PART II
GUIDE TO DAILY OPERATIONS

UNIVERSITY OF PENNSYLVANIA
INSTITUTIONAL REVIEW BOARDS

28 August 2009
INTRODUCTION

The Guide to Daily Operations describes the Institutional Review Board (IRB) standard operating policies. These procedures, though based on policy, are flexible and take into account numerous details of the day-to-day activities of the IRB. Forms, checklists, and worksheets that are part of the Guide are controlled or uncontrolled. Controlled forms contain information that becomes part of the record of the IRB's review and determinations. Uncontrolled forms, checklists, and worksheets are not part of the permanent record.

The Organization of the Guide to Daily Operations

The Guide to Daily Operations is the companion to the IRB Standard Operating Policies. The purpose of the Guide is to facilitate day-to-day operations of the IRBs. The organization of this Guide:

- **GA 100: General Administration** includes sections on the IRB's responsibilities and authority. It includes sections that address the activities that require IRB review, maintenance of SOPs, training, personnel management, and conflicts of interest. These activities form the infrastructure of the human subject protection program.

- **OR 200: IRB Organization** addresses the make-up and management of the IRB.

- **FO 300: Functions and Operations** details the procedures to ensure that the IRB meets its regulatory mandate to oversee research. It includes procedures for submission requirements, determining and documenting research that is exempt from IRB review, meeting administration, and documentation.

- **RR 400: Review of Research** contains the procedures for initial review and continuing review of research. The procedures in this section describe the criteria for approval, the methods employed to assure adequate continuing review and the actions the IRB may take because of such review.

- **SC 500: Reviews Requiring Special Consideration** includes procedures for research that involves vulnerable populations and for types of research that require additional considerations by the IRB, such as clinical trials involving investigational medical devices and prospective research in emergency settings, among others.

- **CO 600: IRB Communication and Notification** contains the procedures to ensure timely and adequate notification of IRB decisions regarding research projects to Investigators and other entities that may have an interest in the outcome of IRB review.

- **IC 700: Informed Consent** focuses on the general requirements for informed consent and documentation of the informed consent process, exemptions to informed consent process or documentation, and the assent of minors. This section also includes template consent forms and checklists of required and optional elements of consent.

- **RI 800: Responsibilities of Investigators and Sponsors** provides instructions to Investigators and Sponsors regarding the IRB's requirements for Investigators, from initial submission through continuing review and study completion.

- **QA 900: Quality Assurance** In order to ensure that the IRB meets a high standard of performance and to prepare the IRB for audits by regulatory agencies, this section includes checklists and procedures to ensure adequate and consistent procedures by IRB staff and key members.
Format

Each individual procedure consists of the following parts, where applicable --

- Process Overview – Defines the scope of the procedure
- Responsibility – Assigns roles
- Tools – Lists the forms, templates, checklists and/or documents available to integrate the policies and procedures into the daily operations of the IRB and ensure compliance
- Procedures Employed to Implement the Policy - Details the individuals and daily activities of IRB staff and members to carry out the requirements of the policy
- Further Guidance – Provides additional information and references
GA 102 A
ACTIVITIES REQUIRING IRB REVIEW

1. PROCESS OVERVIEW AND DEFINITIONS
This procedure provides guidance on administrative review of activities requiring IRB review.

2. RESPONSIBILITY
Upon request, the Executive Director, Executive Chair, Associate Director, IRB Chairs, or Administrators determines if an activity involves human research.

3. TOOLS
Research Determination Form
Claim of Exemption Form
Human Research Determination/Exempt Review Form
Letter Templates: Not Human Research

4. PROCEDURES EMPLOYED TO IMPLEMENT POLICY
IRB Administrator or higher
When the IRB receives an application for review, the IRB Administrator conducts an initial review of the proposal to verify that the University of Pennsylvania IRB has jurisdiction. If the activity does not meet the regulatory definition or if the IRB is not otherwise charged (through policy) with the review of the activity, the IRB administrator (or higher) documents the determination on the human research determination/exempt review form and communicates the determination in writing to the investigator.

5. FURTHER GUIDANCE
The Belmont Report is a statement of ethical principles (including beneficence, justice, and autonomy) for human research by the U.S. Department of Health, Education, and Welfare.

OHRP Decision chart to assist in determining whether a project is human research.
www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm Chart 1: Is an Activity Research Involving Human Subjects?

HHS Office for Human Research Protections (OHRP) Engagement of Institutions in Research
http://www.hhs.gov/ohrp/humansubjects/assurance/engage.htm

Guidance on Research Involving Coded Private Information or Biological Specimens

Pritchard, Ivor A. Searching for “Research Involving Human Subjects”: What is Examined? What is Exempt? What is Exasperating; IRB: Ethics and Human Research 23, no.3 (2001), 5-12

GA 102 B
RESEARCH INVOLVING PERFORMANCE SITES

1. PROCESS OVERVIEW & DEFINITIONS
Definitions:

1. Institutional Review Board (IRB): A specially constituted review body established or designated by an entity to
protect the rights and welfare of human subjects recruited to participate in biomedical or social and behavioral science research.

2. **IRB of Record:** The IRB of record assumes IRB responsibilities for another institution for a specific protocol, a specified group of protocols or for all research covered by the other institution. An IRB Authorization Agreement is required, designating the IRB of Record.

3. **IRB Authorization Agreement (or Cooperative Agreement):** A formal agreement between the University of Pennsylvania and another institution that identifies the University of Pennsylvania Institutional Review Board or the collaborating institutions as the IRB of record for that institution and defines the responsibilities for both the Penn IRB and the other institution.

4. **Individual Investigator Agreement:** A formal agreement between the University of Pennsylvania and another institution not routinely engaged in research involving two types of collaborating individual investigators to fall under the oversight of the University of Pennsylvania's Federalwide Assurance: collaborating independent investigators and collaborating institutional investigators.

5. **A collaborating independent investigator is:**
   - not otherwise an employee or agent of the assured institution;
   - conducting collaborative research activities outside the facilities of the assured institution; and
   - not acting as an employee of any institution with respect to his or her involvement in the research being conducted by the assured institution.

   **A collaborating institutional investigator is:**
   - not otherwise an employee or agent of the assured institution;
   - conducting collaborative research activities outside the facilities of the assured institution;
   - acting as an employee or agent of a non-assured institution with respect to his or her involvement in the research being conducted by the assured institution; and
   - employed by, or acting as an agent of, a *non-assured institution* that does not routinely conduct human subjects research.

6. **Office for Human Research Protections (OHRP):** The office within the Department of Health and Human Services responsible for implementing DHHS regulations (45 CFR 46) governing biomedical and behavioral/social science research involving human subjects.

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

8. **Performance Site(s) Engaged in Research:** A performance site becomes "engaged" in human subjects research when its employees or agents 1) intervene or interact with living individuals for research purposes, or 2) obtain individually identifiable private information for research purposes. Further, a performance site is considered to be "engaged" in human research when it receives a direct Federal award to support the research.

9. **Performance Sites Not Engaged in Research:** A performance site is "not engaged" in human research if its employees or agents do not 1) intervene or interact with living individuals for research purposes, or 2) obtain individually identifiable private information for research purposes. If a University of Pennsylvania investigator or his/her staff, including site personnel contracted by Penn, performs all research related activities as well as screening, recruiting, or consenting at the performance site, the performance site would be considered "not engaged" in research, unless the non-Penn performance site releases identifiable private information to Penn researchers without first obtaining participants’

### 2. RESPONSIBILITY

When human research involves performance sites, it is the responsibility of the investigator to ensure that appropriate approvals and/or agreements are complete prior to the initiation of the study.
The performance site “engaged” in research may have the proposed research reviewed and approved by: Its own assurance holding IRB; another designated Assurance holding IRB; or University of Pennsylvania IRB.

For example, Penn may allow another organization to serve as the IRB of record when:
1) Research related activities occur at another institution and a Penn investigator is involved as a collaborator in the research;
2) A faculty member conducting research holds a joint appointment with a neighboring institution and the research activities occur at the other institution.
4) Penn has an institutional conflict of interest in the proposed research and the Vice Provost for Research or the Conflicts of Interest Standing Committee requires reliance on another IRB as a means of managing the conflict of interest.

Penn may agree to serve as the IRB of record when:
1) Research related activities occur at Penn and an investigator at another institution is involved as a collaborator in the research;
2) A faculty member conducting research holds a joint appointment with a neighboring institution and the research activities occur at Penn;
3) A collaborating institution requests reliance on Penn’s IRB because the collaborating institution does not have an IRB;
4) An institution has conflicts of interest and review by the Penn IRB is considered as a means of managing the institutional conflict.

It is the responsibility of the IRB of Record and the Assurance holding institution to assure that the resources and facilities are appropriate for the nature of the research under its jurisdiction.

The IRB may extend – for one or more research protocols – the applicability of its FWA to cover two types of collaborating individual investigators:

3. TOOLS
Appendix A2, Performance Site Documentation
OHRP website listing of Federalwide Assurances
ORHP Guidance: Extension of an FWA to Cover Collaborating Individual Investigators and Introduction of the Individual Investigator Agreement, January 31, 2005
IRB Authorization Agreement (federally funded research)
IRB Authorization Agreement (non-federally funded research)
Individual Investigator Agreement

4. PROCEDURES EMPLOYED TO IMPLEMENT POLICY

Administrators
The IRB Administrator verifies that the submission includes any required IRB authorization agreements or individual investigator agreements for performance sites.

IRB Administrator
If Penn PI is the lead site for an multi-center study, the IRB administrator will complete Appendix A2, Performance Site Documentation, and contact the PI for more information.

Executive Director
For performance sites “engaged” in research where the University of Pennsylvania has agreed to serve as the IRB of Record through an IRB Authorization agreement, the IRB will maintain a current authorization in the IRB records.

If the administrator identifies omissions in documentation, the Executive Director, Human Research Protections, or designee, will contact the Investigator specifying the required documentation needed from the performance site(s) or investigator.
If the performance site is not routinely engaged in research (e.g. physician practice), the investigator at the performance site may be covered under the University of Pennsylvania’s FWA provided that the investigator submits an Individual Investigator Agreement to the IRB for approval.

