliance based on the investigative team review, then the incident will be reported to the IRB Chair, Director or authorized designee, for initial acknowledgement to confirm timeliness of receipt and to confirm that convened review is appropriate. Additional information may be requested in the acknowledgement and this additional information will be provided to the convened Board for review. When the report is determined to be complete, the report will be scheduled for convened review.

The convened IRB will receive a detailed explanation of the reported issues and any proposed/implemented corrective actions and, as applicable, a copy of the protocol, consent form, and the initial application form. The Director/Associate Director, IRB Chair or assigned IRB member will present the report to the convened IRB. The convened IRB will review the report and make a determination of whether the report qualifies as serious or continuing noncompliance (or both) and whether the corrective action plan proposed is sufficient to address the incidence(s) reported or if further action may be necessary (actions that can occur outlined below). If the convened IRB is unable to make the determination related to whether the incidence(s) reported qualify as serious or continuing noncompliance (or both), the convened IRB will outline specific requests for additional information to provide the additional information necessary to make the final determination. The responses, once received, will be scheduled for the next meeting of the appropriate convened IRB to make the final determination.

3.5 Actions that the IRB Considers in Responding to Serious or Continuing Noncompliance

3.5.1. The IRB may take the following actions in response to a determination of serious or continuing noncompliance:

- No action
- Modification of the research protocol
- Modification of the information disclosed during the consent process
- Additional information provided to past participants
- Notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research)
- Requirement that current participants re-consent to participation
- Modification of the continuing review schedule
- Monitoring of the research
- Monitoring of the consent process
- Suspension of the research
- Termination of the research
- Obtaining more information pending a final decision
- Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)

3.5.2 Appropriate IRB staff will document the results of the IRB's determinations in the meeting minutes. The IRB will notify the investigator in writing of the results of the investigation and of any remedial actions required by the IRB. The letter may include a request for the investigator to respond in writing. Any response required may be reviewed using expedited procedures or may be referred to the convened IRB.

3.5.3 The IRB minutes will include a description of the nature of the event, the findings, actions taken, and plans for continued investigation or action.

3.6 Notifications

If the noncompliance is determined to be serious or continuing, CO 602 will be followed. Additionally, the Penn IRB must report to AAHRPP within 48 hours after the organization or any researchers (if the researcher is notified rather than the organization) becomes aware of:

- Any negative actions taken by a government oversight office, including, but not limited to, OHRP determination letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA restrictions placed on IRBs or ECs or researchers. Organizations outside the US must report any sanctions taken by their country's regulatory agencies.
- Any litigation, arbitration, or settlements initiated related to human research protections.
- Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding the organization's HRPP.

4. REFERENCES

[45 CFR 46.103\(b\)\(4\)&\(5\)](#); [21 CFR 56.108\(b\)](#)

1. PURPOSE

This policy describes the IRB actions associated with suspending or terminating previously approved research.

2. POLICY STATEMENT

Federal regulations require that the IRB have the authority to suspend or terminate approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unexpected serious harm to participants. Suspensions and terminations represent an action by the IRB to temporarily or permanently withdraw approval for some or all research procedures. This policy describes the IRB actions associated with suspending or terminating previously approved research.

3. SPECIFIC POLICIES

3.1 Administrative Hold

A voluntary action initiated by the investigator to place specific research activities on temporary hold. When a study is currently approved by the IRB, the PI may voluntarily place the study on hold as follows:

- Administrative hold of screening/enrollment
- Administrative hold of interaction/intervention
- Administrative hold of follow-up

The investigator will notify the IRB in writing of its decision for Administrative Hold. The notification will include the criteria for the Administrative Hold and will notify the IRB when research related activities resume. Such notifications may be combined with other submissions such as an amendment, deviation, or reportable event.

The investigator will notify the IRB in an expedited manner (within 10 business days) when the administrative hold is related to: participants being placed at greater risk than was previously known or recognized, adverse impact on participants' rights or welfare, or adverse impact on the scientific integrity of the study.

3.1.1 The following officials are authorized to suspend IRB approval pending review by the IRB responsible for continuing review of the protocol: the Vice Provost for Research, Deans of Schools, the Executive IRB, and the Chair of the IRB responsible for continuing review of the protocol, the Institutional Director(s) of Research Compliance, and any other Penn officials who is authorized to take such action by virtue of his/her/their office or of a policy or procedure of the relevant organization.

The University of Pennsylvania official who suspends a protocol shall immediately notify the Principal Investigator of:

- The requirement to suspend the study or to halt the portion of the IRB approved protocol that poses immediate, material risk to participant health and welfare;
- The reasons for the suspension;
- The opportunity to respond in person or in writing to the official and IRB on the suspension,

In addition, the University of Pennsylvania official who suspends a protocol shall immediately notify the IRB. The decision to suspend the research will be reported to the convened IRB and the Committee's discussion will be summarized in the meeting minutes.

The Director of Human Research Protections or Associate Director will report the suspension to the Vice Provost for Research and any appropriate compliance offices. The IRB will immediately initiate the appropriate procedure for review of the basis for the suspension.

If the suspension of some or all of the protocol involves the withdrawal from the research or modification of participation of current participants, the IRB will direct the investigator to contact the participants to:

- Describe any monitoring and follow-up for safety reasons that will be conducted and
- Provide contact information for the Principal Investigator and the IRB where the participant may report any adverse events or unanticipated problems.

3.2 Sponsor-Imposed Suspension

A determination may come from the sponsor of the study to place specific research activities on hold. This determination may be made for interim data analysis; inadequate drug availability; in response to a DSMB report/recommendation; or a pre-planned stopping criterion. The investigator notifies the IRB in writing of sponsor-imposed suspensions.

The investigator will notify the IRB in an expedited manner (within 10 business days) when the suspension is related to: participants being placed at greater risk than was previously known or recognized, adverse impact on participants' rights or welfare, or adverse impact on the scientific integrity of the study.

3.3 Suspension for Cause

Suspension for cause is an action to stop temporarily some or all research procedures pending future action by the IRB or by the Investigator or his/her/their study personnel. The IRB reviews a study for suspension at convened IRB meeting. Examples of these types of circumstances include:

- Falsification of study safety data;
- Failure to comply with prior conditions imposed in writing by the IRB under suspension of the study;
- Repeated or deliberate failure to obtain or document informed consent from human participants, which may include:
 - Repeated or deliberate omission of a description of serious risks of the experimental therapy when obtaining informed consent; and/or
 - Repeated or deliberate failure to provide informed consent in a language understandable to the participant;
- Repeated or deliberate failure to limit administration of the investigational drug or device to those participants under the Investigator's supervision;
- Repeated or deliberate failure to comply with conditions placed on the study by the University, IRB, sponsor, or FDA;
- Repeated or deliberate failure to obtain prior review and approval of new protocols and on-going human participants research by the IRB;

- Repeated or deliberate failure to maintain accurate study records or submit required adverse event reports to the IRB;
- Repeated or deliberate falsification or concealment of study records, e.g., by substituting in study records the results of biological samples from participants who met the inclusion criteria for samples of participants who did not meet the inclusion criteria, or by fabricating participants.
- Research is not being conducted in accordance with the IRB's requirements.
- Research has been associated with unexpected serious harm to participants.

In addition, the Committee may request an ad hoc review from an independent source with expertise in the type of research being conducted or expertise in the specific area of concern.

The IRB notifies the Investigator in writing of its decision to suspend the study for cause and provide a rationale for its actions. This letter includes an opportunity for the PI to respond to the IRB's determinations and to attend an IRB meeting to discuss the suspension and provide clarification of the issues.

3.4.1 The IRB will take the appropriate actions to protect the rights and welfare of currently enrolled participants in suspended or terminated research. Consideration may include, but is not limited to, the following actions:

- Whether procedures for withdrawal of enrolled participants is appropriate
 - Whether participants should be informed of the termination or suspension.
 - Transfer of participants to another investigator.
 - Any follow up care needed to ensure participant safety.
- For FDA regulated research:
- 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 address 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.

- Permit or require follow-up of participants for safety reasons, and if so, require reporting of adverse events or outcomes to the IRB.
- The IRB may request the development of an education plan and/or the completion of a directed audit by the Office of Clinical Research.
- Suspensions are reinstated for approval after corrective actions are completed to the IRB's satisfaction. The IRB may approve the study with or without additional restrictions (e.g., mandating a data and safety monitoring committee to oversee the research at designated intervals, increase in the frequency of IRB review, observation of the consent process).

3.5 Termination for Cause

An action initiated by the IRB to stop permanently some or all research procedures.

The IRB reviews a study for Termination for Cause at a convened IRB meeting. Terminations by someone other than the convened IRB must be reported to and reviewed by the convened IRB.

In addition, the IRB may request an ad hoc review from an independent source with expertise in the type of research being conducted or expertise in the specific area of concern.

The IRB notifies the Investigator in writing of the decision to terminate the study for cause and provide a rationale for its actions. This letter includes an opportunity for the PI to respond to the Committee's determinations and to attend an IRB meeting to discuss the termination and provide clarification of the issues.

3.6 Reporting of Suspensions for Cause or Terminations

All Suspensions or Terminations are promptly (within a period no longer than 30 days) reported per IRB SOP Policy CO 602. The distribution of the report shall also be in accordance with SOP Policy CO 602. The institution may determine that suspensions or terminations associated with a particular study, or an Investigator are repetitive and warrant action for issues of serious and continuing non-compliance.

4. REFERENCES

[45 CFR 46.103\(5\)\(ii\); 21 CFR 56.108\(b\)\(3\)](#)

SC 500 REVIEW REQUIRING SPECIAL CONSIDERATION

SC 500	REVIEW REQUIRING SPECIAL CONSIDERATION
501	<p>VULNERABLE POPULATIONS</p> <ul style="list-style-type: none">- Incarcerated persons- Children- Pregnant individuals, Fetuses & Neonates- Other Vulnerable Groups
502	<p>RESEARCH WITH TEST ARTICLES</p> <ul style="list-style-type: none">- Research involving drugs or biologics- Research involving medical devices<ul style="list-style-type: none">• Significant risk medical devices• Non-significant risk medical devices• Investigations exempted from IDE regulations- Gene therapy research- Prospective research in emergency settings- Expanded access of an investigational drugs or devices- Emergency use of an investigational article or product- Humanitarian use devices- Treatment Use Requests

1. PURPOSE

This section presents the policy concerning review of research that involves groups that could be potentially vulnerable to undue influence or coercion, present conditions that may affect risk/benefit determinations or bear an unequal burden in research.

2. POLICY STATEMENT

The IRB shall apply additional protections as necessary to protect potentially vulnerable research participants. Not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. The extent of additional protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations. In addition, when an IRB regularly reviews research involving a vulnerable population consideration will be given to inclusion of one or more individuals who are knowledgeable about and experienced in working with these participants.

3. SPECIFIC POLICIES

3.1 Incarcerated persons

If an investigator indicates that incarcerated persons will participate in the research, or that participants may reasonably be expected to be incarcerated at some time point during the study, the IRB will adhere to the requirements found at 45 CFR 46, Subpart C. A majority of the IRB (exclusive of incarcerated person members) will have no association with the prison involved apart from membership on the IRB. At least one IRB member who is an incarcerated person or incarcerated person representative with appropriate background and experience to serve in that capacity will be present at the meeting.

3.1.1 When Participants Become Incarcerated persons During a Research Protocol.

This policy applies whenever any human participant in a research protocol becomes an incarcerated person at any time during the protocol, *e.g.*, after the research has commenced. This is necessary because it is unlikely that review of the research and the consent document contemplated the constraints imposed by the possible future incarceration of the participant. If a participant becomes an incarcerated person after enrollment in research, the Principal Investigator is responsible for reporting in writing this situation to the IRB immediately. Each incarcerated person will be informed in advance that participation in the research will have no effect on his/her/their parole.

At the earliest opportunity after receiving the Principal Investigator's notice or otherwise becoming aware of the incarcerated person status of a participant the IRB will review the protocol again with an incarcerated person representative as a member of the IRB.

The IRB will take special consideration of the conditions of being an incarcerated person. Upon this review, the IRB can either (a) approve the involvement of the incarcerated person-participants in the research in accordance with this policy and all applicable regulations; or (b) determine that this participant must be withdrawn from the research.

Additionally, the IRB should confirm that, when appropriate, the informed consent process includes information regarding when subsequent incarceration may result in termination of the participant's participation by the investigator without regard to the participant's consent.

3.1.2 Epidemiologic Research Involving Incarcerated persons.

A Subpart C determination is not required for epidemiologic research involving if the following criteria are met:

- The research presents no more than minimal risk and no more than inconvenience to the incarcerated person-participants.
- Incarcerated persons are not a particular focus of the research.
- The sole purposes of the research are one of the following:
 - To describe the prevalence or incidence of a disease by identifying all cases
 - To study potential risk factor associations for a disease

3.1.3 Incarcerated person Research within the State of NJ

Research with incarcerated persons within the state of NJ requires review and approval by the New Jersey Department of Corrections Departmental Research Review Board (DRRB). The IRB will consult with the Office of General Counsel for research protocols involving incarcerated persons in New Jersey.

3.2 Children

3.2.1 Definition

Federal regulations define “children” 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.

Under New Jersey and Pennsylvania law, persons under the age of eighteen (18) generally meet this definition of “children”, with the exceptions noted below. As a result, permission of the child’s parent(s) or guardian(s) must generally be obtained prior to the participation child’s participation in the research.

The following exceptions to the general rule apply, where a person under the age of 18 does not meet the federal definition of “child” and may provide legally effective consent to participate in research if either:

New Jersey Law	Pennsylvania Law
<ul style="list-style-type: none"> • The research involves the provision of medical care or treatment, (including care or treatment deemed to be experimental) and the person: <ul style="list-style-type: none"> - is married, or - is or has been pregnant. • The person is an emancipated minor. If an emancipated minor provides consent for himself or herself, the court order should be copied and included in the research records with the consent document. 	<ul style="list-style-type: none"> • The research involves the provision of medical care or treatment, (including care or treatment deemed to be experimental) and the person: <ul style="list-style-type: none"> - has graduated from high school, or - is married, or - is or has been pregnant. • The person is an emancipated minor. If an emancipated minor provides consent for himself or herself, the court order should be copied and

	included in the research records with the consent document.
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3.2.2 All individuals defined as “children” will be afforded the protections under Subpart D, 45 CFR 46.401 - 409 and 21 CFR 50.50 - 54, Additional Protections for Children Involved as Participants in Research and as delineated in IRB Policies.

Subpart D Protections are not applicable for minors who do not meet the definition of children. The IRB may consider these participants potentially vulnerable and may choose to apply additional protections.

When a research protocol involves minors who do not meet the definition of children, the IRB will carefully balance the potential risks and benefits of the proposed research and will consult with the Office of General Counsel and the Vice Provost for Research as deemed necessary.

If the research includes enrollment of participants in states other than PA and NJ or other countries, the principal investigator is responsible for providing the IRB with sufficient information to verify the age at which participants in such jurisdictions have the ability to consent to participation in research, including any medical treatments or procedures if applicable.

The IRB may, if it appears advisable, require the submission of an opinion rendered by an attorney from any applicable jurisdiction on the age at which an individual can consent to participation in research.

3.2.3 Federal regulations at 45 CFR 46 Subpart D and 21 CFR 50 Subpart D define “guardian” as “an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.”

Pursuant to New Jersey and Pennsylvania law, only the birth parent or a person adjudicated as an adoptive parent(s) or legal custodian/ guardian may provide the legally effective parental permission on behalf of a child to general medical care.

Except for research involving no greater than minimal risk, if a court appointed guardian provides consent, documentation of the court order or legal authorization to consent to general medical care must be copied and included in the investigator’s research records with the documentation of permission.

3.2.4 For any protocol involving children, the IRB must determine which of the four categories of research apply to that study, if any. The IRB must document the rationale for this choice.

(Category 1) 45 CFR 46.404 or 21 CFR 50.51– Research not involving greater than minimal risk to the children. To approve this research the IRB must make the following determinations:

- the research presents no greater than minimal risk to the children; and
- adequate provisions are made for soliciting the assent of the children and the permission of the parents or guardians

(Category 2) 45 CFR 46.405 or 21 CFR 50.52– Research involving greater than minimal risk to the children but presenting the prospect of direct benefit to the individual child participants involved in the research. To approve this research the IRB must make the following determinations:

- the risk is justified by the anticipated benefits to the participants;
- the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the participants as that provided by available alternative approaches; and
- adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians

(Category 3) 45 CFR 46.406 or 21 CFR 50.53— Research involving greater than minimal risk and no prospect of direct benefit to the individual child participants involved in the research, but likely to yield generalizable knowledge about the participant’s disorder or condition. To approve this research the IRB must make the following determinations:

- the risk of the research represents a minor increase over minimal risk;
- the intervention or procedure presents experiences to the child participants that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
- the intervention or procedure is likely to yield generalizable knowledge about the participant’s disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; and
- adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians

(Category 4) 45 CFR 46.407 or 21 CFR 50.54— Research that the IRB believes does not meet the conditions of categories 1-3 but finds that the research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children. To approve this research the IRB may refer the protocol to HHS or FDA for review. Research may only proceed only if:

- The federal agency, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determined either:
 - That the research fell into categories 1 through 3; or
 - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of children and the research will be conducted in accordance with sound ethical principles.

3.2.5. Research under Category 3 or 4 that involves wards of the state or any other agency.

The IRB requires the Principal Investigator to justify that the research is (please note: This justification will be required to be incorporated into the application to the IRB, not by using the standard worksheet for enrollment of minors):

- Related to their status as wards; or
- Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards

The IRB will 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*.