The Executive Director will make all final determinations regarding the University of Pennsylvania IRB’s willingness to serve as the IRB of Record for a performance site “engaged” in research.

University of Pennsylvania Audit of External Performance Site’s Conduct of Research

The University of Pennsylvania IRB may conduct its own audit of the external site’s conduct of research depending on several factors, including but not limited to, the following:

- The level of risk of the research study;
- The number of reported unanticipated problems involving risk to participants;
- The degree of local oversight provided;
- Complaints from participants; or
- Issues of noncompliance

5. FURTHER GUIDANCE


1. PROCESS OVERVIEW
Describes how the IRB maintains up-to-date policies and procedures that adhere to regulatory mandates and ethical principles.

2. RESPONSIBILITY
The Executive Director is responsible for establishing and periodically reviewing and modifying IRB standard operating policies and procedures. The Executive Director is responsible for communicating changes in policy to the members of the HRPP. The Executive Chair and Executive Director are responsible for approving IRB policies.

3. PROCEDURES EMPLOYED TO IMPLEMENT POLICY
Executive Director, Associate Director
Monitor appropriate sources and contacts for policy updates, note policies that may need revisions and indicate priority.

Executive Director or Designated Staff
At least annually, meet regarding changes to SOPs. Discuss changes and determine if additional procedures are required or if forms need revisions. Revise policies, procedures, and forms, as needed.

Executive Chair and Executive Director
Approve changes to SOPs.

Executive Director or Designated Staff
Archive previous Policies. Notify webmaster to update website. Notify research community & distribute new SOPs & forms as needed.
GA 104
EDUCATION AND TRAINING

1. PROCESS OVERVIEW
Describe the education and training requirements and options for IRB members and staff.

2. RESPONSIBILITY
The Executive Director and Associate Director are responsible for establishing training requirements. The Associate Director is responsible for conducting or overseeing all relevant training programs for IRB members and staff and for guiding the development of IRB member training programs.

3. TOOLS
Training Checklist and Documentation – IRB Members
Training Checklist and Documentation – IRB Staff

4. PROCEDURES EMPLOYED TO IMPLEMENT POLICY
   Executive Director
   Establish education and training requirements for IRB members and staff.

   Associate Director
   Develop training materials and programs. Develop and implement an orientation checklist for all new staff.

   Assure the development of new staff member educational materials as needed.

   Ensure that staff is aware of all training courses offered by IRB.

   Based on requirements and budget, determine training & education schedule (i.e. schedule speakers, acquire training materials & publications)

   Notify members of each IRB as to available training materials & schedule. At least annually, send Training Checklist & Documentation form and reminders as needed.

   IRB Members and staff
   Complete required initial and ongoing training.

5. FURTHER GUIDANCE
   Course Content for IRB Members:
   - University of Pennsylvania IRB Standard Operating Policies
   - DHHS Regulations 45 CFR 46
   - FDA Regulations 20 CFR 50 and 56
   - Applicable State and Federal Laws
   - IRB Member Responsibilities
   - Types of Review including Exempt, Expedited, Convened IRB, Prime Grant
   - Primary and Secondary Reviewer Assignments and Responsibilities
   - Distribution of Materials for Review
   - Pre-review by IRB Administrator
   - Encourage Contact with Investigators for Additional Information/Clarification
   - Assessment of Risks
   - Informed Consent Process, Documentation, Required Elements, Waiver
   - Confidentiality and HIPAA
   - Vulnerable Populations and Supplemental Reviewer’s Comment Forms
   - Monitoring Plan or Committee
• Identification of External Sites and Requirements
• Documentation and Discussion of Review Criteria
• Motions and Votes
• Conflicts of Interest
• Determination of Review Intervals
• Attendance, Notification of Absence

Each new IRB member receives the book entitled “Institutional Review Board Member Handbook” by Robert Amdur, and access to the IRB website, which includes links to:

• University of Pennsylvania IRB Standard Operating Policies
• HHS Regulations - §45 CFR 46
• FDA Regulations – §21 CFR PART 50, 56
• Significant Differences in the FDA and the HHS Regulations http://www.fda.gov/oc/gcp/comparison.html
• Expedited Categories
• OHRP Decision Charts (2004)
• IRB Submission Forms and Guidance Documents
• University of Pennsylvania’s Federalwide Assurance (FWA)
• IRB Reviewer Worksheets (uncontrolled)
• The Belmont Report
• Websites of Interest

IRB Member Continuing Education
Each year, IRB members are encouraged to complete a self-evaluation tool assessing their performance and attendance.

IRB members are encouraged to participate in at least one additional continuing education opportunity each year. The following are available and participation is encouraged:

• Presentations by Penn Investigators;
• IRB seminars with the primary focus in study conduct, forms and regulations training;
• Any other local, regional or national educational opportunities on human research protections.

The IRB reference materials are available for IRB members to obtain additional information regarding the history and conduct of research activities.

Training for New IRB Administrative Staff
New IRB staff members will complete the CITI web-based training modules.

The new IRB staff member is required to attend and observe at least one IRB meeting.

The new IRB administrators will attend PRIM&R within the first three years of employment.

New IRB Staff members will spend one week under the mentorship of the Associate Director for Education and Training, along with any additional designated IRB staff, which will provide an overview of the following:

• The Belmont Report
• Federal Regulations:
  • DHHS 45 CFR 46; and
  • FDA 21 CFR 50 and 21 CFR 56
• IRB Review Process
• Expedited Review Process
• Exempt Review Process
• IRB Policies and Procedures
Job Description and Key Functions

New IRB Staff members are required to review the following:

- §45 CFR 46 & Expedited Categories
- §21 CFR 50 & §21 CFR 56 – FDA Regulations
- FDA Information Sheets
- OHRP Flow Charts
- OPRR (OHRP) Common Findings & Guidance (11/98)
- Ethical Guidelines:
  - Nuremberg Code
  - Declaration of Helsinki
  - The Belmont Report
- FWA
- Vulnerable Populations: Chapter 6 – IRB Member Guidebook
- OHRP Guidance Documents:
  - Certificates of Confidentiality
  - Continuing Review
  - IRB Written Procedures
  - Prisoner Research
  - Research Use of Stored Data or Tissues
- IRB Standard Operating Policies & Guide to Daily Operations

All IRB staff members are encouraged to attend the following during each year (12 months) of employment:

- A minimum of one local, regional or national conference in human research protections
- A minimum of one educational session including but is not limited to:
  - IRB Seminars
  - Bioethics Conferences
  - Other research or human protections related education offerings sponsored by Penn schools or departments
GA 105
MANAGEMENT OF IRB PERSONNEL

1. PROCESS OVERVIEW
Define management policies and procedures to promote the long-term commitment of employees and ensure the efficient and effective administration and enforcement of IRB decisions.

2. RESPONSIBILITY
The Executive Director of the IRB is responsible for establishing personnel requirements and for hiring and evaluating the ongoing performance of IRB staff.

3. TOOLS
Training Checklist – IRB Staff
Training Checklist – IRB Members

4. PROCEDURES EMPLOYED TO IMPLEMENT POLICY
   
   **Executive Director**
   Establish the requirements for IRB staff.
   Compose job descriptions.

   **Executive Director or designated IRB staff**
   Complete personnel recruitment and hiring actions.

   **Executive Director, Associate Directors, and delegated staff**
   Ensure that IRB staff is adequately oriented and trained.

   **Director or delegated IRB staff**
   Evaluate the progress of each new staff member 4 months from his or her hire date.
   This evaluation will include:
   
   - A check of research studies processed by the new staff member; and Agendas and minutes composed by the new Staff member (Administrator or Senior Administrator only).
   - A check of IRB correspondence generated, data entry into the PennERA system, and file maintenance (Administrative Assistants)
   - A plan of action is developed, if necessary, at the four-month evaluation period in the areas identified as needing additional education, training, and development.

   New staff members should demonstrate their ability to perform satisfactorily all key functions of the job at the four-month evaluation point. At that time, the supervisor will deem that:
   
   - The new staff member is satisfactorily performing the key functions of his or her job description and discuss with the new staff member his or her progress and together develop an action plan for any areas of deficiency; or
   - There has not been enough of an opportunity to evaluate the new staff member on specific key functions and will request an extension of the introductory period;
   - The job performance is unsatisfactory and will request an extension of the introductory period and offer to the staff member written notice of the deficiency with an explanation of how the performance or conduct needs to improve in order to continue employment; OR will terminate employment.
GA 106 A
MANAGEMENT OF CONFLICTS OF INTEREST: IRB MEMBERS, CONSULTANTS, AND STAFF

1. PROCESS OVERVIEW
Describe steps to identify and manage financial relationships and possible conflicts of interest for IRB members, consultants and staff.

2. RESPONSIBILITY
The Institutional Official is responsible for articulating and enforcing the conflict of interest policy (COI) at the University of Pennsylvania.

The Administrative Coordinator for Quality Assurance is responsible for monitoring the COI status and disclosures of IRB members.

The IRB Chairperson and IRB Administrator are responsible for identifying COI disclosures before beginning every IRB meeting.

The IRB Administrator or Administrative Assistant is responsible for including in the agenda and periodically sending an e-mail reminder to IRB members prior to the meeting. Sample reminder:

** Conflict of Interest **
All members of the meeting should disclose any potential conflicts may not participate in the initial or continuing review of a protocol except to provide information requested by the IRB. Please review the scheduled agenda for this meeting upon receipt and notify us as soon as possible if you believe that you have a possible conflict with any of the studies being reviewed by the full board. Please supply a brief explanation in reference to the nature of the conflict. Most importantly, if you feel you have a potential conflict with a study that you are assigned to review as a primary or secondary reviewer, please notify us immediately, as the study may need to be reassigned.

The IRB Administrator is also responsible for documenting all COI disclosures in IRB meeting minutes and for ensuring that members, consultants or staff who identify conflicts of interest are not present for the deliberations or vote.

3. TOOLS
IRB Member Agreement

4. PROCEDURES EMPLOYED TO IMPLEMENT POLICY
IRB Members and Consultants
Disclose all financial and professional COI to IRB Administrator when joining the IRB, and periodically update that information.

Leave the room during IRB deliberations and vote where a COI exists or may appear to exist.

IRB Administrator
Document that IRB members with a COI leave the room during deliberations and voting for protocols subject to their COI disclosures.

IRB Coordinator for Quality Assurance
Maintain documentation of IRB member COI via disclosure forms.
IRB Chairperson, IRB Administrator, IRB Members
Ensure that IRB members with a COI leave the room during deliberations and voting subject to their COI disclosures.

5. FURTHER GUIDANCE

FDA Information Sheets, FAQs, Section II, question 12

HHS Guidance on Financial Relationships
GA 106A
MANAGEMENT OF INVESTIGATOR CONFLICTS OF INTEREST

1. PROCESS OVERVIEW
Describe steps to identify and manage financial relationships and possible conflicts of interest for investigators and research staff.

2. RESPONSIBILITY
The Institutional Official is responsible for articulating and enforcing the conflict of interest policy (COI) at the University of Pennsylvania.

The staff of the Office of the Vice Provost for Research is responsible for notifying the IRB of any disclosures reported directly to their office from the Office of Research Services or from Investigators.

The staff of the Office of the Vice Provost for Research is responsible for supplying copies of the Conflict of Interest Standing Committee (CISC) letters and management plans to the IRB.

The Associate Director is responsible for attending the meetings of the CISC.

The Associate Director is responsible for reviewing CISC letters and management plans to determine the appropriate IRB action needed. If IRB follow-up is required, the Associate Director is responsible for contacting the PI to request the needed changes and notifying the appropriate Administrator that changes are forthcoming. When modifications requested by the IRB are received, the Associate Director will pre-review these submissions to ensure that the needed changes have been made to study documents.

The Associate Director is responsible for maintaining the IRB COI tracking log and for updating PENN ERA with the COI status for individual studies.

IRB Administrators are responsible for flagging COI disclosures submitted to the IRB and for ensuring that COI disclosures are forwarded to the Quality Assurance Coordinator and the IRB Associate Director.

The Quality Assurance coordinator is responsible for forwarding the scanned protocol, consent document, and disclosure for all paper submissions to the Conflicts of Interest Standing Committee.

The IRB is responsible for requiring signature by the investigator of the of the COI management plan as a condition of IRB approval of the research protocol.

The IRB is responsible for making template language available for conflict of interest disclosures in consent forms through the IRB website.

The IRB Administrator is responsible for documenting all COI disclosures in IRB meeting minutes and in written communications to the investigator.

3. TOOLS
Penn Confidential Financial Disclosure Statement

4. PROCEDURES EMPLOYED TO IMPLEMENT POLICY
Investigators and research staff
Disclose all financial and professional conflicts of interest via completion of the COI Disclosure Form. Include COI disclosure form with initial submission. Report to the IRB any changes in COI. Disclose COIs for new study team members at the time members join the study team.

Staff of the Office of the Vice Provost for Research
Notifications of COIs:
Upon receipt of any conflict of interest disclosure that involves human subjects research that was not supplied by the IRB, the staff of the Office of the Vice Provost for Research will send notification of a conflict of interest disclosure to the IRB Conflicts of Interest E-mail Box with the following information:

1. PI Name
2. Study Title
3. IRB Protocol Number (If Available)
4. Date of Disclosure

CISC Correspondence:
The staff of the Office of the Vice Provost for Research will send copies of CISC letters and management plans to the IRB Conflicts of Interest E-mail account. The staff of the Office of the Vice Provost for Research will update the IRB when signed management plans are received.

IRB Administrator
Initial Submission
Upon receipt of COI form for a paper submission, scan COI disclosure forms and the IRB Application and forward these documents to the Quality Assurance Coordinator and the Associate Director.

Upon receipt of an HS-ERA submission that contains a COI disclosure, notify the Associate Director via email; provide the study title, PI name and Protocol number.

Ensure that approval of the management plan is a requirement for IRB approval of the research protocol. Document this stipulation for approval in the IRB minutes and in the PennERA electronic IRB database. Communicate the requirement in the official IRB written communication to the investigator that outlines the outcome of the IRB’s review and requirements for IRB approval.

Subsequent Disclosures:
Upon receipt of COI form for a currently-approved protocol, scan COI disclosure forms and the IRB Application and forward these documents to the Quality Assurance Coordinator and to the Associate Director.

For HS-ERA submissions that contain a COI disclosure, notify the Associate Director via email; provide the study title, PI name and Protocol number.

Requests for Continuing Review:
Upon receipt of a request for continuing review where a new or outstanding conflict is identified, scan COI disclosure forms and the IRB Application and forward these documents to the Quality Assurance Coordinator and to the Associate Director.

For HS-ERA requests for continuing review where a new or current conflict is identified, notify the Associate Director via e-mail; provide the study title, PI name and Protocol number.

Quality Assurance Coordinator

Initial Submissions and Subsequent Disclosures with a COI identified:
Forward scanned documents from paper submissions to the Conflicts of Interest Standing Committee.

Requests for Continuing Review where a new or outstanding conflict is identified:
Forward scanned documents from paper submissions to the Conflicts of Interest Standing Committee.

Response to Notifications by Office of Vice Provost of Research:
Upon notification of a new COI disclosure in the COI e-mail box that was not previously reported to the IRB, scan study documents and forward them to the CISC.

**Associate Director**

Upon receipt of the signed CISC management plan for an investigator or study, the Associate Director will determine the appropriate IRB action according to the guidelines for each of the CISC determinations listed below:

**CISC Determination**: Unmanageable conflict or a significant financial interest prohibiting participation in clinical research.

**IRB Action Required**:

*For studies that are pending initial approval by the IRB:*
The Investigator must be removed from study personnel before the study is approved. The Associate Director will update Penn ERA and the IRB COI Tracking log with the required IRB action. The Associate Director will notify the IRB administrator of the pending modification and will verify that the Investigator has been removed from the study personnel before the study is approved.

*For studies that are approved and currently enrolling:*
The Investigator must be removed from the study personnel. The Associate Director will update Penn ERA and the IRB COI Tracking log with the required IRB action. The Associate Director will contact the PI requesting a modification to remove the investigator from the study personnel. The Associate Director will notify the IRB Administrator of the pending modification. Study enrollment should be placed on hold until a modification to remove the investigator has been submitted to the IRB and approved.

*For studies that are closed to enrollment:*
The Investigator must be removed from the study personnel. The Associate Director will update Penn ERA and the IRB COI Tracking log with the required IRB action. The Associate Director will contact the PI requesting a modification to remove the investigator from the study. The Associate Director will notify the IRB Administrator of the pending modification.

**CISC Determination**: Significant financial interest with ameliorating circumstances that permit research participation and a management plan that requires the PI to follow-up with the IRB to determine if disclosure of the COI in the consent form is required.

**IRB Action Required**:

*For studies that are pending initial approval by the IRB:* The COI disclosure must be included in the consent form. The Associate Director will update Penn ERA and the IRB COI Tracking log with the required IRB action. The Associate Director will notify the IRB Administrator of the pending modification. The revised consent form must be reviewed and approved prior to approval of the study.

*For studies that are approved and currently enrolling:* The COI disclosure must be included in the consent form. The Associate Director will update Penn ERA and the IRB COI Tracking log with the required IRB action. The Associate Director will contact the PI requesting a modification to the consent form. The Associate Director will notify the IRB Administrator of the pending modification. Study enrollment should be placed on hold until a modification to remove the investigator has been submitted and approved. Subjects enrolled prior to the change in the consent document will not need to be re-consented.

*For studies that are closed to enrollment:* No change to the consent form is required. The Associate Director will notify the PI that a change in the consent form is not required, however, if the study enrollment status
should change, a modification will be required before new subjects can be enrolled. Subjects enrolled prior to the change in the consent document will not need to be re-consented. The Associate Director will update Penn ERA and the IRB COI Tracking Log with a note that a consent modification is required prior to any new enrollment.

**CISC Determination:** Conflict exists but it does not meet the threshold for significant financial interest prohibiting research participation and a management plan is supplied that requires the PI to follow-up with the IRB to determine if disclosure of the COI in the consent form is required.

**IRB Action Required:**
*For studies that are pending initial approval by the IRB:* The COI disclosure must be included in the consent form. The Associate Director will update Penn ERA and the IRB COI Tracking log with the required IRB action. The Associate Director will contact the PI requesting a modification to the consent form. The Associate Director will notify the IRB Administrator of the pending modification. The revised consent form must be reviewed and approved prior to approval of the study.

*For studies that are approved and currently enrolling:* The COI disclosure must be included in the consent form. The Associate Director will update Penn ERA and the IRB COI Tracking log with the required IRB action. The Associate Director will contact the PI requesting a modification to the consent form. The Associate Director will notify the IRB Administrator of the pending modification. Study enrollment should be placed on hold until a modification to remove the investigator has been submitted and approved. Subjects enrolled prior to the change in the consent document will not need to be re-consented.

*For studies that are closed to enrollment:* No change to the consent form is required. The Associate Director will notify the PI that a change in the consent form is not required, however, if the study enrollment status should change, a modification will be required before new subjects can be enrolled. Subjects enrolled prior to the change in the consent document will not need to be re-consented. The Associate Director will update Penn ERA and the IRB COI Tracking Log with a note that a consent modification is required prior to any new enrollment.

**CISC Determination:** No conflict and no management plan provided.

**IRB Action Required:**
*For studies that are pending initial approval by the IRB:* The Associate Director will update Penn ERA and the IRB COI Tracking Log with the CISC determination. The Associate Director will notify the IRB Administrator that the CISC determination has been received.

*For studies that are approved and currently enrolling:* The Associate Director will update Penn ERA and the IRB COI Tracking Log with the CISC determination.

*For studies that are closed to enrollment:* The Associate Director will update Penn ERA and the IRB COI Tracking Log with the CISC determination.

5. **FURTHER GUIDANCE**
Food and Drug Administration, *Guidance*, Financial Disclosure by Clinical Investigators

**OP 201**
**COMPOSITION OF THE IRB**
1. OVERVIEW
State the requirements for the composition of the IRB(s) responsible for reviewing research conducted in the University of Pennsylvania system.

2. RESPONSIBILITY
Institutional Official is responsible for ensuring that the IRB has adequate resources to identify and recruit qualified potential members and for appointing new members to the IRB.