- The advocate is an individual who has the background and expertise to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research
- The advocate is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigators, or the guardian.

3.3 Pregnant individuals, Fetuses, and Neonates

The University requires adherence to DHHS regulations regarding additional protections required for research involving pregnant individuals, fetuses, and neonates for research that is supported by HHS. In addition to the other responsibilities assigned to the IRBs under 45 CFR Part 46 Subpart A, the University of Pennsylvania requires each IRB to review research involving these participants by applying the protections of 45 CFR 46 Subpart B for HHS supported research. The IRB will provide for equivalent protections when the research is not supported by HHS.

Pennsylvania Law places additional restrictions on research on the fetus. The IRB will consult with the Office of General Counsel on a case-by-case basis for research protocols involving this class of participant.

3.4 Other vulnerable groups

Federal regulations require that the IRB consider additional protections for other vulnerable populations such as but not limited to mentally disabled persons and economically or educationally disadvantaged individuals. The IRB will consider these additional protections as part of the criteria for approval.

Although the federal regulations do not list all vulnerable groups, the IRB considers vulnerable groups to include employees of the sponsor, investigator or the University, as well as those within potentially compromised autonomy. The IRB will determine special protections for these groups on a case by case basis taking into account the risks and benefits and other protections afforded by institutional policies and state and federal law.

3.4.1. Adults with Impaired Decision-Making Capacity

Cognitively impaired adults are individuals who have a diminished capacity for judgment and reasoning due to a psychiatric, organic, developmental, or other disorder that affects cognitive or emotional functions. Other individuals may be considered decisionally impaired or have limited decision-making ability because they are under the influence of or dependent on drugs or alcohol, suffering from degenerative diseases affecting the brain, are terminally ill, or have severely disabling physical handicaps.

There are no federal regulations specific to research involving adults with impaired decision-making capacity. The IRB takes special care to consider issues such as the selection of participants, privacy and confidentiality, undue influence, and risk-benefit analysis. Decisions should be made with the utmost deference to the ethical principles underlying human research as set forth in the Belmont Report.

The National Bioethics Advisory Commission (NBAC) has issued 21 recommendations for IRBs, the research community, and Federal regulators to consider regarding the decision-making capacity of particularly vulnerable participants.

The following criteria may be taken into consideration for adult participants with impaired decision-making capacity involved in a research protocol:

- The objectives of the research cannot be met by conducting the research in a population that does not have the disorder that may affect decision making capacity.

- The research is designed for a disease or condition relevant to the vulnerable population under study.
- The research is either minimal risk, more than minimal risk with a prospect of direct benefit, or more than minimal risk without a prospect of direct benefit, but of vital importance to the vulnerable population.
- Adequate provisions are made for obtaining consent from the participant’s legally authorized representative. The use of a legally authorized representative will be consistent with applicable state law(s).
- Adequate provisions are made for obtaining assent from the participant, unless the IRB determines that assent is not appropriate as a condition of participation or that some or all participants are not capable of providing assent.
- The protocol must describe when and how the participants will be assessed for capacity for formal consent or assent and understanding of the proposed research, and the process for a second confirming assessment. Competency should be evaluated on an individual basis to avoid incorrect assumptions as to an individual’s ability to make decisions. Criteria for determining competence might vary according to the degree of risk or discomfort presented by the research procedures and the extent to which therapeutic gain can be anticipated. See section IC 703, 3.1.1 Mentally disabled or cognitively impaired participants for additional considerations the IRB may make surrounding informed consent.

The IRB may also consider additional safeguards to protect participants. These include:

- Requiring the involvement of participant advocates
- Requiring independent monitoring
- Requiring waiting periods
- Appointing a monitor to supervise the informed consent process

Such decisions may be based on the amount of risk involved in the research and the likelihood that participants will derive health benefits from their participation.

3.4.1.1 Applicable New Jersey State Statutes

NJ state law dictates requirements for medical research on persons with cognitive impairments, lack of capacity, or serious physical or behavioral conditions and life threatening diseases. The IRB will consult with the Office of General Counsel for research protocols involving this class of participants in New Jersey.

NJ state law also requires informed consent of an in-patient being treated for mental health or mental illness, in connection with experimental research, and the experimental research must be “directly related to the goals of the patient’s treatment program.” The IRB may consult with the Office of General Counsel on a case-by-case basis for research protocols involving this class of participants in New Jersey.

3.4.1.2 Inclusion of Adults with Impaired Decision-Making Capacity in Non-Therapeutic Clinical Trials when following ICH-GCP (E6):

A non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the participant) should ideally only enroll participants who are able to personally give consent and who sign and date the written consent document.

However, non-therapeutic clinical trials may enroll participants with consent of a legally acceptable representative provided the following conditions are fulfilled:

- The objectives of the clinical trial cannot be met by means of a trial that enrolls only participants who can give consent personally.

- The foreseeable risks to the participants are low.
- The negative impact on the participant's wellbeing is minimized and low.
- The clinical trial is not prohibited by law.
- The opinion of the IRB is expressly sought on the inclusion of such participants, and the written 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. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear unduly distressed.

3.4.2 Research involving students or employees of the University.

When research involves students or employees of the University, the IRB requires the investigator to provide information regarding the measures that will be put into place to reduce the likelihood of undue influence and to address confidentiality concerns.

3.4.3 Research involving other vulnerable populations

The context of the research is an important consideration for the IRB when reviewing research that involves potentially vulnerable participants. Members of the following groups may be considered potentially vulnerable. The IRB will consider the context of the research and determine whether additional protections may be needed if members of the following groups are a targeted study population:

- Members of disenfranchised racial or ethnic communities
- Members of disenfranchised groups, such as the LGBTQ+ community
- Members of the Armed Forces and veterans
- Refugees, undocumented immigrants, etc.
- Educationally disadvantaged persons
- Economically disadvantaged persons
- Homeless persons
- Institutionalized individuals
- Individuals with mental illness and/or substance use disorders

3.5 Mandatory Reporting Requirements

Penn researchers are expected to comply with State and Local requirements for mandatory reporting of abuse. Any researcher desiring not to comply with reporting requirements must consult with the Office of General Counsel.

4. REFERENCES

[The Belmont Report](#); [45 CFR 46.111\(b\)](#); [21 CFR 56.111\(b\)](#); [45 CFR 46.107](#); [21 CFR 56.107](#); [45 CFR 46 Subpart B](#) ; [45 CFR 46 Subpart C](#); [45 CFR 46 Subpart D](#) ; [50 CFR Subpart D](#); [OHRP FAQs prisoner research](#); [OHRP FAQs on research involving children](#); [Research Involving Persons with Mental Disorders That May Affect Decision Making Capacity \(December 1998\)](#) <http://bioethics.gov/>; [OPRR Protecting Human Research Subjects Guidebook \(1993\)](#), Chapter 6, Section J, “Students, Employees and Normal Volunteers”; [NJSA §26:14-3 & 4](#); [NJSA §30:4-24.2](#); [NJAC §10A](#)

1. PURPOSE

This section presents the policy concerning review of specific types of research that require additional considerations by the IRB

2. POLICY STATEMENT

Certain categories of research involve either methodologies that might require additional considerations or for which there are federally mandated determinations that IRBs are required to make and document. These categories of research include, but are not limited to:

- Clinical investigations involving drugs or biologics
- Clinical investigations involving medical devices
- Gene therapy research
- Prospective research in emergency settings
- Expanded access of an investigational drugs or devices, including single patient treatment use and compassionate use requests
- Emergency use of an investigational article or product
- Humanitarian use devices

3. SPECIFIC POLICIES

3.1 Research Involving Drugs or Biologics

All research involving use of FDA regulated drugs or biologics require submission of an Investigational New Drug Application to the FDA unless the research meets the criteria for exemption from the requirements as outlined below or the research involves the use of a drug other than the use of a marketed drug in the course of medical practice.

For sponsored research, applications for research on the use of a drug, unless that research is exempt from the IND regulations, must be accompanied by documentation from the FDA that includes a valid IND number. The IND number must either match the number on the sponsor protocol with the same title as the proposed research or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA. **The research must not begin until a valid IND is in effect.** This includes recruiting, obtaining consent, and screening participants for a specific study that is subject to an IND.

A study may qualify for IND exemption if it meets one of the FDA exemptions from the requirement to have an IND

- Exemption 1: A clinical investigation of a drug product that is lawfully marketed in the United States if all the following apply:
 - The investigation is not intended to be reported to the FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;
 - If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;

- The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
- The investigation is conducted in compliance with the requirements of 21 CFR 312.7.
- Exemption 2: A clinical investigation involving an in vitro diagnostic biological product if all the following apply:
 - The diagnostic involves one or more of the following: blood grouping serum, reagent blood cells, and anti-human globulin
 - The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and
 - The diagnostic test is shipped in compliance with 21 CFR 312.160
- Exemption 3: A drug intended solely for test in vitro or in laboratory research animals if shipped in accordance with 21 CFR 312.160
- Exemption 4: A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND

When an exemption determination is needed, this assessment will be based on the information provided by the investigator and/or the sponsor. If information provided by the investigator and/or the sponsor is unclear or incomplete, the IRB staff may request submission of the Research with Drugs form to compile necessary information. Information provided may be used to complete the Internal Drugs Checklist, which is used to guide the exemption determination. It is the responsibility of the investigator and/or sponsor to provide accurate information. Exemption determinations may be made by the IRB; the School of Medicine's Office of Clinical Research; the Radiology Department IND office for investigational imaging agents, Radiation Research Safety Committee (RRSC) for Nuclear Med. Agents (radiopharmaceuticals) or may be determined by the FDA.

3.2 Research Involving Medical Devices

Research with medical devices falls into three categories:

- Investigations of significant risk devices
- Investigations of non-significant risk devices
- Investigations exempted from the IDE regulations
- Research involving medical devices for the collection of data but where the medical device is not under investigation to evaluate the safety and effectiveness of the device

When a device risk determination is needed, the convened IRB will determine whether the study presents a significant risk or a non-significant risk of harm to study participants. This assessment will be based on the information provided by the investigator and/or the sponsor. If information provided by the investigator and/or the sponsor is unclear or incomplete, the IRB staff may request submission of the Research with Devices form to compile necessary information. Information provided may be used to complete the Internal Devices Checklist, which is used to guide device risk determinations made by the convened board. It is the responsibility of the investigator and/or sponsor to provide accurate information.

The IRB's risk determination will be documented in the IRB meeting minutes. If an investigator submits a Non-Significant Risk research protocol that is determined by the IRB to be a Significant Risk study, the investigator and the Sponsor, if necessary, will be notified in writing. No further action will be taken by the IRB on the research until the sponsor or investigator has met the requirements for a SR study described in 21 CFR 812.

3.2.1 Significant Risk Device Investigations

Applications for research on the use of a significant risk medical device must be accompanied by documentation from the FDA that includes a valid IDE number.

The IDE number must either match the number on the sponsor protocol with the same title as the proposed research or be listed on communication from the sponsor specific to the proposed research, or on communication with the FDA.

3.2.2 Non-significant Risk Device Investigations

When research involves use of a medical device and the investigators/sponsor indicates that the device may qualify as non-significant risk, the IRB either confirms (1) that appropriate documentation is provided from the FDA to classify the device as non-significant risk or (2) the device does not qualify as a significant risk device, according to the following regulatory criteria outlined below.

An investigational device that presents a potential for serious risk to the health, safety, or welfare of a participant AND:

- (1) Is intended as an implant; or
- (2) Is purported or represented to be for a use in supporting or sustaining human life; or
- (3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health; or

or

Otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

If the above criteria above are not met, the device may be designated as non-significant risk. No application is required to be submitted to the FDA. If the IRB cannot determine the risk of the device, the IRB may defer the determination to the FDA.

When research is conducted to determine the safety or effectiveness of the non-significant risk device the following abbreviated IDE requirements must be ensured by the designated Sponsor:

- The device is not a banned device.
- The sponsor labels the device in accordance with 21 CFR 812.5.
- The sponsor obtains approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device and maintains such approval.
- The sponsor ensures that each investigator participating in an investigation of the device obtains from each participant enter investigator's care, consent under 21 CFR 50 and document it, unless documentation is waived.
- The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
- The sponsor maintains the records required under 21 CFR 812.150 (b) (1) through (3) and (5) through (10);

- The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140 (a) (3) (i) and make the reports required under 812.150 (a) (1), (2), (5), and (7); and
- The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

3.2.3 Investigations exempted from IDE regulations

Clinical investigations that are exempt from IDE regulations still require IRB review and approval. An investigation of a medical device in human participants' research that is exempt from the IDE regulations must fall into one of the following categories and will be determined along with the review and approval of a submission:

- A device legally marketed in the US that is used or investigated in accordance with the indications in the FDA-approved labeling.
- A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
- A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.
- A diagnostic device (that is, an in vitro diagnostic device) if the testing:
 - Is noninvasive
 - Does not require an invasive sampling procedure that presents significant risk,
 - Does not by design or intention introduce energy into a participant, and
 - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
- A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put participants at risk.
- A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

When an exemption determination is needed, this assessment will be based on the information provided by the investigator and/or the sponsor. If information provided by the investigator and/or the sponsor is unclear or incomplete, the IRB staff may request submission of the Research with Devices form to compile necessary information. Information provided may be used to complete the Internal Devices Checklist, which is used to guide the exemption determination. It is the responsibility of the investigator and/or sponsor to provide accurate information. Exemption determinations may be made by the IRB; the School of Medicine's Office of Clinical Research; the Radiology Department IND office for investigational imaging agents, Radiation Research Safety Committee (RRSC) for Nuclear Med. Agents (radiopharmaceuticals) or may be determined by the FDA.

3.2.4 Research involving medical devices for the collection of data

Expedited review category 4 allows for the "collection of data through noninvasive procedures" and specifically notes: "Where medical devices are employed, they must be cleared/approved for marketing." Studies intended to evaluate the safety and effectiveness of the medical device do not qualify under this category of review. The use of marketed medical devices for the collection of data on research studies may be part of a research protocol undergoing expedited or convened review. This type of use is generally considered not to be FDA regulated as it does not meet the definition of a

clinical investigation intended to evaluate the safety and effectiveness of the medical device. In essence, the device is not the participant of the investigation.

3.3 Gene Therapy Research

Gene therapy research may require special considerations. If the project involves gene transfer (administration of recombinant vectors) to human participants for other than clinical purpose review by the NIH Recombinant DNA Advisory Committee (RAC) may be required. The FDA must review any such study prior to final IRB approval. In addition, the protocol will require review by the University of Pennsylvania Institutional Biosafety Committee and may require review by the University's Human Research Advisory Committee, if the research does not have an unaffiliated Sponsor.

3.4 FDA Regulated Prospective Research in Emergency Settings

The IRB, with the concurrence of a licensed physician who is either a member of IRB or a consultant and who is not participating in the research being reviewed, may waive the requirement for informed consent in certain emergency research if it finds and documents the following:

The research activity is subject to the regulations codified by the Food and Drug Administration (FDA) at 21 CFR Part 50 and will be carried out under an investigational new drug application (IND) or investigational device exemption (IDE).

The application clearly identifies the protocols that will include participants who are unable to consent.

The protocol is performed under a separate IND or IDE and clearly identifies such protocols as protocols that may include participants who are unable to consent.

The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device product already exists.

3.4.1 The human participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

3.4.2 Obtaining informed consent is not feasible because:

The participants 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 participants' 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.

3.4.3 Participation in the research holds out the prospect of direct benefit to the participants because:

1. Participants are facing a life-threatening situation that necessitates intervention;

2. 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 participants; and
3. Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

3.4.4 The clinical investigation could not practicably be carried out without the waiver.

3.4.5 The proposed investigation or research plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, attempting to asking 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 representatives and make this information available to the IRB at the time of continuing review.

3.4.6 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 participants 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 participant's participation in the clinical investigation.

3.4.7 Additional protections of the rights and welfare of the participants will be provided, including, at least:

- Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the participants will be drawn;
- Public disclosure to the communities in which the clinical investigation will be conducted and from which the participants 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 participant's family member who is not a legally authorized representative and asking whether he/she/they objects to the participant'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 participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, of the participant'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 participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, that he/she/they may discontinue the participant's participation at any time without penalty or loss of benefits to which the participant is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the participant's condition improves, the participant is also to be informed as soon as feasible. If a participant is entered into a clinical investigation with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the participant's legally authorized representative or family member, if feasible.

3.4.8 If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided above of this 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.

3.5 HHS Regulated Prospective Research in Emergency Settings

For research that is not FDA regulated, requests for waivers of informed consent will be evaluated in accordance with 45 CFR 46.116 and 117 and the OHRP Guidance on Informed Consent Requirements in Emergency Research.

When research is not subject to FDA regulations, but follows DHHS regulations, the IRB finds, documents, and reports to DHHS that the following conditions have been met relative to the research:

- The IRB found and documented that the research is not subject to regulations codified by the FDA at 21 CFR 50.
- The research participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
- Obtaining consent is not feasible because:
 - The participants are not able to give their consent as a result of their medical condition.
 - The intervention involved in the research is administered before consent from the participants' legally authorized representatives is feasible.
 - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in research.
- Participation in the research held out the prospect of direct benefit to the participants because:
 - Participants are facing a life-threatening situation that necessitated intervention.
 - Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence supported the potential for the intervention to provide a direct benefit to the individual participants.
 - The risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
- The research could not be carried out without the waiver.