Executive Chair and Executive Director are responsible for recruiting and making recommendations for membership to the Vice Provost for Research.

3. TOOLS
IRB Roster
IRB Member and Chair Self-Evaluation Forms

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY
*Executive Chair, Executive Director, IRB Chair*
Ensure the overall diversity of the IRB membership (gender, race, ethnicity, community affiliation and professional experience) through non-discriminatory selection methods.

Following established criteria described in SOP 202, select new members, and replace members who resign or otherwise leave IRB service.

*IRB Administrator*
Maintain a roster of all regular and alternate members.

*Associate Director for Education & Training*
Maintain a list of potential consultants.

*IRB Coordinator for QA*
Maintain a file on all members, to include their curriculum vitae, letters of nomination and other evidence of professional ability.

5. FURTHER GUIDANCE
FDA Information Sheets, FAQ section II, questions 14, 15.
OP 202
MANAGEMENT OF THE IRB

1. OVERVIEW
Describe staff administration and oversight of the IRB(s) to ensure the membership has the expertise and commitment to meet its regulatory and institutional mandates.

2. RESPONSIBILITY
Executive Director is responsible for day-to-day management of the activities of IRB members. Executive Chair and IRB Chair is responsible for management of the activities of the IRB members relevant to meeting conduct and review of research. IRB Coordinator for Quality Assurance is responsible for maintaining IRB member files and documentation.

3. TOOLS
Appointment Letter
Confidentiality Agreement
Conflicts of Interest Agreement
Unaffiliated Member Checklist
PennERA Module Access Form
Penn Community Request Form (for unaffiliated members)

Reviewer Duties
IRB Member Responsibilities
IRB Standard Operating Policies
IRB Member Handbook (Amdur)
FDA Information Sheets
IRB Webpage: IRB Member Training

4. PROCEDURES EMPLOYED TO IMPLEMENT POLICY
IRB Administrative Staff
When an individual contacts the IRB regarding membership, obtain contact information and forward the contact information via e-mail to the Associate Director. Copy the Senior Coordinator for Quality Assurance. Executive Director, IRB Executive Chair, or Associate Director for Education and Training
Discuss the responsibilities and time commitment of IRB membership with the interested parties. Invite the prospective member to observe an IRB meeting; and if they wish to do so, notify the IRB Administrator and the Administrative Coordinator for Quality Assurance via e-mail. Request the Curriculum Vitae (CV) for review and forward the CV to the IRB Administrators, Executive Chair and Administrator for Quality Assurance.

Consult with IRB Administrators and Executive Chair to determine if the particular expertise is required on a board. Determine initial length of appointment.

If the individual decides to join the IRB, the Associate Director will notify the Administrative Coordinator for Quality Assurance, and the appropriate IRB Administrator.

Administrator for Quality Assurance
Create an IRB member file.

Forward an e-mail to the Assistant to the Vice Provost for Research and request generation of an IRB Member letter for signature by the Vice Provost for Research. Copy the IRB Director and appropriate Administrator.

Upon receipt of signed letter from Assistant to the Vice Provost of Research, send to the new member a packet including the following:
- Appointment Letter
- Confidentiality Agreement
- Conflicts of Interest Agreement
- Unaffiliated Member Checklist (if appropriate)
- PennERA Module Access Form
- Penn Community Request Form (for unaffiliated members)
- Reviewer Duties
- IRB Member Responsibilities
- IRB Standard Operating Policies
- Member Handbook (Amdur)
- FDA Information Sheets

Send e-mail to Board Administrator notifying receipt of signed letters. Forward the PennERA Module Access form to the PennERA Administrator.

Maintain IRB member files.

**Associate Director or Senior Administrator**
Contact new member to schedule training.

**IRB Administrator**
Update IRB rosters and information in PennERA. Maintain currency of rosters. Notify Administrative Coordinator for Quality Assurance.

**Executive Director**
Update OHRP roster on a quarterly basis.
OP 203
DUTIES OF IRB MEMBERS

1. PROCESS OVERVIEW
Describe steps to ensure that the periodic review and adjustment of IRB membership and composition.

2. RESPONSIBILITY
IRB Chairs and IRB Administrative Staff are responsible for clearly articulating all IRB members’ duties to potential and current IRB members. IRB Members are responsible for fulfilling their duties as specified.

3. TOOLS
   - IRB Member Self-Assessment Worksheet
   - IRB Chair Self-Assessment Worksheet
   - Unaffiliated Member Checklist

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

IRB Member Evaluations
On an annual basis, the Executive Chair and IRB Chair (where appropriate) will convene a meeting with IRB Senior Administrative Staff to review the IRB Member membership. The Chair and IRB staff will provide performance and attendance of individual IRB members.

During that meeting, those in attendance will evaluate members’ contributions. If their continued membership is mutually satisfactory, they are eligible for reappointment. IRB members and Chairs who need to enhance and promote growth in their performance as an IRB member may be offered guidance or further education.

IRB Chair Performance Evaluations
Annually, the Executive Chair will meet with the Vice Provost for Research. During that meeting, the Executive Chair and the Vice Provost for Research will discuss the contributions of each IRB Chair and determine if they are eligible for reappointment.

Periodic Review and Adjustment of the Membership and Composition of the IRBs
In addition to the annual review, Executive Chair, IRB Chairs, and IRB senior administrative staff may also review and recommend adjustments in memberships and composition of the IRB to meet regulatory and organizational requirements. The composition of each IRB may change as needed.

Factors taken into consideration include the following:
- appropriate knowledge of applicable regulatory and legal requirements;
- knowledge of professional standards and practices;
- knowledge of the local research context and research sites, and their capabilities and limitations;
- knowledge of community standards and attitudes; scientific, scholarly, clinical, and professional expertise;
- racial, ethnic, and cultural diversity; and,
- representation of research subjects’ perspectives.

3. FURTHER GUIDANCE
OHRP IRB Guidebook
FDA Information Sheets FAQ, section II, question 17
F0 301
RESEARCH SUBMISSION REQUIREMENTS

1. PROCESS OVERVIEW
Outline the required documents and supporting information required from Investigators for IRB assessment.

2. RESPONSIBILITY
The Executive Director is responsible for defining current research submission requirements.
The IRB Administrator is responsible for ensuring that reviewers receive all required materials for review.
The IRB Administrative Assistant is responsible for submission receipt, tracking, correspondence, acknowledgements, agenda notes and distribution of packets.

3. TOOLS
Pre-review Completeness Worksheet
A-2: Drugs, Biologics, and Devices Worksheet
A-2: Concurrent Review Worksheet

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

IRB Administrative Assistant
Document receipt of all submissions by date stamping the submission and enter the data into the PennERA database).

Enter agenda notes for convened board continuing reviews.

Distribute materials to reviewer(s) and all appropriate reviewer worksheets and checklists.

IRB Administrator
Determine if the activity meets the regulatory definition of human research.

Evaluate submission to determine appropriate level of review: exempt, expedited, or convened IRB.

Ensure that Exempt and Expedited submissions are complete.

Prepare submissions for IRB review by the convened board. Perform pre-review using appropriate pre-review worksheets.

Verify documentation of required signatures.

Request any materials missing from the submission.

Enter agenda notes for convened board continuing reviews and modifications.

Update the PennERA system with agenda notes and other correspondence as necessary.

REVIEW MATERIALS

Initial Review Materials

The IRB Application, Section III, lists Initial review materials distributed to reviewers. The IRB Chair, Primary and Secondary Reviewers receive a full packet. All other members receive a partial packet.

Need chart for initial review
<table>
<thead>
<tr>
<th>Continuing Review Materials</th>
<th>Primary Reviewer, Secondary Reviewer, Chair</th>
<th>Other IRB members</th>
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<tbody>
<tr>
<td>Currently Approved Protocol</td>
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<tr>
<td>Currently Approved IRB Application</td>
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<tr>
<td>Current Investigators Brochure</td>
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<tr>
<td>Continuing Review Form (“Progress Report”)</td>
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<td>Informed Consent Document</td>
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<td>Modification Requests</td>
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<th>Modification Review Materials</th>
<th>Primary Reviewer, Secondary Reviewer, Chair</th>
<th>Other IRB members</th>
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<tr>
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<td>Currently Approved IRB Protocol</td>
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<td>Currently Approved IRB Application</td>
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<td>Tracked changes version of documents</td>
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<td>“Clean” copy of document</td>
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3. FURTHER GUIDANCE

ICH Good Clinical Practice (GCP) Guideline

OHRP Guidance Documents: Expedited Review, Coded Specimens, Flow Charts
FO 302
IRB MEETING ADMINISTRATION

1. PROCESS OVER VIEW
The purpose of this written procedure is to standardize the administrative support of the convened IRB meeting.

2. RESPONSIBILITY
IRB Administrator is responsible for IRB meeting procedural conduct and documentation.
IRB Chair (or Co-Chair) is responsible for IRB meeting review conduct and leadership.

3. TOOLS
Primary Reviewer Worksheet
Informed Consent Worksheet
Subpart B, C, and D Checklists

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

IRB Administrator
Upon receipt by the IRB of a submission for initial review by the convened IRB – conduct pre-review and either assign the submission to the next appropriate board and notify the PI of the board assignment or notify the PI of additional materials required for review.

Assign primary and secondary reviewers based on appropriate expertise. Request consultation or assign to another board, if necessary to assure appropriate expertise.

During the convened meeting, The IRB Administrator is responsible for determining that the quorum is maintained throughout the meeting. If the quorum fails at any time during the meeting, the Administrator will inform the Chair that the IRB may not take any formal actions. Failure of the quorum may result from early departures, an IRB member leaving the room due to conflicts of interest, or absence of a nonscientist member.

Administrative Assistant
Assemble and distribute reviewers’ packets. Create full board continuing review and modification notes for the agenda.

After the IRB meeting, complete the minutes for review by the IRB Administrator of the continuing reviews and the modifications.

IRB Administrator
During the meeting, determine that the quorum is met and that appropriate members are present.

After the IRB Meeting, complete the initial review minutes using the PennERA database system.
Review the continuing review and modification minutes entered by the Administrative Assistant.

IRB Chair and IRB Administrator
Ensure that any member who has a conflict of interest does not participate in the IRB’s deliberations.

Ensure that agenda items requiring review by the convened IRB are adequately addressed, votes are taken, and that a risk level and review period is established, if appropriate.

6. FURTHER GUIDANCE
What is a quorum?
A quorum consists of a majority of IRB members present to discuss and vote on the convened board actions. A quorum must also include at least one non-scientist.

Notes:
1. For research involving prisoners, the prisoner representative must be present.
2. Alternates share one roster position. If both members attend the meeting, only one member votes and only one vote is counted toward the quorum.

What is a majority?
A "majority" is the first whole number that exceeds 50%.

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<thead>
<tr>
<th>IRB membership:</th>
<th>Quorum is (including a non-scientist):</th>
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Conflicts of Interest
Members who have a conflict of interest must leave the room during the deliberation and vote of a protocol (they may answer any questions and then leave the room). IRB members who leave the room and are not present for the deliberation and vote, and do not count towards the quorum.

IMPORTANT NOTE: If there is only one* non-scientist present at the meeting and this person leaves the room, a quorum is LOST.

OHRP Compliance Activities: Common Findings and Guidance #10, #20, #26, #43, #68, #69, #70

OHRP Guidance on Written IRB Procedures

FDA Information Sheets: Significant Risk and Non significant Risk Medical Device Studies


45 CFR 46 Waiver Of Informed Consent Requirements in Certain Emergency Research (Federal Register, Vol. 61, No. 192, pp. 51531-51533, October 2, 1996)
FO 303
ADMINISTRATIVE REVIEW AND DISTRIBUTION OF MATERIALS

1. PROCESS OVERVIEW
Describe the system for receiving and distributing the materials submitted by Investigators and the requirements for document pre-review and distribution prior to IRB review.

2. RESPONSIBILITY
The Executive Director, Associate Director, IRB Senior Administrator; or IRB Administrator is responsible for conducting appropriate assessment of submissions for triage purposes. IRB 8 reviews social and behavioral science research.

In general, IRB 6 reviews research conducted at Pennsylvania Hospital. Other biomedical science research that requires convened board review is assigned to the next appropriate IRB meeting. In general, Phase I and II clinical trials and research involving novel or “high risk” procedures are generally assigned to either IRB 1 or 5. IRB 3 reviews research that will be conducted within the Clinical & Translational Research Center (CTRC). Other biomedical research may be assigned to IRBs 2, 3, 4, or 7, depending on IRB meeting schedules, number of agenda items, and expertise of IRB members.

The Administrative Assistant (with overview by the IRB Administrator) is responsible for distributing complete review material packets to IRB members and other relevant parties. The materials provided to IRB members are listed on the submission forms. IRB members may contact the IRB Administrator or Administrative Assistant to obtain some or all of the materials distributed to the primary reviewer.

3. TOOLS
None

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY
**IRB Administrator**
Assess submission completeness and contact Investigators for any missing elements.

**IRB Administrator and Administrative Assistant**
Assemble IRB member read ahead packets of hard copy materials. Send to IRB members. Send pertinent protocols to consultants. Upon protocol assignment, the reviewers and IRB staff have full access to all application materials submitted via the electronic HS-ERA system including the application (initial, continuing review, or modification) and all documents submitted in support of the application including, as applicable:

- Informed consent and assent documents
- Recruitment materials, including advertisements
- Questionnaires and surveys
- Supporting protocol (e.g. industry sponsor or DHHS-approved protocol)
- DHHS-approved informed consent document
- Investigator’s brochure (drugs)
- Device manual or report of prior investigations (devices)
- Relevant federal grant application
FO 304
DOCUMENTATION AND DOCUMENT MANAGEMENT

1. PROCESS OVERVIEW
This procedure outlines the necessary maintenance of IRB office records associated with research activities under the jurisdiction of the Institutional Review Board (IRB).

2. RESPONSIBILITY
All IRB staff are responsible for maintaining complete files on all research reviewed by or submitted to IRB and for all applicable regulatory compliance requirements.

3. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY
   A. Creating a Study Folder
      Administrative Assistant (Front desk personnel)
      Upon receipt of a new study, enter the study information into the PennERA database.
      Create a file label.

      Administrative Assistant and IRB Administrators
      Build file in accordance with the guidelines provided below.

      IRB Coordinator for QA
      Do routine quality assessments of records to ensure maintenance of files in accordance with regulations and institutional policy.

      Records Administrator
      Ensure that all records are accessible for inspection and copying by authorized representatives of the Sponsor, funding department or agency, federal (FDA, OHRP) and institutional auditors at reasonable times and in a reasonable manner.

   B. Using Electronic Systems
      Associate Director
      Ensure that the IRB's electronic systems and records are maintained in a manner that contains a complete history of all IRB actions related to review and approval of a protocol, including continuing reviews, modifications and reports of unanticipated problems.

      With the assistance of personnel from the Information Technology staff, oversee computerized systems used to generate documentation, track submissions and studies, and ensure communication of requirements to investigators and research staff.

      Ensure training of IRB staff members, along with other delegated staff, on the proper use of all electronic systems used to document study review and compliance activities.

      Maintain specific operations and procedures manuals to train staff and assure consistency of operations.

5. FURTHER GUIDANCE

Guidelines for documents listed on the tab dividers

The documents/review types are not color-coded.
On the tab list the type of action received and the approval date. i.e., CR, Modification, Recruitment Materials, etc.

Protocol File:
Documents submitted as part of the initial submission
- Cover letter with date on letter
- IRB Application
- Consent form (s)
- DHHS-approved sample consent documents
- HIPAA Authorization form
- Full protocol, version and date
- Investigator’s brochure
- Package inserts with date revised/updated
- Advertisements
- Recruitment brochures
- Data collection forms
- Questionnaires

**Continuing Reviews (reviewed expedited or convened IRB)**

All documents that were included as part of the submission

- Cover letter with version date
- CR form
- Progress report with version date, if any
- Reports of unanticipated problems posing risks to subjects or others
- Consent form
- HIPAA Authorization form
- Protocol summary
- Sponsor’s protocol
- Investigator’s brochure

**Modifications**

All documents included in submission, with the exception of tracked/highlighted copies.

- Cover letter outlining changes
- Summary of changes (if document included separately from cover letter)
- Documents revised as part of the submission

**General File Organization Tips:**

- For protocols reviewed by the convened IRB:
  
  * Separate protocol files into manila folders reflecting the “year in review”
  
  * Arrange end tab folders in reverse chronological order
  
  * Place a green sticker on exempt studies
  
  * Place a purple sticker on “not research” or “not humans subjects” studies

**Regulatory Documents/Documentation:** 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 subjects 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 women, fetuses, and neonates
  - Research involving prisoners
  - Research involving children

- For each protocol's initial and continuing review, the frequency for the next continuing review.

**FORMS, TEMPLATES, & WORKSHEETS**

**Submission Forms**

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<th>Form</th>
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<td>Biomed Application I</td>
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<td>Coordinating Center Application</td>
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<td>Limited Data Set Application</td>
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<td>Penn CHOP Agreement Determination Form</td>
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<td>Supplemental Form: Subpart D</td>
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<td>Continuing Review Form for Biomedical Research</td>
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<td>Continuing Review Form of Social/Behavioral Science</td>
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<td>Self-Assessment Form</td>
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<td>Data Use Agreement</td>
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<td>Human Research Determination Worksheet</td>
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**Reviewer Forms and Worksheets**

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RR 401 A
ADMINISTRATIVE REVIEW

1. PROCESS OVERVIEW
This procedure provides guidance to determine if a project meets the regulatory definition of research with human subjects.

2. RESPONSIBILITY
IRB Sr. Administrators and Administrators are responsible for evaluating submissions to determine the requirement for IRB review.

The Executive Director, Associate Directors, and Executive Chair are responsible for providing consultation to staff for determining the requirement for IRB review.

3. TOOLS
Research Determination/Exemption Form

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Administrative Assistant
Once review is complete, draft the letter of final approval using the appropriate PennERA template and secure the signature of the IRB Administrator who conducted the review, or authorized designee.

Update the PennERA database entries.

IRB Administrator
Review the submission to determine if the activity meets the HHS definition of “research” involving “human subjects” AND if the activity meets the FDA definition of “clinical investigation” involving “human subjects”. If the research meets neither definition, the Administrator documents the verification on the Human Research Determination/Exempt Review Form. Formal determinations of research with human subjects are reviewed and acknowledged at the level of IRB Associate Director or higher.

When the project does involve research with human subjects, the IRB Administrator will notify the investigator and guide the investigator on additional submission requirements.

5. FURTHER GUIDANCE

OHRP Decision Chart 1
RESEARCH EXEMPT FROM IRB REVIEW

1. PROCESS OVERVIEW
Federal regulations [45 CFR 46.101(b)] describe categories of research that may qualify for exemption. At the University of Pennsylvania, the IRB makes the final determination of exemption. This procedure outlines the process for verifying exempt protocol status.

2. RESPONSIBILITY
IRB Sr. Administrators and Administrators are responsible for evaluating submissions that claim exemption from IRB review.

The Associate Director or higher is responsible for approving claims of exemption and for providing feedback to IRB Administrators regarding the review of claims of exemption.

3. TOOLS
Claim of Exemption Form
Research Determination/Exempt Review Worksheet

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY
Administrative Assistant (Front Desk Personnel)
Log submission into PennERA database, assemble file and place in bin for distribution.

Senior Administrator
Assign the IRB and administrator, update assignment in PennERA, and forward complete submission to IRB Administrator for review.

IRB Administrators, Sr. Administrators
Review the proposed project to determine if the research qualifies for exemption and meets the additional ethical standards adopted by Penn.

The Administrator may:
- Review the request;
- Request minor revisions to the submitted documents in order to approve the request, and review the revisions prior to forwarding the submission to the Executive Chair or designee for approval; or, Recommend that the protocol undergo expedited review or review by the convened IRB.
- Document the determination and its justification on the Exemption/Research Determination Worksheet.
- Request additional information; confer with the Executive Director, Associate Director, Executive Chair or others for assistance in making the determination.

If the protocol is determined to be exempt from IRB review, the IRB Administrator will complete the Exempt Review Form and place for approval or contact the investigator with recommendations or required changes.