- The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact representatives and make this information available to the IRB at the time of continuing review.
- The IRB has reviewed and approved consent procedures and a consent document in accord with 45 CFR 46.116 and 46.117.
 - These procedures and the consent document are to be used with participants or their legally authorized representatives in situations where use of such procedures is documented and 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 participant’s participation in the research consistent with the paragraph of this waiver.
- Additional protections of the rights and welfare of the participants are provided, at least
 - Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research is conducted and from which the participants are drawn.
 - Public disclosure to the communities in which the research is conducted and from which the participants are drawn, prior to the initiation of the research, of plans for the research and its risks and expedited benefits.
 - Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.
 - Establishment of an independent data monitoring committee to exercise oversight of the research.
 - If obtaining 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 participant’s family member who is not a legally authorized representative and asking whether he/she/they objects to the participant’s participation in the research.
 - The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
 - Procedures are in place to inform, at the earliest feasible opportunity, each participant, or if the participant remained incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, of the participant’s inclusion in the research, the details of the research and other information contained in the consent document.
 - There is a procedure to inform the participant, or if the participant remained incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, that he/she/they may discontinue the participant’s participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
 - If a legally authorized representative or family member is told about the research and the participant’s condition improves, the participant is also informed as soon as feasible.
 - If a participant is entered into research with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the research is provided to the participant’s legally authorized representative or family member, if feasible.
 - For the purposes of this waiver “family member” means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of

brothers and sisters; and any individual related by blood or affinity whose close association with the participant is the equivalent of a family relationship.

3.6 Emergency Use of Investigational Article or Product

An investigational article may be used in an emergency prior to IRB review, provided that the patient is in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

Such emergency use is reported to the IRB within 5 working days. An investigator that expects subsequent use of the investigational drug with other patients should request IRB review and approval of a treatment protocol after the initial emergency use. However, when prior IRB review and approval is not feasible for a subsequent expanded access emergency uses at a particular institution, the IRB does not prohibit a subsequent emergency use based on lack of time to obtain prospective IRB review, as long as that use will be reported to the IRB within 5 working days of initiation of treatment.

In such a situation, obtaining informed consent shall be considered feasible except in certain emergency situations where the investigator has adequately documented the necessary exception under the guidelines described in 21 CFR 50.23. The investigator must submit documentation to the IRB for review within 5 working days after emergency use of the test-article. In review of the documentation, the IRB will ensure that the investigator and a physician not otherwise participating in the clinical investigation adequately certified the following in writing prior to use of the test-article:

- The human participant was confronted by a life-threatening situation necessitating the use of the test article.
- Informed consent could not be obtained from the participant because of an inability to communicate with, or obtain legally effective consent from, the participant.
- Time was not sufficient to obtain consent from the participant's legal representative.
- There was available no alternative method of approved or generally recognized therapy that provided an equal or greater likelihood of saving the life of the participant.
- If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the participant, and time is not sufficient, prior to administering the test-article, to obtain an independent physician's opinion, the determinations of the investigator must be reviewed in writing within 5 days after the use of the test article by a physician not otherwise participating in the clinical investigation. In this event, a copy of the independent review must be submitted to IRB within 5 working days after the use of the test article.

3.6.1 Under FDA regulations, patients given emergency use test articles are considered research participants and data from the emergency use may be used in research through reporting to the sponsor and the FDA. Under HHS regulations, whenever emergency care is initiated without prior IRB review and approval, the patient may *not* be considered to be a research participant and the data derived from use of the test article may not be used in a prospective systematic investigation designed to develop or contribute to generalizable knowledge.

3.7 Humanitarian Use Devices

Humanitarian use devices (HUD) are intended to benefit patients by providing treatment or diagnosis of diseases that affect fewer than 8,000 individuals in the US per year. A Humanitarian Device Exemption (HDE) is an FDA approval for a physician to use a HUD in clinical treatment or as the participant of a clinical investigation. The IRB will approve the use of all Humanitarian Use Devices at this institution.

3.7.1 Review Procedure

For a HUD to be used for treatment or diagnosis at the University of Pennsylvania, the IRB and the FDA must approve it and a Humanitarian Device Exemption (HDE) must be issued by the FDA. HUD applications will be received via HS-ERA.

The IRB will verify that the device does not pose an unreasonable risk of illness or injury to the recipient, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

The IRB will evaluate the use of the HUD, as proposed, in the context of current labeling of the device.

The initial review of a submission to use an HUD for treatment is to be completed by a convened IRB. Continuing review may occur using an expedited procedure, unless the convened IRB (at time of initial review) determines that continuing review must return to the full board.

The IRB may approve the use of the HUD without an informed consent if: 1) a sufficient patient information booklet exists, and 2) the patient will be signing a clinical consent for the procedure. The patient information booklet must state that effectiveness for the labeled indication has not been demonstrated. On a case-by-case basis, the IRB may determine that a consent form is needed.

The IRB may impose more stringent restrictions for use of the HUD as a means of ensuring additional protection, as deemed necessary.

3.7.2 Physician Responsibilities

The physician will provide all applicable information regarding the use of the HUD in his/her/their application materials submitted to the IRB. The physician will fulfill continuing review requirements at the designated IRB intervals.

The physician will provide the consent form or the patient information brochure (prepared by the manufacturer) to the patient and review it with the patient prior to use.

The physician utilizing the HUD for treatment or diagnosis must use the HUD only in accordance with the labeling of the device, intended purpose, and in the designated population for which the FDA approved its use. Any off-label use of an HUD requires review by the IRB.

The physician must also ensure that the device is used only by designated individuals (qualified through training and expertise) in designated facilities approved for HUD use.

3.7.3 Use of HUD in Research

Studying the safety and effectiveness of an HUD does not require an IDE if the use is within the approved HDE labeling. However, IRB approval is required, and informed consent and HIPAA authorization must be obtained, since this constitutes research.

If an investigator plans to collect data for a new use of the device, then the IDE regulations must be followed, and as described previously, IRB approval is required, and informed consent and HIPAA authorization must be obtained. Continuing review by a convened IRB is required.

3.7.4 HIPAA and HUD

When the use of a HUD is for diagnosis or treatment, and not associated with research or data collection, a research HIPAA authorization form is not needed.

3.7.5 Considerations for Prompt Reporting

Whenever a physician or health care provider receives or otherwise becomes aware of information from any source that reasonably suggests that a HUD has or may have caused or contributed to the death or serious injury of a patient, the physician or health care provider must report such findings to the FDA and the IRB as soon as possible, in keeping with the IRB Policy on reporting Unanticipated Problems Involving Risks to Participants or Others. This reporting is in addition to, not a substitute for, FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.30.

The physician or health care provider shall promptly report any FDA action(s) regarding the HUD to the IRB. Modifications to the HUD or the clinical use of the HUD are to be promptly reported to the IRB in accordance with the IRB policy for amendments.

3.8 Expanded Access Use Requests

For research requesting the use of an investigational article for treatment purposes, the IRB requires prospective convened board approval or Chair concurrence of the use of the investigational article prior to administration of the investigational article.

Upon receipt of the protocol utilizing a treatment use IND/IDE or compassionate use IDE (or can be referred to as an expanded access application), an IRB Administrator with the assistance of the Director, Associate Directors, or Senior IRB Administrative staff determines the appropriate level of review.

3.8.1 Expanded Access INDs

Expanded access INDs are a mechanism for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments, but which do not require immediate treatment.

3.8.1.1 Expanded Access Single Patient Treatment INDs

In non-emergency situations, an investigator may obtain a treatment IND for use outside of a controlled clinical trial for a single patient. In such a situation, the investigator must provide the IRB with the required regulatory documentation. The IRB must determine all requirements for informed consent are met.

The IRB must prospectively approve the use of the treatment IND in a single patient at a convened board meeting, unless the FDA has been informed of Alternative IRB Review Procedures. If the FDA has been informed of Alternative IRB Review Procedures, the IRB Chairperson will provide prospective concurrence before the treatment use begins.

3.8.1.2 Expanded Access Intermediate or Large Population Treatment INDs

An investigator may obtain an expanded access treatment IND for an intermediate-size patient population or a large (widespread) patient population. The IRB must prospectively approve the use of the treatment IND in intermediate and large populations at a convened board meeting unless an exception can be granted (see section 3.8.3).

3.8.2 Expanded Access IDEs

3.8.2.1 Compassionate Use IDE

In non-emergency situations, an investigator may obtain a compassionate use IDE for use outside of a controlled clinical trial for a single patient. A compassionate use IDE is a mechanism for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may

provide a benefit in treating and/or diagnosing their disease or condition. This provision is typically approved for individual patients but may be approved to treat a small group.

In such a situation, the investigator must provide the IRB with the required regulatory documentation. The IRB must prospectively approve the use of the compassionate IDE at a convened board meeting, unless the FDA has been informed of Alternative IRB Review Procedures. If the FDA has been informed of Alternative IRB Review Procedures, the IRB Chairperson will provide prospective concurrence before the treatment use begins.

Subsequent treatment use requires FDA approval for a compassionate use IDE. If any problems occurred as a result of device use, these should be discussed in the IDE Report and reported to the reviewing IRB as soon as possible.

3.8.2.2 Treatment Use IDE

In non-emergency situations, an investigator may obtain a treatment IDE for use outside of a controlled clinical trial for an intermediate-size patient population or a large (widespread) patient population. A treatment IDE is a mechanism to expand access to additional patients with life-threatening or serious diseases in a trial if the data suggests that the device is effective.

In such a situation, the investigator must provide the IRB documentation of the treatment IDE to the FDA and treatment IDE number from the FDA, a protocol application with supporting documents, and an informed consent form. The IRB must prospectively approve the use of the treatment IDE and determine all requirements for informed consent are met. The IRB must prospectively approve the use at a convened board meeting unless an exception can be granted (see section 3.8.3). Subsequent treatment use requires FDA approval for a treatment IDE. If any problems occurred as a result of device use, these should be discussed in the IDE Report and reported to the reviewing IRB as soon as possible.

In the case of an emergency, refer to section 3.6 Emergency Use of Investigational Article or Product.

3.8.3 Exceptions to Convened Review Requirement for Expanded Access INDs/IDEs

3.8.3.1 Single Patient Expanded Access INDs/IDEs

Single patient expanded access applications may be processed via expedited review when there is documented notification of expedited review to the FDA by the submitter (e.g., in the cover letter to FDA and/or box 10b is checked on FDA form 3926).

The level of review required is dependent upon the following factors:

- The time sensitivity of the request
- The level of risk involved in both the treatment/compassionate use itself
- Whether the treatment/compassionate use is thought to be in the best interest of the participant
- Whether the treatment/compassionate use holds out the prospect of direct benefit to the participant
- Whether the risk/benefit ratio specifically related to the treatment/compassionate use request is favorable

3.8.3.2 Intermediate Size Population and Treatment Use INDs/IDEs

Such applications require convened IRB review, given the treatment/compassionate use may pose greater than minimal risk, unless an emergent situation presented itself.

The IRB staff will consider whether there is adequate time and resources to allow for the protocol to be scheduled and reviewed by the appropriate convened IRB without negatively affecting potential benefit to a patient. The Director and / or physician IRB Chair will be consulted as needed.

The following applications **may** be eligible for expedited review*:

- The treatment/compassionate use is time sensitive
- The treatment/compassionate use is in the best interest of the patient and/or the prospect of direct benefit exists
- The risk/benefit ratio for the proposed treatment/compassionate use request is favorable

A physician IRB Chair is responsible for reviewing and approving the protocol.

*Submissions that do not meet the above criteria require convened review. Protocols requiring convened review will be scheduled for the appropriate convened IRB.

3.8.4 Ongoing Review of Expanded Access INDs/IDEs

The IRB does not require formal continuing review submissions (i.e. progress report, monitoring summary, etc.) for annual renewals of expanded access protocols that meet the requirements needed for protocols determined to be greater than minimal risk research. Annual reports for expanded access protocols may be provided at the end of the compassionate/treatment use if the report exists. As the treating physician is required to submit a summary report to the FDA and (if applicable) the sponsor, the treating physician may provide this report at the end of the compassionate/treatment use.

3.9 Research conducted in the context of Advanced Life Support Services, Mobile Intensive Care Units, Specialty Care Transport Services, or Air Medical Services

NJ State Law requires that any “prospective research activity involving drug trials or invasive procedures” conducted in the context of Advanced Life Support Services, Mobile Intensive Care Units, Specialty Care Transport Services, or Air Medical Services undergo review by the NJ State Office of Emergency Medical Services (OEMS) MICU Advisory Council.

Research of this type within the state of NJ will be referred to the Office of General Counsel prior to IRB review. The IRB will withhold IRB approval until approval from the Commissioner through OEMS MICU Advisory Council is received.

4. REFERENCES

[21 CFR 812](#); [21 CFR 814](#); 21 CFR 803.30; [FDA Device Advice](#); [FDA Information Sheets, Medical Devices](#); [21 CFR 50.24](#); [Federal Register 61\(192\): 51531-51533](#); [FDA Draft Guidance, Exception from Informed Consent Requirements for Emergency Research, August 29, 2006](#); [OHRP Guidance, informed consent requirements in emergency research, October 31, 1996](#); [Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors Significant Risk and Nonsignificant Risk Medical Device Studies](#), January 2006; [Humanitarian Device Exemption \(HDE\): Questions and Answers Draft Guidance for HDE Holders, Institutional Review Boards, Clinical Investigators, and Food and Drug Administration Staff](#), March 2014; NJAC § 8:41-5.1

IDE Early/Expanded Access

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm#treatmentuse>

FDA Physician Request for an Individual Patient IND under Expanded Access for Non-emergency or Emergency Use
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm107434.htm>

Treatment Use of Investigational Drugs - Information Sheet
<http://www.fda.gov/RegulatoryInformation/Guidances/ucm126495.htm>

CO 600 COMMUNICATIONS

CO 600	COMMUNICATIONS
601	INVESTIGATIVE STAFF
602	OTHER ENTITIES

1. PURPOSE

This policy describes the IRB actions that must be communicated to the investigator and the importance of open communication among IRBs, investigators, staff, and university committees and officials.

2. POLICY STATEMENT

It is important that staff, participants, and other interested parties have a means of communicating information about the conduct of a research project directly to the appropriate institutional officials. It is vital that IRB members, department heads, and other officials with responsibility for oversight of research have open and ready access to the highest levels of authority within the institution. IRB staff and members do not have the opportunity to communicate directly with study participants. The researcher and research staff interacts with participants; therefore it is vital that open and frequent communication with the investigative team be maintained.

3. SPECIFIC POLICIES

3.1 Investigator Notifications

3.1.1 Initial Submission: The investigator will be notified in writing of the IRB's decision as soon as possible after the meeting. If the approval is withheld pending clarification, based upon receipt and review of requested materials or responses from the investigator or sponsor, the IRB must receive the response within a reasonable timeframe of the date of notification.

3.1.2 Renewals and Revisions: Investigators will be notified in writing as soon as possible as to the action taken by the IRB for any continuing reviews or revisions.

3.1.3 Notification of Final Approval: Investigators will be notified in writing of the final approval. The IRB-approved consent form will be dated with the period of approval and submitted to the investigator with the final approval letter.

3.1.4 Disapproval: Correspondence will provide the reason(s) for disapproval and will give the investigator an opportunity to respond in person and in writing to the IRB.

3.2 Investigator Appeal of IRB Action

If an investigator disagrees with a determination of the IRB (substantive or procedural), the investigator may appeal to the Vice Provost for Research. An appeal must be in writing, state the decision being appealed and the basis of the appeal, and be filed within 30 calendar days of the decision. The Vice Provost may use his/her/their sole discretion to determine the process for the appeal and grant or deny the appeal, including:

- Notifying the IRB of the appeal and requesting a response and relevant information from its records before making a decision
- Appointing a factfinder to review the matter and prepare a report for review by the IRB
- Seeking assistance from consultants or internal administrative units such as the Office of the General Counsel who will report their findings to the IRB

- Requesting that the IRB consider additional information or actions in relation to the decision under appeal
- The investigator is bound by the IRB decision prior to and during the appeal. The decision on an appeal by the Vice Provost for Research is final.

If, after taking into consideration any additional information, the IRB decides to disapprove a protocol or requires protocol modifications as a condition for approval, neither the Vice Provost for Research, the Provost, nor any other any University of Pennsylvania official or committee may overturn the IRB's decision.

3.3. Noncompliance

The IRB, through the Senior Management (Director and Associate Directors), will notify the investigator in writing of the findings of the convened IRB and any additional actions required in response to the findings, as well as notification of reporting to outside oversight agencies, if applicable. In addition, any required reporting to outside oversight agencies (i.e. FDA or OHRP) shall also be sent to the individual's Supervisor (Department/Division Chair or Dean), any appropriate internal Penn entities (including entities with required Sponsor reporting), and the Vice Provost for Research.

3.4. Scientific Misconduct

The IRB's responsibility is to protect the rights and welfare of research participants, which could be placed at risk if there is scientific misconduct on the part of an investigator or any member of the investigative team. It is, therefore, the duty of the IRB to be receptive to and act on good faith allegations of scientific misconduct. Allegations of Misconduct in Science, as defined by University Policy must be referred to the Vice Provost for Research.

4. REFERENCES

[45 CFR 46.109](#); [21 CFR 56.109](#)

1. PURPOSE

This policy describes the IRB actions that must be communicated to various parties involved in the research program.

2. POLICY STATEMENT

The University of Pennsylvania complies with all applicable local, state, and federal regulations that pertain to reporting requirements. Federal regulations require institutions to have written procedures in place for prompt reporting to the IRB, appropriate institutional officials, and department and agency heads of:

- Unanticipated problems that involve risks to participants or others;
- Serious or continuing noncompliance with regulations; and,
- Suspension or termination of IRB approval of research; and

The specific procedures for investigating and making pertinent determinations concerning those situations are addressed in SOP RR 404.