When the IRB Administrator makes the determination that the research does not meet the criteria for exemption, the Administrator will notify the investigator, and will request any additional information needed for expedited or convened board review.

Administrative Assistants
Once the determination has been approved by the Associate Director (or higher), draft the determination letter to the investigator for signature by the IRB Administrator.

Secure IRB Administrator’s signature.
Make copies for the protocol file.

Update the PennERA database and ensure that entries are complete, including notification of approval on the next available agenda.

Send letter to investigator via interoffice mail or e-mail.

*Associate Director or higher*
Assist the Administrators in determining if the study meets the exemption criteria.

Approve claims of exemption.

5. FURTHER GUIDANCE
OHRP Compliance Activities: Significant Findings and Concerns of Noncompliance, #18, #19
RR 402
EXPEDITED REVIEW

1. PROCESS OVERVIEW
The Executive Chair or other experienced IRB member reviewers designated in writing by the Executive Chair conducts expedited review. Expedited reviewers may request revisions to the submitted documents and review the revisions prior to forwarding the submission to the Executive Chair or Designee for approval. The Executive Chair or designee may exercise all of the authorities of the IRB, except that he/she may not disapprove the research.

2. RESPONSIBILITY
Senior IRB Administrators or higher are responsible for identifying submissions that qualify for expedited review and assigning the review to a qualified reviewer. In general, IRB administrators designated by virtue of education, training and IRB membership will conduct expedited review.

3. TOOLS
Expedited Review Form

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY
The expedited reviewer receives the following materials
- Original Signed Cover Letter
- Signed IRB Application Section I (Face sheet)
- IRB Application Section II (Protocol Summary)
- IRB Application Section III (Documents Checklist)
- Sponsor’s full protocol
- Cover letter with additional information that may help in the review
- Grant application (minus appendices & budget information, for federally-funded studies, e.g., NIH, CDC, DOD)
- The complete DHHS-approved protocol (when one exists).
- Informed consent form (and parental permission/assent form for research involving children)
- The DHHS-approved sample informed consent document (when one exists).
- Performance site approvals for sites other than the university.
- HIPAA Authorization or Waiver
- Supporting Documents:
  - Supplemental form(s) for research involving pregnant women, fetuses, neonates, or children
  - Questionnaires, surveys, diaries, personality tests, quality of life assessment or other surveys or inventories, data collection forms that will be completed by subjects, interview & focus group scripts, consent and recruitment scripts. **Exception:** IRB review is not required for widely recognized, accepted, standard tests in a given field.
  - Recruitment materials, including advertisements, brochures, letters to physicians and patients, and broadcast materials, etc

Administrative Assistant (Front Desk Personnel)
Log submission into PennERA database as per 401B-5.

Administrative Assistant
Once review is completed, draft the approval for signature by the Administrator

Secure signature from Administrator

Make copies for the protocol file.

Update the PennERA database entries.

Ensure that notification of approval/status verifications are reported on the next available IRB agenda
Send letter to investigator via interoffice mail or e-mail

**Expedited Reviewer**
The expedited reviewer conducts initial and continuing review of research by the expedited procedure. Staff members who conduct expedited review are members of the full board IRB, experienced as IRB members, and designated by the Executive Chair. Appropriate training involves specially created educational training sessions conducted by IRB senior staff.

Reviewers self-identify conflicts of interest and refer the research to another reviewer if a conflict exists.

The reviewer will confirm that the research satisfies the criteria in the “Categories of Research That May be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure” and ensure that the specific permissible category or categories justifying the expedited review are documented on the Expedited Review Form and in the agenda/minutes.

The reviewer’s decision regarding approvability of new research and continuation of ongoing research is based on satisfaction of all of the conditions outlined in 45 CFR 46.111(a)(1-7) and 21 CFR 56.111(a)(1-7).

The reviewer uses the Expedited Review Worksheet to document the review. If the reviewer determines that the proposed research does not meet the criteria for expedited review, the submission is referred to a convened IRB meeting.

The reviewer will make all additional findings and determinations required by regulations and IRB policy for research involving children, prisoners, pregnant women and fetuses, waivers and alteration of consent, and waivers of consent documentation, and HIPAA authorizations or waivers.

The reviewer may recommend approval of the research or require modifications to secure approval. The reviewer may not disapprove the research. If the investigator does not make the required modifications to secure approval, the application is referred to the convened IRB for review.

When revisions are requested, the reviewer reviews the modified documents and, if acceptable, the reviewer forwards the submission and the reviewer worksheet to the Executive Chair or designee for approval.

Note: If additional expertise is required, the IRB Administrator will consult with the Executive Director or Associate Director to identify an IRB member with the appropriate expertise and forward the protocol to the IRB member for review.

_Executive Chair or Senior IRB Administrative Staff_

Verify scientific and scholarly merit in relationship to the level of risk.

Verify that that the conditions outlined in 45 CFR 46.111(a)(1-7) and 21 CFR 56.111(a)(1-7).

_The Convened IRB_

Review the IRB agenda for notifications of research proposals/activities approved under an expedited review procedure

Request additional information, as necessary, to resolve any protocol related concerns or issues.

5. FURTHER GUIDANCE

Note: OHRP has concluded the expedited review Category 5 intended to include research involving existing information or specimens that were previously collected for non-research purposes, as well as research involving
existing information or specimens that were previously collected for research purposes—provided they were not collected for the currently proposed research.

FDA Information Sheets

OHRP IRB Guidebook
INITIAL REVIEW: CRITERIA FOR IRB APPROVAL

1. PROCESS OVERVIEW
This procedure elaborates the regulatory criteria the IRB must consider in the approval process. In addition, certain other criteria that are unique to the University of Pennsylvania system may apply and may be stipulations for IRB approval.

2. RESPONSIBILITY
IRB Administrator is responsible for ensuring that IRB reviewers have all the tools and resources they need to complete their research reviews and for selecting primary and secondary reviewers with the relevant expertise to perform reviews and make necessary recommendations on approval decisions by the IRB.

The IRB Senior staff, Executive Chair, and Chair are responsible for providing IRB members adequate submission review training and ongoing guidance, and IRB Reviewer is responsible for conducting a thorough review and making all appropriate approval recommendations for consideration by the IRB.

The primary reviewer is responsible for conducting an in depth initial review.

3. TOOLS
Subpart Determination Forms (controlled)
   B1: Research Involving Pregnant Women or Fetuses
   B2: Research Involving Neonates of Uncertain Viability
   B3: Research Involving Nonviable Neonates
   B4: Research Involving Fetal Material
   C: Research Involving Prisoners
   D1: Research Involving Children
   D2: Research Involving Children who are Wards of the State
Worksheet: Is an IDE Necessary (uncontrolled)
Primary Reviewer Worksheets (uncontrolled)

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY
   IRB Member Assigned to Review
   Conduct an in-depth review of the protocol submission focusing the review on the criteria for IRB approval.

   Ascertain whether third party verification of submitted information is necessary.

   Prepare summary of findings and recommendations for presentation at the next convened IRB meeting.

   Present to the convened IRB a summary of findings along with stipulations required for approval.

5. FURTHER GUIDANCE
   OHRP Compliance Activities: Common Findings and Guidance #3, #14, #15, #72
RR 404
CONTINUING REVIEW

1. PROCESS OVERVIEW
Describe the processes for the continuing review that occurs after initial research approval.

2. RESPONSIBILITY
The Executive Director is responsible for establishing the processes for conducting ongoing reviews of research. The Associate Director is responsible for quality assurance and quality improvement activities for continuing review processes.

3. TOOLS
Request for Continuing Review Form for Biomedical Research
Request for Continuing Review Form for Social/Behavioral Research
Continuing Review Worksheet

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

A. Site Visits and Third Party Verification
Upon request by the IRB, the IRB Associate Director will conduct the site visit, form a site visit team, or refer the request to the Office of Human Research or other audit and compliance office.

Once completed, the IRB Associate Director will forward the Site Visit Report to the IRB Administrator who will place the report on the agenda for discussion by the convened IRB.

The convened IRB will review the report and determine any necessary follow-up actions.

The IRB Administrator will document the discussion in the minutes and notify the Investigator in writing of the IRB’s review and any stipulations or recommendations.

B. Modifications
Upon receipt, the IRB Administrative Assistant (Front desk Personnel) will:
- Date-stamp the current submission
- Attach all information related to the modification to the study file and give to the administrator for pre-review

The IRB Administrator will review the submission to determine if the modification is eligible for expedited review, or place on the agenda for the next appropriate IRB meeting if review by the convened IRB is required. The IRB Administrator will consult with the IRB Senior Administrative Staff, Chair, or Executive Chair if unsure about appropriate the level of review.

When a modification is eligible for expedited review, the IRB Administrator will pre-review the submission.

The Administrative Assistant will enter data in PennERA, and will forward the request for modification to the Executive Chair or designee for review and approval.

C. Continuing Review
The IRB Records Administrator is responsible for ensuring that auto-generated electronic e-mail reminders forwarded to investigators at 90 and 45 days prior to the expiration date, and on the day the IRB approval expires.

Upon receipt of the submission to the IRB, an Administrative Assistant (Front desk personnel) date-stamps the submission with the current date.
The IRB Administrator reviewers the submission to determine completeness. When a continuing review is eligible for expedited review, the IRB Administrator will conduct the pre-review and will forward the Protocol file to the Executive Chair or designee for review and approval.

The Administrative Assistant retrieves the corresponding IRB file, and ensures that protocols submissions requiring expedited review are forwarded the Executive Chair for review and approval.

Once the Executive Chair (or designee) review is complete, the Administrative Assistant:
- Retrieves the study file, generates the continuing review approval letter, and if appropriate the approved informed consent documents.
- Forwards the approval letter and date stamped informed consent documents to the Investigator via intramural or email
- Completes database entry and final collation of the file.

For protocols requiring review by the convened IRB, the IRB Administrator identifies the Primary Reviewer and assigns the protocol to the next appropriate IRB meeting agenda. The IRB administrator also ensures that all database entries are complete. If the submission clearly does not meet the criteria for reporting to the IRB, the IRB Administrator will contact the investigator or study staff and provide them with a copy of the IRB SOP on unanticipated problems and other events requiring reporting to the IRB. The IRB administrator will consult with the IRB Executive Chair or designee as necessary to determine the level of review required.