Senior IRB Management (Director and Associate Directors) will review the reports, and the Institutional Official will receive the report, along with any appropriate internal Penn entities.

3. SPECIFIC POLICIES

3.1 Communication to Institutional Official of IRB Actions

All IRB minutes shall be available to the Institutional Official if they are requested. IRB Minutes shall be available to the Senior Associate Vice Provost for Human Research by way of the Office of Clinical Research Compliance Unit as well as the Research Compliance Officer as the Vice Provost for Research has delegated this responsibility to the Senior Associate Vice Provost for Human Research and the Research Compliance Officer.

3.2 Communications to Others

3.2.1 Prospective Emergency Research: If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in 21 CFR 50.24 Exemption from Informed Consent Requirements for Emergency Research, notification of disapproval will be conveyed to the sponsor as well as the investigator.

3.2.2 Device studies: If the IRB determines that a study submitted as a non-significant risk presents significant risk, the IRB will notify the investigator.

3.2.3 Other Reportable Events:

- The IRB determines that a problem represents an unanticipated problem that involves risks to participants or others;
- The IRB or institutional official suspends or terminates its approval of research; or,
- The IRB determines that noncompliance represents serious or continuing noncompliance.

3.3 Report Content

Following a complete investigation of the situation or incident, the Director of Human Research Protections will prepare a final report that includes the following:

- An overview of the situation or incident
- Any findings that would impact the IRB review, as applicable
- A full explanation as to why and how the incident occurred
- The actions taken, including any corrective actions
- Any sanctions taken

3.4 Report Recipients

The event(s) reported by the Director of Human Research Protections and/or Associate Director, will be shared with government agencies, if applicable, and sponsors to the extent legally and contractually required (with most notification coming from the appropriate internal entities managing the relevant agreement), and with any others at the discretion of the IRB and the Institutional Official. The report will be sent to, or shared with, the following individuals and agencies:

- Office of Human Research Protections (OHRP) when the research is subject to regulation by the OHRP
- Food and Drug Administration (FDA) when the research is subject to regulation by the FDA
- Funding agency when funded by a government entity (e.g., the Departments of Defense, Education, and Justice require copies of such reports)
- Licensing and accrediting bodies, where the report or some portion thereof implicates standards or regulations administered by those bodies
- Principal investigator (PI)
- PI's Department Chair/Division Chief or Dean
- The Office of Clinical Research, when the PI is within the Perelman School of Medicine
- Appropriate internal entity managing the grant or contract or other research agreement

3.5 Reporting Timeframe

The Institutional Official will be notified of the convened IRB findings by being copied on the reporting letter.

The Institutional Official, or delegate, will report the event to appropriate federal department and agency heads within 30 days of the formal determination by the convened IRB. Note: If the report requires input from several research support entities or specific responses from the study team, it may be delayed to produce a comprehensive report. If federally funded, the Institutional Official, or delegate, will submit any report on behalf of the institution.

3.6 Provisions related to IRB Authorization Agreements

If Penn is serving as the IRB of Record for another organization or University according to an IRB authorization agreement, the Penn IRB will maintain responsibility for reporting applicable events that occur at relying sites. The Penn IRB will provide a draft report to the IRBs at relevant relying institutions with the opportunity to review and comment on the draft report. The Penn IRB will provide a copy of the finalized report to the relying site IRB. The relying site IRB maintains the right to make its own additional report.

If Penn is relying on another IRB to serve as the IRB of Record according to an IRB authorization agreement, the Penn IRB will receive a copy of any external reports made by the IRB of Record related to events that occurred at Penn. The

Director of Human Research Protections will review the report and determine whether the Penn IRB will elect to submit its own additional report to the FDA, OHRP or other regulatory agencies.

4. REFERENCES

[45 CFR 46.103](#); [21 CFR 56.108](#); [FDA Reporting Requirements: suspension or termination of IRB approval](#); [OHRP compliance overview](#)

IC 700 INFORMED CONSENT AND HIPAA AUTHORIZATION

IC 700	INFORMED CONSENT AND HIPAA AUTHORIZATION
701	GENERAL REQUIREMENTS AND DOCUMENTATION
702	WAIVERS AND ALTERATIONS
703	CONSENT DOCUMENTATION
704	ASSENT
705	SURROGATE CONSENT AND AUTHORIZATION

IC 701 GENERAL REQUIREMENTS AND DOCUMENTATION OF INFORMED CONSENT

1. PURPOSE

This policy describes the general requirements for obtaining informed consent and participant authorization and for documentation of informed consent and participant authorization.

2. POLICY STATEMENT

Informed consent must be legally effective and prospectively obtained. Except as described at IC 702 no investigator may involve a human being as a research participant unless he/she/they has obtained legally effective informed consent of the participant or the participant's legally authorized representative. Consent shall be sought only under circumstances that provide the prospective participant or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The consent document must be organized in a way that facilitates comprehension and presents information in a way that does not merely provide lists of isolated facts, but rather facilitates understanding of the reasons why one might or might not want to participate

Participant authorization must be obtained for prospective use or disclosure of protected health information for research conducted within one or more of the covered entities of the University of Pennsylvania. Except as described at IC 702 no investigator may involve a human being as a research participant unless he/she/they has obtained legally effective authorization of the participant or the participant's legally effective representative.

The IRB requires documentation of informed consent by use of a written consent form approved by the IRB and signed by the participant or the participant's legally authorized representative. Authorization may be obtained by the use of a separate HIPAA Authorization Form or combined with an IRB-approved informed consent document. As part of the IRB's reviews to determine that the approval criteria found in the regulations at 45 CFR 46.111 and 21 CFR 56.111 have been met, the IRB reviews the consent form and determines that the form meets the applicable regulatory requirements. Specifically, that informed consent will be sought from each prospective participant or the participants LAR in accordance with the informed consent regulations found at 45 CFR 46.111(a)(4) and 21 CFR 56.111(a)(5) and that informed consent will be appropriately documents in accordance with the regulations found at 45 CFR 46.111(a)(5) and 21 CFR 56.111(a)(5).

3. SPECIFIC POLICIES

3.1 The Consent Form May be:

3.1.1 A written consent document that embodies the elements of informed consent and if necessary, the required elements of HIPAA authorization. This form may be read to the participant or the participant's legally authorized representative, but, in any event, the investigator shall give either the participant or the representative adequate opportunity to read it before it is signed (this may include an electronic format). Each participant shall receive a copy of the signed consent document or signed combined consent authorization document.

3.1.2 A "short form" written consent document stating that the elements of informed consent as required have been presented orally to the participant or the participant's legally authorized representative. The short form may be used when an investigator unexpectedly encounters a participant who does not speak English. Please reference IC 703 Documentation section 3.2 for specific details on requirements surrounding the use of short forms.

3.2 Required Elements of Informed Consent:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the participant's participation, a description of the procedures to be followed, and identification of any procedures which are experimental or investigational.
2. A description of any reasonably foreseeable risks or discomforts to the participant, if any.
3. A description of any benefits to the participant or to others which may reasonably be expected from the research, if any.
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant.
5. A statement describing the extent to which, if any, the confidentiality of records identifying the participant will be maintained and that notes the possibility that the Food and Drug Administration and representatives of the IRB may inspect the records.
6. For research involving more than minimal risk, or if the research proposes compensations for research related injury, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained. 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.
7. An explanation of whom to contact for answers to pertinent questions about the research and research participants' rights, and whom to contact in the event of a research-related injury to the participant.
8. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and that the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
9. One of the following statements will be required for 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 removal, could be used for future research studies or distributed to another investigator for future research studies without additional informed consent; --or-
 - A statement that participant'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

3.3.1 When appropriate, one or more of the following elements of information shall also be provided to each participant:

- A statement that the particular treatment or procedure may involve risks to the participant (or to the embryo or fetus if the participant is or may become pregnant) which are currently unforeseeable.
- Anticipated circumstances under which the participant's participation may be terminated by the investigator without regard to the participant's consent.
- Any additional costs to the participant that may result from participation in the research.
- The consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation by the participant.
- A statement that significant new findings developed during the course of the research which may relate to the participant's willingness to continue participation will be provided to the participant.
- The approximate number of participants involved in the study.
- A statement that participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant 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 participants, and if so, under what conditions;
- 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 Other Informed Consent Requirements

3.4.1 Second Person Language

The language of the consent document should be in the second person style, so the consent form conveys a dialogue with information being provided and that there is a choice to be made by the participant rather than presumption of the participant's consent with the use of the first person style.

3.4.2 Lay Language/Participant Comprehension

The information provided in the informed consent documents must be in language understandable to the participant. The informed consent document should not include complex language that would not be understandable to all participants. Technical and scientific terms should be adequately explained using common or lay terminology. Informed consent as a whole, must present information in sufficient detail related 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 participants or LAR's understanding of the reasons why one might, or might not, want to participate.

3.4.3 Exculpatory Language

Informed consent documents may not contain any exculpatory language through which the participant is made to waive or appear to waive legal rights or releases or appears to release the investigator, the sponsor, the university from liability for negligence.

3.4.4 FDA-Regulated Test Articles

For all research involving test articles regulated by the U.S. Food and Drug Administration (FDA), informed consent documents should include a statement that the purpose of the study includes evaluation of the safety or the safety and the effectiveness of the test article. The consent form must also include a statement that the FDA has access to the participant's medical records.

3.4.5 IRB review of consent process.

The IRB will take the following into consideration when reviewing the protocol and consent form:

- Who will conduct the consent process;
- Matters of timing of obtaining informed consent and any waiting period between informing the participant and obtaining consent;
- That the process provides ample time for the person conducting the consent interview and the prospective participant to exchange information and ask questions.

3.4.6 When applicable: translations of consent documents will also be submitted for IRB approval and will be reviewed in an expedited manner. There are two options available to obtain approval of translated consent forms.

Option #1: The IRB-approved consent form is translated by the sponsor or site and submitted to the IRB. The IRB will have a member or consultant fluent in the language of the consent; review the translated document for accuracy. In their opinion it must match the English version.

Option #2: The investigator (or sponsor) may submit the IRB-approved version of the consent to a translator for translation. A second translator may then back translate the consent to the original English. Both original and back-translated consent must be submitted.

Option #3: The investigator (or sponsor) may submit the IRB-approved version of the consent to an official certified translator or translation service for translation. The translator will submit a signed statement that the consent document is a true and accurate translation.

When translated documents are utilized, the investigator should also provide a plan for verbal interpretation of all participant materials as well as ongoing interactions throughout the study.

3.4.7 When following ICH-GCP (E6): The IRB determines that the following disclosures are included:

- That the monitor, the auditor, and the regulatory authorities will be granted direct access to the participant's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the participant or the participant's legally acceptable representative is authorizing such access.
- The approval of the IRB.

In addition, when following ICH-GCP (EG): The IRB determines that the consent includes the following, if applicable:

- If a participant 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 consent document and any other written information to be provided to participants is read and explained to the participant or the participant's legally acceptable representative, and after the participant or the legally acceptable representative has orally consented to the participant's participation in the trial and, if capable of doing so, has signed and personally dated the consent document, the witness should sign and personally date the consent document.
- By signing the consent document, the witness attests that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant or the participant's legally acceptable representative, and that consent was freely given by the participant or the participant's legally acceptable representative.
- Prior to participation in the trial, the participant or the participant's legally acceptable representative should receive a copy of the signed and dated written consent document and any other written information provided to the participants.

3.4.8 When following FDA regulations, the IRB determines that the consent form includes the following statement regarding posting of the trial on clinicaltrials.gov, as applicable:

"A description of this clinical trial will be available on <http://www.clinicaltrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time."

3.4.9 A concise and focused presentation of the key information that is most likely to assist a prospective participant or LAR in understanding the reasons why one might, or might not, want to participate in research. This part of the informed consent form must be organized and presented in a way that facilitated comprehension. Generally, the beginning of an informed consent should include a concise explanation of the following:

- The fact that consent is being sought for research and that participation is voluntary
- The purposes of the research, the expected duration of the prospective participant's participation and the procedures to be followed in the research
- The reasonably foreseeable risks or discomforts to the prospective participants
- The benefits to the prospective participant or others that may reasonably be expected from the research

- Appropriate alternative procedures or course of treatment, if any, that might be advantageous to the prospective participant

However, based upon the facts of an individual protocol, the IRB may require that different (or additional) information be presented at the beginning of an informed consent to satisfy this requirement.

3.5 Public Posting of Clinical Trial Consent Forms

The revised Common Rule includes a requirement for the posting of one IRB-approved consent form to a publicly available Federal website for each clinical trial conducted or supported by a Common Rule department or agency. The consent form must have been used in enrolling participants. The consent form must be posted after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any participant.

This requirement may be satisfied by either the awardee or the Federal department or agency. 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 website (e.g., confidential commercial information), the department or agency may permit or require redactions to the information posted.

Two publicly available federal websites that will satisfy the consent form posting requirement have been identified by DHHS: 1) ClinicalTrials.gov and 2) a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

Federal guidance is available on the DHHS website. The investigator should consult with their grant officer if they have questions regarding how to satisfy this requirement.

3.6 Broad Consent

Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or non-research purposes) is permitted on a case by case basis.

When obtaining broad consent, the other requirements for informed consent described in the previous section are applicable. The following elements of broad consent [§46.116(d)] shall be provided to each participant or the participant's LAR:

1. A description of any reasonably foreseeable risks or discomforts to the participant;
2. A description of any benefits to the participant or to others which may reasonably be expected from the research;
3. A statement describing the extent, if any, to which confidentiality of records identifying the participant must be maintained;
4. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled;
5. For research involving biospecimens, a statement that the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit;
6. 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);

7. A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;
8. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens;
9. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite);
10. Unless the participant or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the participant's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;
11. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the participant in all circumstances, a statement that such results may not be disclosed to the participant; and
12. An explanation of whom to contact for answers to questions about the participant's rights and about storage and use of the participant's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.

Investigators must include information regarding the circumstances under which broad consent will be obtained, the proposal for tracking of responses, and the proposed consent form(s) (or oral script if a waiver of documentation of consent is sought) and any other consent materials (e.g., information sheet, audiovisual materials, etc.) in their submission to the IRB. The IRB will review the information provided with the aid of a checklist to ensure that all requirements are satisfied. The outcome of the IRB's review will be communicated to the investigator in the IRB correspondence.

3.7 Observation of the Informed Consent Process

The IRBs have procedures for observation of the informed consent process in ongoing research, when appropriate. As part of the IRB oversight options, an IRB may require that a staff member or an outside third party observe the consenting of research participants to determine:

Whether the informed consent process has been appropriately completed and documented.

An IRB may require observation of the consent process for selected protocols. Examples of protocols that may require observation of the consent process include:

1. High risk studies;
2. Studies that involve particularly complicated procedures or interventions;
3. Studies involving potentially vulnerable populations (e.g., ICU patients, children);
Studies involving study staff with minimal experience in administering consent to potential study participants; or,
4. Other projects where observation is determined to be required by the IRB.

3.8 Remote Informed Consent Process

Obtaining informed consent from a participant (or permission from their legally authorized representative or parent) may occur fully or partially remote via audio or video mediums. The investigator should describe the consent discussion, i.e., the process that will be used to review the IRB approved informed consent document with the participant and obtain

verbal consent or permission. This description should include the medium / platform used (e.g., phone, Zoom video conferencing, etc.). Refer to Section IC 703 for methods of documenting consent remotely.

Investigators within Penn Medicine and Penn Dental must utilize platforms that are compliant with HIPAA regulations, as applicable. Investigators must remain in compliance with GCP and FDA regulations, as applicable. Investigators shall follow IRB guidance as applicable to their school affiliation.

4. REFERENCES

[45 CFR 46.116; 21 CFR 50.20; FDA's Information Sheets: guide to informed consent; OPRR Guidance, obtaining and documenting informed consent of participants who do not speak English](#)

1. PURPOSE

This policy describes the requirements for waiver of certain or all elements of informed consent procedures and waiver of requirements for obtaining informed consent.

2. POLICY STATEMENT

The IRB may approve a consent procedure, which does not include, or which alters some or all of the elements of informed consent (above) or waives the requirement to obtain informed consent if the IRB finds that the research meets specific criteria.

For FDA regulated research, the IRB may not waive informed consent except under the narrow provisions found in:

- 21 CFR 50.23 governing emergency research
- FDA's Guidance on Informed Consent for *in vitro* Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable, April 25, 2006.
- FDA's Guidance on IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects, July 2017

3. SPECIFIC POLICIES

3.1 Waivers or Alterations of One or More Requirements of Informed consent

The IRB may approve an informed consent procedure which does not include, or which alters some or all of the elements of informed consent or waives the requirement to obtain informed consent provided the IRB finds and documents that:

- the research involves no more than minimal risk to the participants and, the waiver or alteration will not adversely affect the rights and welfare of the participants, the research could not practicably be carried out without the waiver or alteration and; whenever appropriate, the participants will be provided with additional pertinent information after participation
- research could not practicably be carried out without accessing or using such information or biospecimens in an identifiable format
- Non-identified information should be used whenever possible to respect participants' interests in protecting the confidentiality of their information and biospecimens.
- The study team has provided a sufficient explanation as to why the study meets all of the four criteria listed above.
- The IRB documents its findings justifying the waiver or alteration of consent.
- If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

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

- In order to approve a request from an investigator to waive the requirement for informed consent, or to omit or alter one or more basic or additional element of consent (an “Alteration”), under this provision the IRB must determine and document that the below criteria are satisfied.
 - The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine a. Public benefit 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.

3.3 Exceptions to Requiring a Waiver

The 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 participants without the informed consent if either of the following conditions are met:

- 1) The information will be obtained by communicating with the prospective participant or their legally authorized representative.

- 2) The identifiable information or biospecimens will be obtained by accessing existing records or stored biospecimens.

For additional information, please see SOP IC 702.

4. REFERENCES

[45 CFR 46.116](#); [45 CFR 46.117](#); [21 CFR 50](#); [21 CFR 50.23](#); [FDA Guidance on Informed Consent for *in vitro* Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable, April 25, 2006](#); [FDA Guidance: IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects, July 2017](#).

1. PURPOSE

This policy describes the requirements for documentation of informed consent and circumstances when the IRB may waive the requirement to document informed consent.

2. POLICY STATEMENT

Unless specifically waived by the IRB, all participants, or their legally authorized representatives, must document that they are consenting to participate in any research project that is conducted at the University of Pennsylvania.

3. SPECIFIC POLICIES

Documentation of Informed Consent

Each participant or his/her/their legally authorized representative must sign and date a copy of the current IRB-approved consent form prior to enrollment or any participation in any phase of the study, unless the requirement is waived by the IRB as allowed and be given a copy of the signed document.

The IRB may approve procedures for documentation of informed consent that involve (a) a written consent form signed by the participant; (b) a short form written consent form with oral presentation; or (c) waiver of signed written consent form.

Each of these three options is described in detail below. It is the responsibility of the IRB to determine which of the procedures described below is appropriate for documenting informed consent in protocols that it reviews. Generally, only option (a) will be appropriate.

3.1 Written Consent Form Signed by Participant or Legally Authorized Representative

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 participant or the participant's legally authorized representative. The investigator should allow the participant or the legally authorized representative adequate opportunity to read the consent document before it is signed. A copy of the document must be given to the person signing the form.

3.1.1 Mentally disabled or cognitively impaired participants: Studies involving participants who may have impaired decision-making capabilities may take place over extended periods. The IRB should consider whether periodic re-consenting of individuals (or consent, if assent was obtained) should be required to ensure that a participant's continued involvement is voluntary. The IRB may require that investigators re-consent participants after taking into account the study's anticipated length and the condition of the individuals to be included (e.g., participants with progressive neurological disorders). Additionally, the IRB should consider whether and when to require a reassessment of decision-making capacity.

3.1.2 The written informed consent document should embody, in language understandable to the participants of the study, all the elements necessary for legally effective informed consent (see section 701 3.2).

3.1.3 Participants who do not understand English should be presented with an informed consent document written in a language understandable to them.

3.2 Obtaining Informed Consent from Non-English Speakers

Non-English speaking participants should not be systematically excluded from research without a sound scientific or ethical rationale to ensure equitable participant selection. In assessing equitable participant selection, the IRB will consider the purpose of the research, the research setting, and the targeted population. Investigators and the IRB must carefully consider the ethical and legal ramifications as well as the risks and benefits of enrolling participants when a language barrier exists. Investigators (particularly those conducting greater than minimal risk and clinical research) *must prospectively review protocol requirements to ensure applicable provisions are in place to support the safety of a non-English speaker to participate in the research.*

Federal regulations at 45 CFR 46.116(a)(3) and 21 CFR 50.20 require that informed consent be obtained in language that is understandable to the participant (or the participant's legally authorized representative). In accordance with these regulations, informed consent discussions must include a *reliable* interpreter when the prospective participant does not understand the language of the person who is obtaining consent. Likewise, the written informed consent document should embody, in a language understandable to the participant, all the elements necessary for legally effective informed consent. For FDA regulated research, the FDA considers understandable to mean that the information presented to prospective participants is in a language and at a level they can comprehend, including an explanation of scientific and medical terms.

Consent may be documented in one of two ways:

- A full-length informed consent document translated into a language understandable to the participant; or
- A “short-form” consent document in the language of the participant (or LAR) that states the general elements of informed consent.

When the targeted population includes a large proportion of non-English speaking participants, investigators should document a plan for translating the informed consent and providing an interpreter for the consent discussion. See section IC 701 3.4 Other Informed Consent Requirements for translation requirements.

- For federally funded research, the [NIH policy 3014-301 – Informed Consent](#) must be followed.
- For FDA regulated research, consult the [FDA guidance Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors AUGUST 2023](#) for best practices.

3.2.1 Using short form consent documents

When non-English speaking participants (or LARs) are incidentally encountered, a short form process is appropriate. Generic “short form” consent documents are made available to investigators in languages typically encountered among participant populations. Investigators are responsible for providing documents in languages not typically encountered.

If investigators use a “short form” to document informed consent, they must also provide participants (or LAR) with

- (i) **A written summary of the information that is presented orally.** The written summary must contain the basic and additional elements of consent; in most cases this will be the full-length informed consent document in English;
AND
- (ii) **An interpreter who speaks English and the participant's (or LAR's) language,** who can take part in the oral informed consent discussion to provide the oral summary and to ensure participant's understanding through facilitating exchange of information related to questions and/or concerns;

AND the investigator must also confirm there is

- (iii) **A witness to the oral presentation.** The role of the witness is to confirm:
 - a. the information, as orally presented to the participant, was presented in the participant's language and was understandable to the participant;

- b. that the participant's questions were interpreted and responses by the person obtaining consent were conveyed in the participant's language and understandable to the participant; and
- c. at the conclusion of the consent discussion, the participant was asked in his/her/their language if he/she/they understood the information and that in response the participant indicated affirmatively.

The participant / LAR should be given copies of both the "short form" consent document and the written summary of the information that is presented orally.

3.2.1.1 Requirement for a Witness

A witness to the oral presentation is required. The witness must be a legal adult and *fluent in both English and the language spoken by the research participant*. It is preferred that the witness be impartial to both the study team and participant. However, if an impartial witness is not otherwise available, the witness may then be an adult family member/friend of the participant, or an adult staff member not otherwise involved with the study. The interpreter may serve as the witness as long as the interpreter is able to confirm the authenticity of the oral consent process, as noted above, and provide a signature as the witness. *The investigator obtaining consent may not be the witness to the consent process.*

3.2.1.2 Requirement for an Interpreter

An interpreter must be utilized to orally present the written summary and facilitate the discussion between the person obtaining consent and the participant, in the participant's language. The interpreter may be present in-person or arranged remotely.

For FDA-regulated research, the interpreter must be through a qualified translation service vendor. If arranged through a qualified vendor, the interpreter must provide either his/her/their name or unique employee ID and have the ability to receive the IRB-approved English language study consent document(s) for use as the source of information to be orally presented through the interpretation services.

3.2.1.3 Signature Requirements

The "short form" consent document written in the participant's (or LAR's) language must be signed by *the participant (or LAR)* and *the witness* to the oral presentation. It is *recommended* that the interpreter also sign the short form, when possible.

The written summary of the information that is presented orally (i.e., the full-length English consent document) must be signed by *the person obtaining consent* and *the witness* to the oral presentation. It is *recommended* that the interpreter also sign, when possible.

Protocols requiring GCP compliance should also document the short form consent process utilizing a consent / enrollment note.

3.2.1.4 Research Requiring HIPAA Authorization

For research requiring HIPAA authorization, when using a short form consent document to complete the primary consent process for a non-English speaking participant, a fully translated standalone HIPAA authorization is also required.

3.2.1.5 Requirements for Prospective IRB Approval to Use a Short Form

Prospective IRB approval to enroll a Non-English speaking participant with a short form is not required when *all of the following conditions are met*:

1. The approved, English version of the informed consent document is used as the written summary. Signature lines may be adapted to permit applicable signatures without additional prospective IRB review / approval. No additional changes may be made without prospective IRB review;
2. One of the generic "short form" consent documents available from the Penn or CHOP IRBs is utilized,

AND

3. A qualified interpreter service will be utilized throughout the course of the participant's consent process and participation.

In this case, the IRB will not stamp the short form consent document.

An exception request (prospective deviation) is required if *any* of the following conditions are met:

- The written summary is not the approved, stamped English version of the informed consent;
 - A short form consent document translated into a language unavailable from the Penn or CHOP IRB is utilized. The IRB may accept short form translations from other AAHRPP accredited IRBs. The study team should consult with the IRB prior to utilization;
- OR
- An individual other than a qualified interpreter will be used for interpretation (e.g., a member of the study, another Penn employee, etc.)

When formal exception requests are submitted, the IRB will stamp the short form consent document.

Expedited review of these versions is acceptable if the protocol, the full English language informed consent document, and the English version of the short form document have already been approved by the convened IRB.

3.2.1.6 On-going/Re-consent for Non-English Speakers

After enrolling a participant using a short form process, the investigator is encouraged (but not required) to pursue a complete translation of the full informed consent document, particularly for greater than minimal risk or FDA regulated research. Refer to IC 701, Section 3.4.6.

- a. If available, a full translation should be provided to the participant in a timely manner. The participant should sign the full translation upon receipt. Re-consent processes involving a fully translated informed consent document should involve an interpreter to facilitate discussion between the person obtaining consent and the participant, but do not require the participation of a witness. Moving forward any updated information provided to participants concerning research study participation must be provided through a fully translated informed consent document.
- b. If not available, the short form process may be leveraged each time an update to the informed consent is required.

3.3 Waiver of Documentation

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all participants if the IRB finds that the study is minimal risk, the only record linking the participant and the research would be the consent document and the principle risk would be potential harm resulting from breach of confidentiality.

The IRB may waive the requirement for the investigator to obtain written informed consent if the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.

The IRB may waive the requirement for the investigation to obtain written informed consent if the participants are members of a cultural group or community in which signing forms is not the norm. If the participants or LARs are members of a distinct cultural group or community in which signing forms is not the norm, documentation of consent may be waived if the research presents no more than minimal risk of harm to the participants and provided there is an appropriate alternative mechanism for documenting consent was obtained.

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.

In cases in which the documentation requirement is waived, the IRB may still require the Principal Investigator to provide participants with a written statement regarding the research.

If a broad consent procedure is used:

- The IRB may not omit or alter any of the required elements of disclosure, and when appropriate, any of the additional elements of disclosure.
- If a study requests broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens, and an individual refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

3.4 Documenting Consent Remotely

The IRB may approve a process that allows the informed consent document to be delivered by mail, facsimile or electronically to the potential participant or the potential participant's legally authorized representative. The investigator should describe the method of documenting signed consent, including the medium / platform used (e.g., mail, fax, DocuSign, etc.). Refer to Section IC 702 for methods of conducting the consent discussion remotely.

Investigators within Penn Medicine and Penn Dental must utilize platforms that are compliant with HIPAA regulations, as applicable. Investigators must remain in compliance with GCP and FDA regulations, as applicable. Investigators shall follow IRB guidance as applicable to their school affiliation.

4. REFERENCES

[46 CFR 46.117](#); [21 CFR 50.27](#); [FDA Guidance Document: Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors AUGUST 2023](#); [NIH Policy 3014-301 - Informed Consent](#)

IC 704 ASSENT

1. PURPOSE

This policy describes the requirements for assent of cognitively impaired adults and of children.

2. POLICY STATEMENT

The principle of respect for persons requires that the choice of an autonomous person be respected. Under the usual conditions of clinical research, this is accomplished by soliciting the informed consent of the prospective research participant. When prospective participants have diminished capacity to consent, the consent of the parent or legally authorized representative is required (see IC705). However, any individual capable of some degree of understanding (generally, a child of seven or older) should participate in research only with assent. When assent is required, however, the decision of the individual assenting should be binding.

The Department of Health and Human Services' (DHHS) [Regulations for the Protection of Human Subjects](#) (Title 45, Part 46 Subpart D of the Code of Federal Regulations) and the Food and Drug Administration (FDA) regulations for the Protection of Human Subjects (Title 21, Part 50, Subpart D) set standards for the informed consent process and assign Institutional Review Boards with the responsibility for ensuring that any research or clinical trials involving children meet the following criteria.

3. SPECIFIC POLICIES

3.1 Use of Assent:

In instances where the participant may not be capable of giving informed consent the IRB must find that adequate provisions are made for soliciting the assent of the participant when in the judgment of the IRB, the participant is capable of providing assent.

3.1.1 "Assent" means a participant's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

3.1.2 In determining whether participants are capable of assenting, the investigator and the IRB shall take into account the age, maturity, and psychological state of the participant involved. This judgment may be made for all participants to be involved in research under a particular protocol, or for each participant, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the participants is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the participant and is available only in the context of the research, the assent of the participant is not a necessary condition for proceeding with the research. Even where the IRB determines that the participants are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived as stated in section IC 702.3.1.

3.1.3. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

3.1.4 If at any time after a minor participant is enrolled in a study through parental permission and assent, and he/she/they legally comes of age, the investigator shall obtain the legally effective informed consent of the participant for continued participation in the research.

3.2 Parental Permission and Assent for Research involving Children

3.2.1 When children are involved in research, the regulations require the **assent** of the child and the **permission** of the parent(s), in place of the consent of the participants.

Given that children have not reached their full intellectual and emotional capacities and are legally unable to give valid consent, involving children in research requires the permission of one or both parents or legally authorized representatives. The IRB will determine whether the permission of both parents is necessary, and the conditions under which one parent may be considered "not reasonably available". In addition, the IRB will determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent.

3.2.2 For research that is FDA regulated, children may be participants of research only if informed consent is obtained from the parents or legal guardian. For other research, parental permission may be waived in accordance with 45 CFR 46.116(c)(2)(d).

The regulations provide that an IRB may find that the permission of one parent is sufficient for research to be conducted if the research is no more than minimal risk or if the research involves greater than minimal risk but presents the prospect of direct benefit to individual participants. Where research is covered by §46.406 - 46.407 of the HHS regulations or §50.53 - §50.54 of the FDA regulations, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

3.2.3 The IRB will determine for each protocol - depending on such factors as the nature of the research and the age, status, and condition of the proposed participants - whether all or some of the children are capable of assenting to participation. Where appropriate, the IRB may choose to review on a case-by-case basis whether assent should be sought from given individual participants.

When the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary. Additionally, in such circumstances a child's dissent, which should normally be respected, may be overruled by the child's parents, at the IRB's discretion.

When the IRB determines that the assent of the child is required, it will also determine that the provisions for obtaining and documenting assent are adequate.

3.2.4 The IRB will comply all federal regulations and also with state and local law.

4. REFERENCES

[45 CFR 46.408 Subpart D](#); [21 CFR 50.55 Subpart D](#)

IC 705 SURROGATE CONSENT

1. PURPOSE

The purpose of this Policy is to provide guidelines for the IRB and investigators in proposing, conducting and reviewing research in participants with decisional impairments.

Informed Consent

Federal regulations require that the researcher obtain the legally effective informed consent of the participant or the participant's legally authorized representative prior to medical research. Federal law defers to state law to determine what surrogate is legally authorized to substitute consent.

New Jersey Law	Pennsylvania Law
<p>New Jersey law requires the informed consent of the participant or the participant's authorized representative with reasonable knowledge of the participant before the individual may participate in medical research.</p> <p>New Jersey law requires a determination by an attending physician with no connection to the proposed research that: 1) a participant is unable to consent, 2) the extent of his/her/their incapacity and 3) the likelihood that he/she/they will regain decision-making capacity.</p> <p>New Jersey law prohibits the receipt of compensation for participation on the part of the individual providing surrogate consent. Likewise, participation in the research may not override an advance directive for health care.</p> <p>Inability to consent according to NJ state law is defined as: "inability to voluntarily reason, understand, and appreciate the nature and consequences of proposed health research interventions, including the participant's diagnosis and prognosis, the burdens, benefits, and risks of, and alternatives to, any such research, and to reach an informed decision."</p>	<p>Pennsylvania law requires the informed consent of the participant or the participant's authorized representative before the administration of an experimental medication, the use of an experimental device, or the use of an approved medication or device in an experimental manner.</p> <p>Pennsylvania law also authorizes surrogate consent to the performance of experimental biomedical or behavioral medical procedure or participation in any biomedical or behavioral experiment by the participant's court-appointed guardian pursuant to a court order issued after fact finding. Finally, Pennsylvania statutory law further authorizes a person named in the participant's power of attorney to consent to medical, therapeutic, and surgical procedures.</p> <p>While Pennsylvania statutory law does not explicitly authorize surrogate consent in the absence of a power of attorney or court-appointed guardian, case law strongly supports surrogate consent by close family members when patients lack capacity to make medical decisions. When the participant is unable to give informed consent, the participant's close family member or significant partner is in the best position to determine the wishes of the participant regarding participation in therapeutic research.</p>

If the research poses no more than minimal risk, and is not FDA regulated, the investigator and IRB may consider waiver of the requirement for informed consent as described in Policy 702.

2. POLICY STATEMENT

It is the policy of the University of Pennsylvania Institutional Review Boards to protect the research participant's right to autonomy. It is also the IRB's policy to protect those with diminished autonomy or reduced capacity to consent to research or to provide authorization for the use and/or disclosure of their protected health information.

However, the IRB recognizes that surrogate consent is necessary in order to offer experimental treatments to participants incapable of making autonomous choices where the research poses more than minimal risk, but where the risks to the participant are reasonable in relationship to any anticipated benefits to participants, and to the importance of the knowledge that may reasonably be expected to result from the research. Accordingly, the following procedure will be followed when the researcher determines that a patient is unable to give informed consent for participation in research and/or is unable to give a HIPAA Authorization.

3. SPECIFIC POLICIES

3.1 Submission and Review of Protocols Involving Participants Unable to Provide Informed Consent for biomedical research.

3.1.1 The investigator shall be responsible for making the determination as to whether the research protocol shall or shall not enroll participants incapable of giving informed consent.

3.1.2 If it is anticipated that the research will involve individuals with diminished capacity to consent, the protocol shall describe the process by which the investigator will determine and document the individual's ability to provide consent. The protocol shall also describe the process by which the investigator shall obtain assent/surrogate consent.