Reportable Events

Reportable Events Process Flowchart
D. Procedures for managing a protocol-specific concern or complaint submitted by investigator, research team, research participant or family member.

The IRB Executive Director will review the details of the complaint and the course of action thus far, and determine whether any additional steps necessary to resolve the complaint. This may involve further discussion with the research participant/family member, the PI, other members of the research team, and/or other health care providers, the Office of General Counsel or others as necessary. The Executive Director and IRB Executive Director will determine whether the issue is adequately resolved or if further action is required. Issues or concerns not resolved by the process outlined above are handled in accordance with the unanticipated problems policy RR 404.

E. Procedures for reviewing suggestions, complaints, or concerns about the IRB review process or the Penn’s HRPP.

The Associate Director for Compliance and Quality improvement will comments, questions and issues received from the Penn community including research participants to identify areas for potential improvement in the effectiveness of HRPP policies and procedures and for ensuring the protection of human subject research participants.
RR 405
CONTINUING REVIEW – CRITERIA FOR RENEWAL

1. PROCESS OVERVIEW
Continuing review of research previously approved by the IRB must be substantive and meaningful. The approval criteria for continuing review are the same as that for initial review. The IRB should obtain and review sufficient information to conduct continuing review of research in accordance with the regulations and the organization’s policies and procedures. Federal guidance describes the minimum information the IRB should receive and review.

2. RESPONSIBILITY
The Executive Director is responsible for establishing and implementing processes for making research renewal decisions.

3. TOOLS
Continuing Review Form for Biomedical Research
Continuing Review Form for Social/Behavioral Research
Continuing Review Worksheet

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

IRB Member(s)
The primary or designated reviewer reviews the materials to determine the status of continuation of the study.

The AA forwards to the Executive Chair (or designee) any protocol requiring expedited continuing review and approval.

If review by the convened IRB is required, the appropriate documents are copied, the Reviewers’ packets prepared and delivered to IRB members in advance of the meeting.

The AA attends IRB meetings and documents continuing reviews conducted by the convened IRB.

IRB Administrator
For protocols requiring convened IRB review, identify the Primary Reviewer and assign the protocol to the next appropriate IRB meeting agenda. If the protocol is due to expire, the Administrator will make every attempt possible to schedule the continuing review for the next available IRB meeting.

Notify the Investigator as to the outcome of the review. If the IRB does not re-approve the research by the specified expiration date, notify the PI in writing of the expiration.

Report expedited approvals on the agenda for the next IRB meeting.

Administrative Assistant
Once the continuing review is complete, the Administrative Assistant will:

- Retrieve the study file, generate the letter, and stamp the approved informed consent documents, if any.
- Secure signature of IRB Administrator.
- Fax and mail the original letter and informed consent documents to the Investigator with a copy to the study contact.
- Ensure that all database entries are complete.

Executive Chair or Designee
For submissions eligible for expedited review, The Executive Chair or authorized designee will review the study and take any of the following actions:

- Approved
- Conditional re-approved pending modifications
- Defer pending receipt of additional information
- Deferred to the convened IRB

**Primary Reviewer and Convened IRB**

When conducting continuing review at a convened IRB, Penn uses a primary reviewer system for continuing review.

The Reviewer presents the findings to the convened IRB. The convened IRB discusses the protocol and makes determinations, recommendations, or stipulations for re-approval. All actions require approval by the majority of IRB members present.

Prior to the meeting, the Primary Reviewer will review the protocol, continuing review form (i.e., progress report), the protocol summary and the currently approved informed consent document.

**Other IRB Members**

Review the continuing review form, protocol summary, and currently approved informed consent document.

**5. FURTHER GUIDANCE**

**Determining Appropriate Interval for Continuing Review**

The following factors that may determine the appropriate review interval, but are not limited to:

- Involvement of vulnerable populations;
- Research determined by the IRB to involve high-risk e.g. gene transfer protocols;
- Classified research;
- Research for which participants would be exposed to additional risks, e.g. breach of confidentiality, phase I studies, disproportionate number or severity of adverse events;
- Previous suspensions of the research due to non compliance, poor record-keeping or other concerns; or,
- Recommendations from other Institutional committees.

**Scenarios for Determining Dates of Approval and Expiration**

**Scenario 1:** The IRB reviews and approves a study for one year, without any conditions, at a convened meeting on October 1, 2002. The date of IRB approval is October 1, 2002 and the date of IRB expiration is September 30, 2003.

**Scenario 2:** The IRB reviews a study at a convened meeting on October 1, 2002, and approves the study for one year, contingent on specific minor conditions the IRB chair or his or her designee can verify. On October 31, 2002, the IRB chair or designee confirms that the required minor changes were made. The date of approval is October 31, 2002 and the date of expiration is September 30, 2003. Continuing review must occur within one year of the date of the convened IRB meeting at which the IRB reviewed and approved the study, that is, by September 30, 2003.

**Scenario 3:** The IRB reviews a study at a convened meeting on October 1, 2002, and has serious concerns or lacks significant information that requires IRB review of the study at subsequent convened meetings on November 3, 2002 and December 5, 2002. On December 5, 2002, the IRB completes its review and approves the study for one year. The date of IRB approval is December 5, 2002 and the date of expiration is December 4, 2003.
Scenario 4: The IRB reviews and approves a study at a convened meeting on January 13, 2003 for a period of one year. The IRB approval date is January 13, 2003 and the expiration date is January 12, 2004. The PI submits an modification to the approved study; the modification is reviewed and approved at a convened meeting on November 1, 2003. The IRB did not change the review period. Therefore, the new date of approval is November 1, 2003 and the date of expiration is January 12, 2004.

OPRR Reports 95-01

OHRP Guidance Contining Review January 2007
1. SCOPE
Describe how the IRB receives notification when a research project is completed. This procedure also outlines the circumstances and methods in which a study’s approval status may be changed and subsequently reinstated.

2. RESPONSIBILITY
Study Completion. Upon study completion, the IRB Administrator ensures the receipt, review, and filing of documentation of study completion.

3. TOOLS
Continuing Review Form for Biomedical Research
Continuing Review Form for Social/Behavioral Research

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Administrative Assistant (Front Desk Personnel)
Study Completion. Date stamp submission.

IRB Administrator
Study Completion. Review submission and obtain any outstanding information or documentation from the Investigator to close the study. If there are inconsistencies, the IRB Administrator, or Administrative Assistant, requests additional information.

Administrative Assistant
Study Completion. Log into PennERA database and place for review by Executive Chair or Designee.

Executive Chair or Designee
If the study may be closed and the contents of the IRB file are complete, authorize closure of the study.

Administrative Assistant
Study Completion. Prepare and send completion letter to investigator. Update PennERA system so that completed studies are listed in the agenda.
1. PROCESS OVERVIEW
Specify the actions the IRB may take resulting from its review of research.

2. RESPONSIBILITY
The Executive Chair and IRB Chairs are responsible for ensuring that all IRB decisions and actions are in accordance with institutional and regulatory requirements for approval and are responsible for ensuring the appropriateness of all IRB decisions and actions.

3. TOOLS
IRB Guidance: Categories of Action

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

*IRB Administrator*
Document IRB decisions in the minutes.
Review and sign all IRB decision letters.

*Administrative Assistant*
Create and distribute IRB decision letters in a timely manner.

5. FURTHER GUIDANCE
OHRP Compliance Activities: Common Findings and Guidance #6, #21, #71
OHRP Guidance on Expedited Review
FDA Information Sheets: Continuing Review after Study Approval
1. PROCESS OVERVIEW
Describe the special considerations for the review of research involving vulnerable populations.

2. RESPONSIBILITY
The Executive Director is responsible for maintaining up-to-date review tools for review of research pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines.

The Executive Chair, Chairs and the IRB Administrators are responsible for ensuring the IRB members are well versed in new and evolving regulations and guidelines pertaining to vulnerable populations, for selecting primary reviewers with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

The IRB Primary Reviewer is responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of potential for coercion, in consultation with any appropriate experts and resources.

3. TOOLS
Supplemental Checklists for Vulnerable Populations
Review Checklists:
Appendix: B: Research Involving Pregnant Women or Fetuses
Appendix B1: Research Involving Neonates of Uncertain Viability
Appendix B2: Research Involving Non-viable Neonates
Appendix B3: Research Involving Fetal Material
Appendix C: Research Involving Prisoners
Appendix D: Research Involving Children

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

RESEARCH INVOLVING VULNERABLE POPULATIONS

IRB Executive Director
Maintain and update checklist to conform to applicable regulations and guidelines.

IRB Administrator
Conduct a pre-review.

E-mail the Investigator with any questions or needed clarification.

Verify that the IRB reviewing the research involving a prisoner has at least one member who is a prisoner or prisoner representative in attendance.

Assist in preparing documents for the certification letter and prepare a draft certification letter to the Secretary (through OHRP) for signature by the appropriate institutional official listed on the FWA.

For research funded or supported by HHS, send the IRB-approved protocol, any relevant HHS grant application or proposal, any IRB application forms required by the IRB, and any other information requested or required by the IRB to be considered during initial IRB review to OHRP for certification.

HHS conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its approval in writing to the institution on behalf of the Secretary under 45 CFR 46.306(a)(2). Upon receipt of OHRP's determination, notify the investigator of the approval status.
**IRB Member (Primary Reviewer)**

Complete the Subpart Determination Checklist.

Contact Primary Investigator, Coordinator, Executive Chair, or IRB Administrator in advance of the meeting to resolve issues or gather information needed for a thorough review.

Determine the need for a consultant. Contact IRB Administrator to arrange for consultant’s review.

Determine if the investigator should attend the meeting. Contact the IRB Administrator to arrange for the investigator’s attendance at the convened IRB.

5. **FURTHER GUIDANCE**

**Research Involving Children**

When determining whether children are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the children targeted for the study population. This determination may apply to all children involved in the study, or on a case-by-case basis, as deemed necessary by the IRB.

The IRB also needs to determine the appropriate ages for assent and the method of documentation of assent.

The IRB needs to assure that special protections afforded to children found in Subpart D have been met for this population.