3.1.3 The IRB shall review such protocols and determine and document whether:

- the risks to the participants are reasonable in relationship to any anticipated benefits to participants and to the importance of the knowledge that may reasonably be expected to result; and,
- the description of the informed consent process to be used is appropriate to the risk of the protocol as assigned by the IRB; and,
- the appropriateness of the assent/surrogate consent content and process; and,
- the appropriateness and effectiveness of the HIPAA Authorization whether it is included as part of the informed consent or assent or provided as a stand-alone document; and,
- all other aspects of the proposed research as provided in Policies RR 402-404 are appropriate.

3.1.4 If the IRB determines that the risk to the participant is greater than minimal risk, it may require additional safeguards to ensure that the rights of such participants are protected. Such additional protections may include, but are not limited to:

- Witnessing assent/informed surrogate consent by a third party.
- Independent assessment of participant's ability to assent, and/or surrogates' ability to consent by an independent participant advocate or participant's primary care physician consistent with legal requirements.
- Independent documentation of the informed consent process.
- The appropriateness of the individual serving as the personal representative/ surrogate.

- Other safeguards as appropriate.

3.1.5 The IRB shall not approve any research involving the use of surrogate consent if they determine that the risk to the participant is high in relationship to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result.

3.2 Determination of Participants Ability to Provide Informed Consent in a Research Study

3.2.1 The investigator shall be responsible for determining whether an individual participant can provide informed consent, except in cases where NJ state law applies (see Section 1 of IC 705).

3.2.2 The investigator will document in the research record, as thoroughly as possible, the reason for the participant's inability to provide informed consent.

3.2.3 The investigator shall apply and document any additional safeguards as directed by the IRB.

3.3 Individuals Able to Provide Effective Surrogate Consent and/or Surrogate

3.3.1 State Law

Definitions: *Guardian* means an individual who is authorized under applicable State or local law to consent on behalf of another.

New Jersey Law	Pennsylvania Law
<p>For research conducted in the state of New Jersey, the below individuals (in the following descending order of priority) may be considered legally authorized representatives of the participant and capable of providing surrogate consent:</p> <ol style="list-style-type: none"> (1) the guardian of the participant who has the authority to make health care decisions for the participant; (2) the health care representative of the participant pursuant to an advance directive for health care; (3) the spouse or civil union partner, as applicable, of the participant; (4) the domestic partner of the participant; (5) an adult son or daughter of the participant; (6) a custodial parent of the participant; (7) an adult brother or sister of the participant; (8) an adult grandchild of the participant; (9) an available adult relative with the closest degree of kinship to the participant. 	<p>For research conducted in the Commonwealth of Pennsylvania, the following individuals may be considered legally authorized representatives of the participant and capable of providing surrogate consent:</p> <ul style="list-style-type: none"> ▪ A court-appointed guardian authorized to consent to the participant's participation in the protocol in a current court order issued within the participant's jurisdiction. ▪ A health care agent appointed by the participant in a power of attorney. ▪ A "health care representative" when the participant cannot speak for themselves and where there has been no guardian appointed by the court or health care power of attorney designated by the patient (PA Act 169). Any member of the following classes, in descending order of priority, who is reasonably available may act as the participant's health care representative. <ul style="list-style-type: none"> ○ The spouse (unless an action for divorce is pending) and adult child or children of another relationship ○ Adult children (18 years of age or older) ○ A parent

<p>New Jersey law does not permit participation if there is disagreement between two or more available persons who may give surrogate informed consent and who are in the same order of priority, if any of those persons expresses dissent as to the participation of the person in the research.</p>	<ul style="list-style-type: none"> ○ An adult sibling ○ An adult grandchild ○ An adult who has knowledge of the patient’s preferences and values, including but not limited to religious and moral beliefs, to assess how the patient would make decisions. <p>If there is disagreement between two or more available persons who may give surrogate informed consent and who are in the same order of priority, Pennsylvania law permits participant participation if a majority agree.</p>
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3.3.2 For human participants research conducted in other states or internationally, requests for the use of surrogate consent will be considered by the IRB in accordance with local state or international law. The investigator or the IRB will contact the legal advisor to the IRB within the Office of General Counsel to assist in determining who under local law may serve as a legally authorized individual.

3.4 Responsibilities of the Authorized Individual in the Surrogate Consent Process

3.4.1 The surrogate should base his/her/their decision on the participant's expressed wishes or, if unknown, what the participant would have desired in light of his/her/their prognosis, values, and beliefs. In the event of a disagreement among potential patient surrogates, an attempt to reach consensus shall be made through the intervention of a participant advocate appointed by the IRB if available. If consensus is not possible, a court appointed guardian should be obtained before the participant is enrolled in the study. When a surrogate provides consent, for a participant’s participation in a research project it is preferable for that surrogate to remain the responsible party for all subsequent research decisions including but not limited to withdrawal of consent.

3.5 Requirement for Re-Consent

3.5.1 If at any time after the participant is enrolled in a study through surrogate consent, he/she/they regains the capacity to provide informed consent, the investigator shall obtain the legally effective informed consent of the participant for continued participation in the research.

3.5.2 Decision-making capacity of participants may fluctuate. The consent process should be ongoing and involve the legally effective representative if at any time the investigator believes that the participant is unable to provide informed consent for continuing in a research project in which the participant initially gave informed consent.

4. REFERENCES

[Fiori, 543 Pa. 592, 673 A.2d 905 \(1996\); PA Act 169](#)

RI 800 RESPONSIBILITIES OF INVESTIGATORS

RI 800	RESPONSIBILITIES OF INVESTIGATORS
801	IRB-REQUIRED INVESTIGATOR ACTIONS
802	PRINCIPAL INVESTIGATORS

1. PURPOSE

This policy describes what the IRB requires of investigators in the conduct of research.

2. POLICY STATEMENT

The regulations require that organizations have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and appropriate federal officials of unanticipated problems involving risks to participants or others, defined as an untoward event that is serious, unexpected and related to the research. Events meeting the definition must be reported under this policy to the appropriate regulatory oversight agency. For research subject to the FDA regulations, reportable events include the events meeting reporting criteria to the IRB, per the regulations.

It is the Investigator's responsibility to keep the IRB informed of unexpected, protocol related, reportable events or unanticipated problems that pose risk to participants or others. An investigator is responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events. Investigators are also responsible for informing government funding agencies and other sponsors of any unanticipated serious events, as appropriate.

3. SPECIFIC POLICIES

3.1 IRB Review of Research

All human participants' research that is conducted by or under the direction of any employee, faculty, staff, student or agent of the University of Pennsylvania in connection with his/her/their institutional responsibilities must be reviewed by the IRB.

If the research is a Department of Health and Human Services (DHHS)-approved protocol, the investigator must provide the IRB with (as applicable) a copy of the DHHS-approved sample informed consent document and the DHHS-approved protocol.

3.2 Informed Consent

The investigator must obtain informed consent from participants prior to their enrollment into the research unless the IRB has waived this requirement. The investigator must use the informed consent document approved by the IRB. Approval dates are indicated on the header or footer of the consent document. Consent documents are valid only during the dates indicated on the form; and the investigator may use the forms only during the period for which they are valid. Investigators must follow University guidelines for obtaining consent.

3.3 Reporting of Unanticipated Problems Increasing Risks to Participants or Other Reportable Events

The IRB must be informed of unanticipated problems involving risks to participants or others and other reportable events as defined by SOP RR 404.

3.4 Changes in Approved Research

Changes in approved research, during the period for which approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to human participants. Investigators or sponsors must submit requests for changes to the IRB in writing. Upon receipt of the protocol change, the

Director of Human Research Protections or designee will determine if the revision meets the criteria for expedited review. Minor changes involving no more than minimal risk to the participant will be reviewed by the expedited review process.

3.5 Periodic and Final Reports

The length of time approval is given to a research protocol will be not less than once per year and is dependent on the risk involved with the research. For protocols requiring continuing review by the convened Committee (IRB Board), the expiration date will be set to align with the following year's Convened Committee date. The expiration date will ensure continuing review of the research at least once per year. The IRB will inform investigators of the expiration date in a letter following the meeting. Investigators are responsible for requesting renewal in anticipation of the expiration of the approval period. Investigators or their designees and /or sponsors are required to provide a periodic report regarding their investigation prior to the end of the approval period, or upon completion of the study. In addition, if so determined by the Board, the investigator is required to submit Interim Reports. For renewal of approval, an IRB notification will be provided as a courtesy to study teams within 90 days from study expiration date for convened review studies and 45 days for expedited review studies. Study teams are responsible for tracking their study expiration dates. The sponsor and/or the investigator or his/her/their designee may submit final reports of study completion.

3.6 Student Conducted Research

Directed or independent Research Projects (e.g., honors or graduate theses), which employ systematic data collection with the intent to contribute to generalizable knowledge require IRB review and approval.

For example, activities that must be reviewed and approved by the IRB include: (i) All master's theses and doctoral dissertations that involve human participants; and (ii) All projects that involve human participants and for which findings may be published or otherwise disseminated.

Classroom activities, the goal of which is to provide training in research methodology, do not require IRB review and approval. Examples are provided in the IRB Guidance: Is IRB Review Required?

All students/fellows applying for IRB review must obtain approval from their faculty advisor prior to submitting to the IRB.

3.7 Financial Conflicts of Interest

The protection of human participants requires objectivity in communicating risks, selecting participants, promoting informed consent, and gathering, analyzing and reporting data.

All investigators must report on their application to the IRB whether they or any other person responsible for the design, conduct, or reporting of the research has any financial interest requiring reporting per University policy. IRB approval will be contingent upon review of the reported interest by the Office of the Vice Provost for Research, acceptance of the management plan by the investigator, as applicable and incorporation of any requirements for disclosure to participants if required by the IRB.

4. REFERENCES

None

1. PURPOSE

This policy describes those individuals who may serve as principal investigators on research protocols involving human participants.

2. POLICY STATEMENT

All research involving the use of human participants conducted at the University of Pennsylvania must be conducted by individuals appropriately trained and knowledgeable concerning the protection of human participants.

3. SPECIFIC POLICIES

3.1 Faculty

All human participants research that is conducted by or under the direction of any employee, faculty, staff, student or agent of the University of Pennsylvania in connection with his/her/their institutional responsibilities must be under the direct supervision of a member of the Standing Faculty, Clinician-Educator or Associate Faculty of the University. Generally, faculty members are considered to be sufficiently knowledgeable to supervise and/or conduct research as determined by their appointment. However, the IRB may at its discretion determine that a faculty member lacks sufficient expertise to carry out any particular research project based on the risks and benefits to the research participants.

When all research activities take place at the Philadelphia Veterans Administration Medical Center (VAMC) and the research is conducted by an investigator whose academic appointment is at the University of Pennsylvania but whose primary hospital appointment is at the VAMC, the research proposal does not have to be submitted to the Penn IRB.

When all research activities take place at the Children's Hospital of Philadelphia (CHOP) and the research is conducted by an investigator whose academic appointment is at the University of Pennsylvania but whose primary hospital appointment is at the CHOP, the research proposal does not have to be submitted to the Penn IRB. Other exceptions are elaborated in the CHOP-Penn IRB Reciprocity Agreement and in the Guide to Daily Operations.

3.2 Non-Faculty, Academic Support Staff, Postdoctoral Fellows, Graduate Students, and Undergraduate Students

Research conducted by University students or employees must be under the direction of a faculty member as defined in 3.1.

3.3 Other Individuals

Individuals not meeting the above criteria as principal investigators may, by demonstrating sufficient cause and necessary expertise, petition the Director of Human Research Protections for permission to submit an application for approval to serve as a principal investigator of a human research protocol. If the person is permitted to function in this role, their listing as Principal Investigator on the protocol will document this decision.

3.4 Training of Investigators

The IRB shall establish standards of training required for all individuals engaged in human research.

4. REFERENCES

None

QA 900 QUALITY ASSURANCE

QA 900	QUALITY ASSURANCE
901	QA/QC PROGRAM
902	AUDITS AND INSPECTIONS BY REGULATORY AGENCIES
903	IRB NONCOMPLIANCE

1. PURPOSE

This section states the policy concerning quality assurance measures for the IRB.

2. POLICY STATEMENT

Quality assurance and improvement of the daily operations of the IRB ensure that they effectively support the IRB's mandate. Therefore, the QA/QI program consists of three components:

- Periodic review of IRB records; and,
- Regular review and assessment of procedures.
- Training and continuing education of IRB staff.

3. SPECIFIC POLICIES

The Director of Human Research Protections has the authority to implement a QA/QI program and act on identified deficiencies by implementing corrective action plans. The Director of Human Research Protections and Associate Directors, in conjunction with Senior IRB staff, are responsible for oversight of the IRB's quality improvement activities. Specific IRB personnel may have designated QA/QI responsibilities.

4. REFERENCES

None

1. PURPOSE

This section states the policy concerning preparation for regulatory audits of the IRB and appropriate behavior toward regulators

2. POLICY STATEMENT

Quality assurance and control of the daily operations of the IRB ensure that they effectively support the IRB's mandate. Therefore, the IRB must have in place mechanisms and policies for dealing with external auditing and accrediting agencies.

3. SPECIFIC POLICIES

3.1 Preparing for an Audit

Certain regulatory and/or accrediting agencies have the authority to audit and inspect the operations of IRBs. These include: FDA, OHRP, sponsors or funding entities of research, or others who may also be authorized by regulations or agreement with the University to audit specific documents and procedures.

For external audits involving OHRP or FDA, the following must be notified immediately:

- Vice Provost for Research
- Office of Clinical Research (if the audit is for a Perelman School of Medicine Investigator)
- Hospital Administration if applicable

The Director of Human Research Protections and IRB staff designated to participate in the audit are required to follow the steps outlined by this institution for preparing the site for an audit.

3.2 Participating in an Audit

Researchers and IRB staff members are expected to know and follow the procedures outlined by this institution for the conduct of an internal or external audit of specific studies or study sites.

Prior to being granted access to IRB documentation, inspectors or auditors must exhibit proof of their authority or authorization to conduct an audit to access IRB documents, and no entity other than those listed on the consent forms may have access to any document that includes participant identifiers. The Director of Human Research Protections is responsible for ensuring the redaction of such information from files prior to an audit as may be required.

Auditors will be provided with adequate working area to conduct an audit and IRB staff and members must make every reasonable effort to be available and to accommodate and expedite the requests of such auditors.

Documents may be copied and taken off-site only by individuals authorized in writing by the Office of General Counsel or the Vice Provost for Research to do so.

3.3 Follow-up after an Audit

Reports of the audit, either verbal or written, should be addressed by the appropriate IRB representatives, or other appropriate individuals or offices, as soon as possible after site-specific audits. Reports of the audit directed to the operation of the IRB should be presented to the Vice Provost for Research and Director of Human Research Protections and addressed as soon as possible.

4. REFERENCES

-None

1. PURPOSE

This section states the policy concerning identification of IRB noncompliance and resolution through root cause identification, as well as corrective and preventative actions.

2. POLICY STATEMENT

Penn pledges to promote and uphold the highest ethical standards in the conduct of human research. Employees and agents of the organization are required to comply with federal regulations, state laws, and institutional policies.

All employees and agents of the University of Pennsylvania share the responsibility for reporting incidents of noncompliance.

The IRB, in consultation with the Research Compliance Officer (RCO) or Vice Provost for Research (VPR), as needed, may use its discretion in determining whether an incident meets the definition of noncompliance, serious noncompliance, or continuing noncompliance. Likewise, the IRB, in consultation with the Research Compliance Officer and/or VPR, as needed, may use its discretion in determining whether noncompliance is reportable to internal and/or external entities.

3. SPECIFIC POLICIES

3.1 Definitions

The definitions as outlined in RR408 Section 3.1 will be applied.

3.2 Reporting Concerns

3.2.1 Reports of noncompliance may come from many sources including, but not limited to, the IRB or IRB office staff member (self-report); university or school-based compliance and audit offices; the P-COMPLY Hotline, a sponsor; or a member of a research team.

3.2.2 Persons raising such concerns are encouraged to express them in writing. However, verbal concerns will be received and appropriately documented.

3.3 Evaluation

3.3.1 An unconflicted IRB Director/Associate Director(s) or staff member will be responsible for the initial review and evaluation of the report describing the potential noncompliance.

- The Director or staff member assessing the initial report may elect to gather additional information and may also consult an IRB Chair, the Research Compliance Officer, the Office of General Counsel, University or School Offices of Audit and Compliance, Vice Provost for Research, or other outside consultants as appropriate.

A written record of findings and supporting information will be maintained by the staff member assessing the potential noncompliance. A report will be drafted to include a description of the incident, and if applicable, an assessment of the root cause, any corrective actions taken in real-time, any preventative actions to prevent the incident from happening in

the future, as well as an assessment regarding whether serious and continuing noncompliance has occurred. The process for this assessment outlined in RR 408 will be followed.

3.3.3 Noncompliance that does not have the potential to qualify as serious or continuing.

If it is determined that there was noncompliance and (1) the noncompliance was clearly not serious and not continuing, (2) the noncompliance was identified, and (3) the appropriate corrective actions were taken to address the issue, then the report will be forwarded to the appropriate unconflicted IRB Chair, an unconflicted IRB Director, Human Research Protections, or an appropriate designee for review and acknowledgement. If the IRB Chair, Director and/or Human Research Protections staff member or designee agrees with the assessment, a copy of the final report will be forwarded to the RCO with no further action is required.

If it is determined that additional corrective actions are required, the actions will be communicated to the appropriate party along with an anticipated timeline for the corrective action to occur. Unless otherwise specified, it will be the responsibility of the party who developed the report to confirm that the corrective action has been implemented.

3.3.4 Noncompliance that has the potential to qualify as serious and/or continuing.

If there is an incident of noncompliance that could qualify as serious or continuing noncompliance based on the initial review and evaluation, the incident will be reported to the IRB Executive Chair (if unconflicted), unconflicted IRB Director, or alternate designee for initial acknowledgement to confirm timeliness of receipt and to confirm that further review is appropriate. Additional information may be requested in the acknowledgement and this information will be provided to the person to whom the incident was initially reported. When the report is complete, the report will be scheduled for convened review by an unconflicted IRB or an alternative review, if appropriate.

If the matter is assigned to a convened IRB, which may be the Executive IRB 9 committee, the designated IRB will receive a detailed explanation of the reported issues and any proposed/implemented corrective actions as well as the IRB SOPs and applicable regulations. The IRB Chair or assigned IRB member will present the report to the convened IRB. The convened IRB will review the report and determine whether the report qualifies as serious or continuing noncompliance (or both) and whether the corrective action plan proposed is sufficient to address the incidence(s) reported or if further action may be necessary (outlined below). If the convened IRB is unable to make the determination related to whether the incidence(s) reported qualify as serious or continuing noncompliance (or both), the convened IRB will outline specific requests for additional information to provide the additional information necessary to make the final determination. The responses, once received, will be scheduled for the next meeting of the appropriate convened IRB to make the final determination. If requested by an IRB Director, RCO or VPR, an alternative review process outside of the IRB (such as an external IRB) may be designated.

The final outcome of this review will be reported to the RCO and the VPR.

3.4 Potential Response to a Serious or Continuing Noncompliance Determination

3.4.1. Actions in response to a determination of serious or continuing noncompliance may include, but are not limited to:

- No action
- Audit request
- Notification to the research community
- Request for additional information pending a final decision
- Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)

3.4.2 The outcome of the incident review will be documented. The IRB will notify the Director, Human Research Protections and Research Compliance Officer in writing of the results of the outcome and of any action required by the IRB. The letter may include a request for the Director, Human Research Protections to respond in writing. Any response required may be reviewed by an IRB Chair or may be referred to the convened IRB or other appropriate party.

3.4.3 The correspondence will include a description of the nature of the event, the findings, actions taken, and plans for continued investigation or action. A copy of this correspondence will be forwarded to the RCO and/or VPR.

3.5 Notifications

If it is determined that there was noncompliance and it is determined to be serious or continuing, CO 602 will be followed. Additionally, the Penn IRB must report to AAHRPP within 48 hours after the organization becomes aware of:

- Any negative actions taken by a government oversight office, including, but not limited to, OHRP determination letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA restrictions placed on the IRB.
- Any litigation, arbitration, or settlements initiated related to human research protections.
- Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding the organization's HRPP.

4. Final Disposition

4.1 The outcome of all reports will be communicated to the RCO for an external review and acknowledgement. Should the RCO disagree with the outcome of any report, the RCO, with approval from the VPR, may stipulate additional steps be taken to address the issues raised. As appropriate, this action should first be discussed with the IRB Director and approached as a coordinated effort.

4.2 The VPR may require that additional stipulations be met in order to address any issues raised in the report.

5. REFERENCES

None

ADDENDUM

ADDITIONAL REGULATIONS FOR SPECIFIC FUNDING/GOVERNMENT OVERSIGHT OFFICES

Version 3

July 2024

Standard Operating Policies, Addendum, Version 3 were reviewed and approved by the Director, Human Research Protections



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DD 100 DEPARTMENT OF DEFENSE REGULATED RESEARCH

Overview

The IRB follows DoD regulation when reviewing human research supported and regulated by the DoD. This addendum to the SOP describes the DoD regulations for reviewing studies that involve greater than minimal risk or has a special consideration(s) e.g., classified research, research with vulnerable populations, etc. The information below provides a brief overview of how the IRB would review such studies. In conducting these reviews, the IRB will refer to and follow the applicable Department of Defense regulations. The Penn IRB does not review classified research. When conducting classified research, the chosen IRB of record must comply with DoD regulations as described below.

Activities overseen by the Human Research Protection Program

Non-exempt classified research must be conducted following the requirements of 3216.02.13. (See references for DoD directive 3216.02.13.).

Surveys performed on Department of Defense personnel must be submitted, reviewed, and approved by the Department of Defense after the research protocol is reviewed and approved by the IRB

The definition of minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests” shall not be interpreted to include the inherent risks certain categories of human participants face in their everyday life. For example, the risks imposed in research involving human participants 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.)

Research involving an experimental participant is defined as an activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving a human being as an experimental participant is a subset of research involving human participants. This definition relates only to the application of section 980 of Reference (g); it does not affect the application of part 219 of Reference (c). This definition does not include activities that are not considered research involving human participants, activities that meet the exemption criteria at section 219.101(b) of Reference (c), and research involving the collection or study of existing data, documents, records, or specimens from living individuals.

In general, no Department of Defense component may conduct or use appropriated funds to support research involving a human being as an experimental participant without the prior informed consent of the participant.

Classified Research

For all Department of Defense conducted or supported non-exempt human participant research involving classified information (as defined in Executive Order 13526), additional requirements must be applied. The review of research involving classified information is rare and requires Secretary of Defense approval. Additional requirements are described in the Department of Defense Instruction 3216.02 13.

Chemical or Biological Agents

Human participant research involving the testing of chemical or biological agents is prohibited, pursuant to Section 1520a of Title 50, United States Code (U.S.C.). Some exceptions for research for prophylactic, protective, or other peaceful purposes apply. Before any excepted testing of chemical or biological agents involving human participants’ research can begin, the DoD component seeking to conduct such research must obtain explicit written approval from the DoD Office for Human Research Protections (DOHRP).

- The organization permits research involving chemical or biological agents under an exception. The Principal Investigator and research team is responsible for obtaining approval from DoD and must submit documentation of this with their IRB application.

Human Participant Research Training

University of Pennsylvania investigators and study staff who conduct human participant research must complete training before the IRB will approve a project(s). Please visit Investigator & Research Staff Training for the current University of Pennsylvania training requirements and options. If research involving a DoD component requires more frequent or other training requirements in addition to those that the University of Pennsylvania requires, the investigator will be responsible for ensuring that the training is completed for those involved in the conduct of the research. Researchers should contact the human research protection officer of the DoD component for their education requirements and obtain documentation confirming the requirements.

Additional Protections for Military Research Personnel

When research involves U.S. military personnel as participants in research, the following guidelines apply:

Recruitment and Enrollment

- Officers are not permitted to influence the decision of their subordinates.
- Officers and senior non-commissioned officers may not be present at the time of recruitment.
- Officers and senior non-commissioned officers have a separate opportunity to participate.
- When recruitment involves a percentage of a unit, an independent ombudsman is present.

DOD Personnel Recruitment

For greater than minimal risk research involving DoD-personnel, when recruitment and consent occur in a group setting, the IRB must appoint an ombudsperson. The ombudsperson:

- Must not have a conflict of interest with the research or be a part of the research team.
- Must be present during the HSR recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary, and that the information provided about the research is consistent with the IRB-approved script and materials, including digitally provided materials.
- Should be available to address DoD-affiliated personnel's concerns about participation.

Compensation

- Participants may be compensated for research participation as long as the participant is involved in the research when not on duty. Enrolled individuals may not receive payment of compensation for research participation during duty hours.
- Federal employees while on duty and non-Federally employed individuals may be compensated for blood draws for research up to \$50 for each blood draw.
- Non-Federally employed individuals may be compensated for research participation other than blood draws in a reasonable amount as approved by the IRB.

Surveys

Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD Information Management Control Officer (IMCO) after the research protocol is reviewed and administratively finalized by the IRB. Documentation of this approval should be provided in the IRB application before enrollment may commence and final approval is issued. When a survey crosses DoD components, additional review is required, and the DOD checklist is required to be completed. The PI is responsible for obtaining all required approvals.

Informed Consent Requirements

If the research involves DoD-affiliated personnel as participants, in addition to the basic and required consent disclosures, the IRB or component HRPO must confirm that the consent documents must include:

- If the research involves risks to their fitness for duty (e.g., health, availability to perform job, data breach), the informed consent document (ICD) must inform DoD-affiliated personnel about these risks and that they should seek command or component guidance before participating.
- If applicable, a statement of potential risks for the revocation of clearance, credentials, or other privileged access or duty.
- 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.

For greater than minimal risk research:

- Consent documents must include the disclosure that participants may, for the duration of the study, be eligible for health care services for research-related injuries at a military treatment facility, and this eligibility for health care services extends beyond participants' participation in the study to such time after the study has ended.
- Written materials must document how organizations will care for participants with research-related injuries, including injuries that are the direct result of activities performed by DoD-affiliated personnel in studies that are collaborative with a non-DoD institution.

Waiver of Consent

Research Participant to Department of Defense requirements is prohibited from using an exception from consent in emergency medicine unless a waiver is obtained from the Secretary of Defense.

The Assistant Secretary of Defense 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 might directly benefit the individual experimental participant.
- The research is conducted in compliance with all other applicable laws and regulations.
 - For classified research, waivers of consent are prohibited.
 - If the research participant does not meet the definition of "experimental participant," the IRB is allowed to waive the consent process.

Informed Consent Process

The following are additional requirements regarding the informed consent process for DoD conducted or supported studies.

Disclosure of Research-Related Injury - Any requirements for disclosure of research-related injury from a DoD component must be included in the informed consent process. See SOP 701 (2.3).

Consent from a Legally Authorized Representative - If consent is to be obtained from the legally authorized representative of an experimental participant, the research must be intended to provide direct benefit to the individual participant. The determination that the research is beneficial to the individual experimental participant must first be made by the IRB.

Genomic Data

Research involving large-scale genomic data from DoD-affiliated personnel is subject to additional requirements:

- The disclosure of DoD-affiliated personnel's genomic data may pose a risk to national security; accordingly, written materials must describe administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of de-identified data or specimens.

- All research involving large-scale genomic data collected from DoD-affiliated personnel must have a certificate of confidentiality from DHHS (Title 42, U.S.C., and Public Law 114-255).
- Research involving large-scale genomic data collected from DoD-affiliated personnel is subject to DoD component security review to ensure the adequacy of the proposed administrative, technical, and physical safeguards, including the secondary use or sharing of de-identified data or specimens.

Vulnerable Populations (Subparts B, C and D)/Prisoners of War

Research involving pregnant individuals/fetuses, incarcerated persons, and children are subject to the DHHS Subparts B, C, and D, respectively.

Research involving pregnant individuals and/or fetuses

- For purposes of applying Subpart B, the phrase “biomedical knowledge” shall be replaced with “generalizable knowledge.”
- The applicability of Subpart B is limited to research involving pregnant individuals as participants in research that is more than minimal risk and included interventions or invasive procedures to the individual or the fetus or involving fetuses or neonates as participants.

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

- Research or experimentation may not be conducted, in the United States or in any other country, on a nonviable living human fetus ex utero or a living human fetus ex utero for whom viability has not been ascertained unless the research or experimentation:
 - May enhance the well-being or meet the health needs of the fetus or enhance the probability of its survival to viability; or
 - Will pose no added risk of suffering, injury, or death to the fetus and the purpose of the research or experimentation is the development of important biomedical knowledge which cannot be obtained by other means.
- The risk standard must be the same for fetuses which are intended to be aborted and fetuses which are intended to be carried to term.
- For human participant research that would not otherwise be approved but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, written approval from the DOHHP must be obtained through the COHPR prior to research starting.

Service members and DoD-affiliated personnel

Service members and DoD-affiliated personnel are considered to be vulnerable to coercion and undue influence by the DoD due to the nature of the command structure of the organization. Therefore, additional protections for DoD-affiliated personnel are required, as follows (DoDI 3216.02 section 3.9 (f)):

- If the research involves DoD-affiliated personnel as participants and if the research includes any risks to their fitness for duty (e.g., health, availability to perform job, data breach), the informed consent document must inform DoD-affiliated personnel about these risks and that they should seek command or component guidance before participating.
- If the research involves DoD-affiliated personnel, the researcher must receive command or component approval to execute the research.
- Military and civilian supervisors, officers, and others in the chain of command are prohibited from influencing their subordinates to participate in research.
- Military and civilian supervisors, officers, and others in the chain of command must not be present at any participant recruitment sessions or during the consent process for DoD-affiliated personnel. Excluded supervisors or those in the chain of command may participate in separate recruitment sessions, if applicable.
- Service members and all Reserve component and National Guard members in a federal duty status are considered to be adults. If a Service member, Reserve component or National Guard member in federal duty status, student at a Service

Academy, or trainee is under 18 years of age, the IRB must carefully consider the HSR recruitment process and the necessity of including such member as a human participant.

Research with Incarcerated Persons

- Research involving incarcerated persons cannot be reviewed by the expedited procedure.
- When the IRB reviews research involving incarcerated persons, at least one incarcerated person representative must be present for quorum.

In addition to allowable categories of research on incarcerated persons 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 participant.

If a participant becomes an incarcerated person, and if the researcher asserts to the IRB that it is in the best interest of the incarcerated person-participant to continue to participate in the research while an incarcerated person, the IRB chair may determine that the incarcerated person-participant may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the organizational official and DoD Component office review the IRB's approval to change the research protocol. Otherwise, the IRB chair shall require that all research interactions and interventions with the incarcerated person-participant (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 participant has become an incarcerated person, shall promptly re-review the research protocol to ensure that the rights and wellbeing of the human participant, now an incarcerated person, are not in jeopardy. The IRB should consult with a participant matter expert having the expertise of an incarcerated person representative if the IRB reviewing the research protocol does not have an incarcerated person representative. If the incarcerated person-participant can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the incarcerated person-participant's confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human participants from continuing as approved, the convened IRB may approve a change in the study to allow this incarcerated person-participant to continue to participate in the research. This approval is limited to the individual incarcerated person-participant and does not allow recruitment of incarcerated persons as participants.

- Research involving a detainee as a human participant 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 children cannot be exempt.
 - If consent is to be obtained from the experimental participants' legal representative, the research must intend to benefit the individual participant.
 - The determination that the research is intended to be beneficial to the individual experimental participant must be made by an IRB.
- Research involving a prisoner of war is prohibited
 - A prisoner of war is a person captured in war; *especially*: a member of the armed forces of a nation who is taken by the enemy during combat

Emergency Medicine Research

When conducting emergency medicine research, the Principal Investigator is responsible for obtaining approval from the DOHRP on behalf of the Secretary of Defense for a waiver of the advance informed consent provision of 10 USC 980. The Principal Investigator is responsible for following the process required by DOHRP.

Multi-Centered Research

If an investigator is the lead investigator/site for a multi-centered study, they have additional responsibilities for overseeing the activities at the University of Pennsylvania as well as the other sites participating in the study. To meet DoD requirements (SECNAVINST 3900.39D, section 6f), the investigator must execute an agreement or statement of work with all collaborating sites that delineates each site's responsibilities. This document should include the following elements:

- A brief description of the research
- Specific roles and responsibilities of each site, including scientific and IRB review; recruitment of participants; and informed consent procedures
- Plan for ongoing data and safety monitoring, reporting requirements, documentation retention, and compliance for the entire research project

If the investigator is not the lead investigator for a multi-centered DoD study, the investigator should ensure to request a copy and sign the study's agreement/statement of work prior to initiating study procedures at the University of Pennsylvania.

Reliance Agreements

The IRB shall adhere to SOP GA 102 when executing reliance agreements between IRBs. These agreements will define the responsibilities of the DoD organization and non-DoD reviewing IRB, including all requirements in Standard I-9 for IRBs serving as reviewing IRBs, and the following additional requirements, including but not limited to:

- The process for serving as a reviewing IRB for DoD institutions collaborating with non-DoD institutions, including who is responsible and the process they go through to obtain DoD approval for a non-DoD institution to be designated to review for DoD research, including ensuring the following conditions are met (DoDI 3216.02 section 3.5):
 - Each institution engaged in non-exempt human participant research must have a current federal assurance of compliance.
 - The non-DoD institution's IRB is registered in accordance with Subpart E of 45 CFR 46.
 - The DoD institution reviews the protocol to ensure all applicable local and DoD requirements are addressed in the protocol.
 - The DoD institution, non-DoD institution, and the non-DoD institution's IRB have a written agreement defining the responsibilities and authorities of each institution in complying with all legal requirements. This agreement must specify that the non-DoD IRB will apply the DoD requirements specified in DoDI 3216.02, including but not limited to non-DoD institutional responsibilities defined under DoDI 3216.02 section 3.6(b).
 - If the research constitutes classified human participant research, the COHRP must approve the agreement to rely on the non-DoD institution's IRB.

International Research

If the DoD research is conducted in a foreign country, the investigators must submit verification of the local ethics review (i.e. approval to conduct research). The investigator must abide by the local laws, regulations and customs as applicable. For more guidance, please see the International Research section of the Guide to Daily Operations.

Serious and Continuing Noncompliance

Determinations of serious or continuing non-compliance of DoD-supported research must be promptly (no longer than within 30 days) reported to the DoD human research protection officer.

Records maintained that document compliance or non-compliance with DoD requirements shall 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.

Reporting Requirements

The following shall be promptly (no longer than within 30 days) reported to the Component Office of Human Research Protections (COHRP):

- When significant changes to the research protocol are approved by the IRB.
- The results of the IRB continuing review.
- Change of reviewing IRB.
- When the organization is notified by any Federal department, agency or national organization that any part of the HRPP is under investigation for cause involving a DoD-supported research protocol.
- Reports of audits of DoD-conducted or DoD-supported human participant research by another federal or state agency, official governing body of a Native American or Alaskan native tribe, other official entity, or foreign government.
 - The PI is responsible for reporting to the IRB and the Component Office of Human Research Protections (COHRP) in alignment with the applicable branch requirements
- Allegations of serious or continuing noncompliance related to research involving human participants that are substantiated by investigation, and subsequent actions taken based on the findings.
 - The IRB will report to the Component Office of Human Research Protections (COHRP) via email.
- Substantiated allegations related to classified HSR must be reported immediately.
 - If allegations are received by the study team, the PI is responsible for reporting to the IRB and the Component Office of Human Research Protections (COHRP) in alignment with the applicable branch requirements
 - If allegations are received by the IRB, the IRB will report to the Component Office of Human Research Protections (COHRP) via email.
- When the organization is notified by any federal body, state agency, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that any part of an HRPP is under investigation for cause involving a DoD-supported research protocol.
- Closure of a DoD-supported study.

Any unanticipated problems involving risks to participants or others for any DoD-supported research must be promptly (no longer than within 30 days) reported to the DoD human research protection officer.

Any suspension or termination of DoD-supported research must be promptly (no longer than within 30 days) reported to the DoD human research protection officer.

Reporting of serious noncompliance, continuing noncompliance, and unanticipated problems will be done in accordance with SOPs 408 and 409.

Data and Safety Monitoring

In alignment with RR 403, where appropriate, the IRB will consider provisions for monitoring data to ensure the safety of participants to be appropriate.

REFERENCES

<http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf>

DED 200 Department of Education

Overview

The IRB follows Department of Education regulation when reviewing human participant research supported and regulated by the Department of Education. The information below provides a brief overview of how the IRB would review such studies. In conducting these reviews, the IRB will refer to and follow the applicable Department of Education regulations.

IRB Membership Requirements

For research funded by the National Institute on Disability and Rehabilitation Research, when an IRB reviews research that purposefully requires inclusion of children with disabilities or individuals with mental disabilities as research participants, the IRB must include at least one person primarily concerned with the welfare of these research participants.

FERPA

- The IRB verifies that the research is in compliance with the Family Educational Rights and Privacy Act (FERPA) by securing this certification from the researcher and the participating schools.
- The IRB works with the organization (e.g., a FERPA committee) to grant exceptions to parental/student consent to release student records for research. .
 - An educational agency or institution may disclose personally identifiable information from an education record of a student without consent if the disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to:
 - Develop, validate, or administer predictive tests.
 - Administer student aid programs.
 - Improve instruction.
- A school district or postsecondary institution that uses this exception is required to enter into a written agreement with the organization or researcher conducting the research that specifies:
 - The determination of the exception.
 - The purpose, scope, and duration of the study.
 - The information to be disclosed.
 - That information from education records may only be used to meet the purposes of the study stated in the written agreement and must contain the current requirements in 34 CFR 99.31(a)(6) on re-disclosure and destruction of information.
 - That the study will be conducted in a manner that does not permit personal identification of parents and students by anyone other than representatives of the organization with legitimate interests.
 - That the organization is required to destroy or return all personally identifiable information when no longer needed for the purposes of the study.
 - The time period during which the organization must either destroy or return the information.

Records

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

- Student's name and other direct personal identifiers, such as the student's social security number or student number.
- Indirect identifiers, such as the name of the student's parent or other family members; the student's or family's address, and personal characteristics or other information that would make the student's identity easily traceable; date and place of birth and mother's maiden name.

- Biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting.
- Other information that, alone or in combination, is linked or linkable to a specific student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify the student with reasonable certainty.

Pupil Rights Amendment

- The IRB verifies that the research is in compliance with the Protection of Pupil Rights Amendment:
- No student shall be required, as part of any research project, to submit without prior consent to surveys, psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:
 - Political affiliations.
 - Mental and psychological problems potentially embarrassing to the student or his/her/their family.
 - Sex behavior and attitudes.
 - Illegal, anti-social, self-incriminating and demeaning behavior.
 - Critical appraisals of other individuals with whom the student has close family relationships.
 - Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers.
 - Religious practices, affiliations, or beliefs of the student or student's parent.
 - Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.
 - Prior consent means:
 - Prior consent of the student, if the student is an adult or emancipated minor; or
 - Prior written consent of the parent or guardian, if the student is an un-emancipated minor. Schools and contractors obtain prior written parental consent before minor students are required to participate in any ED-funded survey, analysis, or evaluation.
- The IRB must verify compliance with U.S. Department of Education regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:
 - The right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student.
 - Any applicable procedures for granting a request by a parent for reasonable access to such survey within a reasonable period of time after the request is received.
 - Arrangements to protect student privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items):
 - Political affiliations or beliefs of the student or the student's parent.
 - Mental or psychological problems of the student or the student's family.
 - Sex behavior or attitudes.
 - Illegal, anti-social, self-incriminating, or demeaning behavior.
 - Critical appraisals of other individuals with whom respondents have close family relationships.
 - Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers.
 - Religious practices, affiliations, or beliefs of the student or the student's parent.
 - Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program).

- The right of a parent of a student to inspect, upon the request of the parent, any instructional material used as part of the educational curriculum for the student.
- Any applicable procedures for granting a request by a parent for reasonable access to instructional material received.
- The administration of physical examinations or screenings that the school or agency may administer to a student.
- The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use.
- The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student.
- Any applicable procedures for granting a request by a parent for reasonable access to such instrument within a reasonable period of time after the request is received.

References:

<http://www2.ed.gov/policy/fund/guid/humansub/guidan1.html>

DE 300 DEPARTMENT OF ENERGY

Overview

The IRB follows Department of Energy regulation when reviewing human participant research supported and regulated by the Department of Energy. The information below provides a brief overview of how the IRB would review such studies. In conducting these reviews, the IRB will refer to and follow the applicable Department of Energy regulations.

DOE requirements apply to all research conducted with DOE funding, at DOE institutions (regardless of funding source), or by DOE or DOE contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research.

- When research involves contractors, DOE “Contractor Requirements Document” describing contractor responsibilities for protecting human research participants must be included in contracts.

No human participant research conducted with DOE funding at DOE institutions (regardless of funding source), or by DOE or contractor personnel (regardless of funding source or location conducted), whether done domestically or in an international environment, including classified and proprietary research, may be initiated without both a Federalwide Assurance (FWA) or comparable assurance (e.g., Department of Defense assurance) and approval by the cognizant IRB in accordance with 10 CFR Part 745.103.

Department of Energy IRB Review Checklist

The IRB reviews and approves the “Checklist for IRBs to Use in Verifying That HHS Research Protocols Are in Compliance with DOE Requirements” submitted by the researchers to verify compliance with the DOE requirements for the protection of personally Identifiable Information.

Research that uses social media data must be submitted to the IRB for human participant research review and determination.

Research that involves the study of humans in a systematically modified environment must be submitted to the IRB for HSR review and determination.

Confidentiality Requirements:

The following items must be addressed in all protocols:

1. Keeping PII confidential;
2. Releasing PII, where required, only under a procedure approved by the responsible IRB(s) and DOE;
3. Using PII only for purposes of this project;
4. Handling and marking documents containing PII as “containing PII or PHI;”
5. Establishing reasonable administrative, technical, and physical safeguards to prevent unauthorized use or disclosure of PII;
6. Making no further use or disclosure of the PII except when approved by the responsible IRB(s) and DOE, where applicable, and then only under the following circumstances: (a) in an emergency affecting the health or safety of any individual; (b) for use in another research project under these same conditions and with DOE written authorization; (c) for disclosure to a person authorized by the DOE program office for the purpose of an audit related to the project; (d) when required by law; or (e) with the consent of the participant/guardian;
7. Protecting PII data stored on removable media (CD, DVD, USB Flash Drives, etc.) using encryption products that are Federal Information Processing Standards (FIPS) 140-2 certified;
8. Using passwords to protect PII used in conjunction with FIPS 140-2 certified encryption that meet the current DOE password requirements cited in DOE Guide 205.3-1;

9. Sending removable media containing PII, as required, by express overnight service with signature and tracking capability, and shipping hard copy documents double wrapped;
10. Encrypting data files containing PII that are being sent by e-mail with FIPS 140-2 certified encryption products;
11. Sending passwords that are used to encrypt data files containing PII separately from the encrypted data file, i.e. separate e-mail, telephone call, and separate letter;
12. Using FIPS 140-2 certified encryption methods for websites established for the submission of information that includes PII;
13. Using two-factor authentication for logon access control for remote access to systems and databases that contain PII. (Two-factor authentication is contained in the National Institute of Standards and Technology (NIST) Special Publication 800-63 Version 1.0.2 found at: <http://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.800-63-2.pdf>).
14. Reporting the loss or suspected loss of PII immediately upon discovery to: 1) the DOE funding office Program Manager or, if funded by a DOE laboratory, the DOE laboratory Program Manager; and 2) the DOE Human Subjects Protection Program Manager, SC-23, and the NNSA Human Subjects Protection Program Manager, NA-SH. If the above individuals are unreachable, immediately notify the DOE-CIRC (1-866-941-2472, by FAX: at 702-932-0189, or by e-mail at: circ@jc3.doe.gov). For additional information, see: <http://energy.gov/cio/office-chief-information-officer/services/incident-management/jc3-incident-reporting>.
15. Classified projects that use PII must also comply with all requirements for conducting classified research.

DOE Personnel Recruitment:

DOE and DOE site contractors are considered vulnerable subjects when participating in research and additional care must be taken to ensure their participation is truly voluntary (e.g., by ensuring they do not report to members of the research team), and that data collected about them is kept confidential.

The IRB must consider if additional protections are required for research involving employees and contractors.

IRB Review Requirements:

The Penn IRB does not review classified research. When conducting classified research, the chosen IRB of record must comply with the Department of Energy regulations noted above. Classified and unclassified human participant research that is funded through the Strategic Intelligence Partnership Program (SIPP) must be reviewed and approved by the Central DOE IRB-Classified. In addition, the IRB of record must:

- Have a voting quorum of at least five members, which must include both a non-scientist and a non-affiliated member.
- The non-affiliated member must be a non-governmental member with the appropriate security clearances. This individual cannot be a current federal employee or contractor.
- Any IRB member can appeal a vote to approve research to the Institutional Official, Secretary of Energy, and Director of the Office of Science and Technology, in that order.

The Penn IRB does not review research involving Human Terrain Mapping (HTM). HTM is defined by DOE as research and data gathering activities primarily conducted for military or intelligence purposes to understand the “human terrain,”—the social, ethnographic, cultural, and political elements of the people among whom the U.S. Armed Forces are operating and/or in countries prone to political instability. Such activities are often referred to as human social culture behavior (HSCB) studies. Investigators who seek to engage in such research must seek special permission from Penn’s IO who will engage other appropriate organizational leaders in the decision-making process.).

Research involving human participants involving multiple DOE sites (e.g., members of the research team from more than one DOE site and/or data or human subjects from more than one DOE site) must be reviewed and approved by one of the Central DOE IRBs prior to initiation, unless review by another appropriate IRB of record is authorized by the DOE and/or NNSA HSP Program Manager.

If authorized by the DOE and/or NNSA HSP Program Manager, research may be reviewed by other appropriate IRB of record. In all cases, an IRB Authorization Agreement (IAA) or Memorandum of Understanding (MOU) must be in place between the organization(s) conducting the HSR and the organization responsible for IRB review.

Reporting Requirements:

Researchers must promptly (no longer than within 30 days) report the following to the human participant research program manager:

- Any significant adverse events, unanticipated risks, and complaints about the research, with a description of any corrective actions taken or to be taken.
- Any suspension or termination of IRB approval of research.
- Any significant non-compliance with HRPP procedures or other requirements.
- The time frame for “promptly” is defined.
- Any compromise of personally identifiable information must be reported immediately.
 - The time frame for “immediately” is defined.

The Human Subjects Protection (HSP) Program Manager (and when an NNSA element is involved, the NNSA HSP Program Manager) must be notified in writing prior to initiation of the HSR portion of a new project, even if it meets the regulatory definition of exempt HSR as outlined in 10 CFR Part 745.104, that involves (DOE 0 443.1C, section 4(d)):

- An institution without an established IRB.
- A foreign country.
- A potential for significant controversy (e.g., negative press or reaction from stakeholder or oversight groups).
- Research subjects in a protected class (prisoners, children, individuals with impaired decision making, or DOE/NNSA federal or DOE/NNSA contractor employees as human subjects, who may be more vulnerable to coercion and undue influence to participate) that is outside of the reviewing IRB’s typical range/scope.
- The generation or use of classified information.

The HSP Program Manager at DOE or NNSA must be notified within 48 hours, with a description of corrective actions taken, of any known or potential incidents of noncompliance.

References:

<http://humansubjects.energy.gov/other-resources/pii.htm>

<http://humansubjects.energy.gov/other-resources/documents/IRB-TemplateForReviewingPIIprotocols2014a.pdf>

DJ 400 DEPARTMENT OF JUSTICE

Overview

The IRB follows Department of Justice regulation when reviewing human participant research supported and regulated by the Department of Justice. The information below provides a brief overview of how the IRB would review such studies. In conducting these reviews, the IRB will refer to and follow the applicable Department of Justice regulations.

- **For National Institute of Justice (NIJ) funded research:**

- All projects are required to have a privacy certificate approved by the NIJ Human Subjects Protection Officer.
- All researchers and research staff are required to sign employee confidentiality statements, which are maintained by the responsible researcher.
- The confidentiality statement on the consent form must state that confidentiality can only be broken if the participant reports immediate harm to participants or others.
- Under a privacy certificate, researchers and research staff does not have to report child abuse unless the participant signs another consent form to allow child abuse reporting.

- **For research conducted with the Bureau of Prisons:**

- Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered research.
- A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
- Except as noted in the consent statement to the participant, the researcher must not provide research information that identifies a participant to any person without that participant's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
- Except for computerized data records maintained at an official Department of Justice site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.
- The researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the researcher.
- If the researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual participants, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.
- Required Elements of Disclosure
 - Identification of the researchers.
 - Anticipated uses of the results of the research.
 - A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable).
 - A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a researcher may not guarantee confidentiality when the participant indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the participant is an inmate, indicates intent to leave the facility without authorization.

- A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility.
- The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
- The research design must be compatible with both the operation of prison facilities and protection of human participants. The researcher must observe the rules of the institution or office in which the research is conducted.
- The research must have an adequate research design and contribute to the advancement of knowledge about corrections.
- Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the provisions of 28 CFR 512.
- All research proposals will be reviewed by the Bureau Research Review Board.

Guidance for Investigators:

For research conducted within the Bureau of Prisons, the researcher must have academic preparation or experience in the area of study of the proposed research.

- For research conducted within the Bureau of Prisons, when submitting a research proposal, the applicant shall provide the following information:
 - A summary statement, which includes:
 - Names and current affiliations of the researchers.
 - Title of the study.
 - Purpose of the study.
 - Methods to be employed.
 - Anticipated results.
 - Duration of the study.
 - Number of participants (staff or inmates) required, and amount of time required from each.
 - Indication of risk or discomfort involved as a result of participation.
 - A comprehensive statement, which includes:
 - Review of related literature.
 - Detailed description of the research method.
 - Significance of anticipated results and their contribution to the advancement of knowledge.
 - Specific resources required from the Bureau of Prisons.
 - Description of all possible risks, discomforts, and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks and discomforts will actually occur.
 - Description of steps taken to minimize any risks.
 - Description of physical or administrative procedures to be followed to:
 - Ensure the security of any individually identifiable data that are being collected for the study.
 - Destroy research records or remove individual identifiers from those records when the research has been completed.
 - Description of any anticipated effects of the research study on organizational programs and operations.
 - Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.

EPA 500 ENVIRONMENTAL PROTECTION AGENCY

Overview

The IRB follows Environmental Protection Agency regulation when reviewing human participant research supported and regulated by the Environmental Protection Agency. The information below provides a brief overview of how the IRB would review such studies. In conducting these reviews, the IRB will refer to and follow the applicable Environmental Protection Agency regulations.

Additional Regulatory Requirements

- EPA prohibits research involving the intentional exposure of pregnant individuals, individuals who are nursing, or children to any substance.
- The EPA requires application of 40 CFR 26 Subparts C and D to provide additional protections to pregnant individuals and children as participants in observational research, i.e., research that does not involve intentional exposure to any substance.
- EPA policy requires submission of IRB determinations and approval to the EPA human research review official for final review and approval before the research can begin.
- For research not conducted or supported by any federal agency that has regulations for protecting human research participants and for which the intention of the research is submission to the EPA, the EPA regulations protecting human research participants apply, including:
 - EPA extends the provisions of the 40 CFR 26 to human research involving the intentional exposure of non-pregnant, non-nursing adults to any substance.
 - EPA prohibits the intentional exposure of pregnant individuals, individuals who are nursing, or children to any substance.
- Research involving intentional exposure of pregnant individuals or children to any substance is prohibited and not approved by the IRB.
- For research intended for submission to the EPA, research involving intentional exposure of pregnant individuals or children to any substance is prohibited and not approved by the IRB.
- The IRB review must review and approve observational research involving pregnant individuals and fetuses using 40 CFR 26 and 45 CFR 46 Subpart B.
- The IRB must review and approve observational research involving children that does not involve greater than minimal risk only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 26.406.
- The IRB may only approve observational research involving children that involves greater than minimal risk but presenting the prospect of direct benefit to the individual participants if the IRB finds and documents that:
 - The intervention or procedure holds out the prospect of direct benefit to the individual participant or is likely to contribute to the participant's well-being.
 - The risk is justified by the anticipated benefit to the participants.
 - The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.

Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 26.406.