HHS-funded or supported studies determined by the IRB to meet 45 CFR 46.407 for children, will be given a “withdrawn approval” status until a determination by the Secretary of the Department of Health and Human Services (DHHS) is received.

The Executive Director will notify the HHS Office of Human Research Protections (OHRP) when the IRB determines a study meets 45 CFR 46.407. Documentation sent to the Secretary includes:

- IRB minutes from the convened meeting documenting the IRB findings;
- The complete IRB application and informed consent documents;
- The relevant protocol and/or grant application; and
- Any supporting material including the Investigator’s Brochure, if applicable.

If OHRP grants approval under Category 46.407, then the IRB may grant final approval. If OHRP requires changes in the process of approval, or any other changes are made after the IRB “approved pending” modifications, an modification must be submitted for review and approved by the Executive Chair designee, unless the Executive Chair determines the changes submitted are major, which require IRB review.

FDA regulated clinical investigations determined by the IRB to meet 21 CFR 50.54 for children, will be given a “withdrawn approval” status until a determination by the Commissioner of Food and Drugs is received.

The Executive Director will notify the FDA when the IRB determines a study is determined to meet 50 CFR 50.54. Documentation sent to the Secretary will include:

- IRB minutes from the convened meeting documenting the IRB findings;
- The complete IRB application and informed consent documents;
- The relevant protocol and/or grant application; and
- Any supporting material including the Investigator’s Brochure, if applicable.

If FDA grants approval under Category 50.54, then the IRB may grant final approval. If FDA requires changes in the process of approval, or any other changes are made after the IRB “approved pending” modifications, an modification
must be submitted for review and approved by the IRB Chairperson or his or her designee, unless the IRB Chairperson determines the changes submitted are major, which require IRB review

Non-Federally funded studies determined by the IRB to meet 45 CFR 46.407 for children, and meet all criteria for approval under 45 CFR 46.111, will be given a “withheld approval” status until the research proposal is reviewed by both an expert panel and a community panel, for recommendations.

When children as wards of the State are involved in research under HHS 45 CFR 46.407 or FDA 21 CFR 50.54, the required additional individual acting on behalf of the child as guardian or in loco parentis may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child’s participation in the research and who is not associated in any way with the Investigators, or the guardian organization.

Research Involving Prisoners
Certification
The submission will include a statement that indicates that the IRB was constituted as per the requirements in 45 CFR 46.304. OHRP does not require that the prisoner certification letter include information about the manner in which the IRB fulfills the requirements of 45 CFR 46.304. The institution may wish to provide the name of the prisoner representative.

The submission to OHRP will include the protocol application; the grant application (including any grant award updates), and a certification letter.

The certification letter will include:
- OHRP Assurance #;
- IRB # for Designated IRB;
- Site(s) where research involving prisoners will be conducted;
- If prisoner research site is “engaged in research”, provide OHRP Assurance #;
- DHHS Grant Award #;
- DHHS Funding Agency Name;
- Funding Agency Grants/Program Officer Name and Telephone #;
- Title of DHHS Grant;
- Title of Protocol (if the same as the title of the grant, indicate as such);
- Version date of the ICD to be used with prisoners;
- Date(s) of IRB Meeting(s) in which the protocol was considered and provide a chronology of: Date of initial IRB review; and/or Date of Subpart C reviews including: type of IRB review (initial, modification, addendum, continuing review); and special IRB review for prisoner issues.
- Principal Investigator; and
- Reason for IRB review (from the applicable reasons):
  - Non-prison study (not previously reviewed and certified under Subpart C) in which participant has become incarcerated (or otherwise fits the definition of prisoner in 45 CFR 46.303(c)) and the PI wishes to continue the individual’s participation in the study;
  - Non-prison study with at-risk population (i.e., probationers, substance abusers) and the PI wishes to continue the individual’s participation in the study if the individual becomes incarcerated;
  - Non-prison study, majority of study population are non-prisoners but PI seeks to enroll some prisoners (as defined in 45 CFR 46.303(c)):
  - Minimal risk DHHS conducted or supported epidemiologic research, majority of study population are non-prisoners but PI seeks to enroll some prisoners (prisoners are not the focus of the study) and the sole purpose of the study is either: To describe the prevalence or incidence of a disease by identifying all cases; or To study potential risk factor associations for a disease.
Initial Subpart C review of study designed to be conducted in a prison or using prisoners as defined in 45 CFR 46.303(c), the PI seeks to enroll already incarcerated subjects.

The prisoner certification letter will also contain the following information:
- Justification for the use of prisoners in the study. If applicable, delineate the protocol to be conducted in the prison from the overall project described in the grant application;
- Study objectives or study aims;
- Brief summary of study procedures;
- Customary treatment or services at the prison (or alternative to incarceration) research site(s) for the condition being studied;
- Description of how risks specific to a prison (or alternative to incarceration) setting are minimized;
- Whether the prison site(s) are “engaged in research” and whether they have obtained an assurance with OHRP;
- Whether a Certificate of Confidentiality was obtained by the PI for the study;
- Description of recruitment procedures in the specific prison (or alternative to incarceration) setting; and/or
- Description of how the consent form was altered for use with a prison population or specific prisoner and whether the subsequently incarcerated participant will be reconsented.

All prisoner research certification letters will be mailed to:
OHRP Prisoner Research Coordinator
Office for Human Research Protections (OHRP)
Department of Health and Human Services
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

3. REFERENCES
OHRP IRB Guidebook
OHRP Guidance on the Involvement of Prisoners in Research Dated May 23, 2003
Penn Human Research Advisory Committee Charter
SC 502
CATEGORIES OF RESEARCH

1. PROCESS OVERVIEW
Define the review process categories of research including research involving devices and emergency research.

2. RESPONSIBILITY
The Executive Director is responsible for maintaining up-to-date review tools for review of research pertaining to these categories based on new and evolving applicable regulations and guidelines.

Executive Chair, Chair, and IRB administrative staff Chair are responsible for ensuring the IRB members are well versed in new and evolving regulations and guidelines pertaining to these categories, for selecting primary reviewers with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

IRB Reviewer is responsible for conducting appropriate review of research planned for these categories in consultation with any appropriate experts and resources.

3. TOOLS
IRB Worksheet: Is an IDE Necessary?
IRB Guidance: Significant Risk and Non-significant Risk Medical Device Studies
IRB Supplemental Form: Investigational Devices

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

A. Research involving drugs or biologics

Administrator Include the Appendix A-1 worksheet in the primary reviewer's packet when the study involves a drug or biologic. Include adequacy of the documentation of IND documentation is submitted.

IRB Member Assigned to Review
IND Exemption: Note whether an IND exemption letter is included in the submission. If not, require documentation of IND exemption.

IND information included with the submission. Make preliminary determination that the documentation of the IND is acceptable. If an IND may be required but not submitted, communicate this finding to the IRB Administrator.

Present status of IND decision at the convened IRB for acceptance or further deliberation.

IRB Administrator
Notify the investigator of additional documentation required for IND submission or IND exemption.

B. Clinical Research Involving Investigational Devices

Administrator Include the IDE worksheet in the primary reviewer's packet when a medical device is the study article.

IRB Member Assigned to Review
Perform the device risk determination to make preliminary determination that the Sponsor's determination is acceptable.

IRB Administrator
Notify the investigator if the IRB rejects the Sponsor's NSR device determination.
**IRB Administrator**
Conduct pre-review and request any necessary revisions for submitted documents for use of investigational devices as outlined for new study submissions.

When pre-review is complete, place the new study on the next available IRB agenda, assign reviewers and prepare the reviewer and IRB packets.

Assist reviewers in obtaining additional information from the investigator regarding the investigational device.

Ensure that the minutes of IRB meetings document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.

**IRB Administrator/Administrative Assistant**
Draft letters requesting revisions and final approval letters using the appropriate template.
Complete appropriate database entries.

C. Gene Transfer Research

*Executive Director or designee and Executive Chair*
For sponsor-investigator research, notify the Office of the Vice Provost for Research to determine the requirement for review by the VPR Human Research Advisory Committee.

*Executive Chair or designee*
Coordinate meeting in accordance with the HRAC Charter.

**IRB Administrator**
For all gene transfer studies, verify review by the Recombinant DNA Advisory Committee (RAC), and the Penn Biosafety Committee.

D. Prospective Research in Emergency Settings

*Executive Director or IRB Associate Director*
Conduct pre-review.

**IRB Administrator**
Provide Investigators and IRB members with appropriate guidelines regarding research in emergency settings.

E. Emergency Use of Investigational Articles

*Executive Chair or IRB Chair*
Review submitted report(s).
Determine whether an emergency meeting of IRB is feasible.

5. FURTHER GUIDANCE

FDA Information Sheets: Medical Devices
IRB Guidance on Emergency Use
1. PROCESS OVERVIEW
Describe communications with investigators and research staff.

2. RESPONSIBILITY
The Executive Director is responsible for overseeing all IRB communications.

IRB Administrative staff are responsible for generating appropriate correspondence in response to IRB meetings and decisions and for distribution of IRB correspondence to appropriate parties.

3. TOOLS
PennERA Letter Templates

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

**IRB Administrator**
Ensure that all communications follow established procedures and format.

Ensure that the determinations and requirements of the IRB are communicated to the Investigator as soon as possible.

Supervise Administrative Assistants to ensure that all communications with Investigators, regulatory bodies, and others as appropriate are accurate and timely.

Ensure that documentation, either electronic or paper, of any communication of determinations, requirements, or actions of the IRB or representatives of the IRB, when acting in a regulated capacity, are maintained, according to procedures in section FO 305: Documentation and Document Management.

Ensure that all verbal communications are documented (either electronically or on paper) and retained in the study file according to procedures in section FO 305: Documentation and Document Management.

Ensure that the appropriate entities are copied on the documentation and notification of any IRB determinations and actions as described in section CO 602 and as noted on this procedure’s attachments.

**Administrative Assistants**
Generate letters as directed.

Distribute correspondence as directed.

Record communications as required.
CO 602 OTHER ENTITIES.

1. PROCESS OVERVIEW
Describe how actions are communicated to other entities.

2. RESPONSIBILITY
The Executive Director is responsible for ensuring required communications with other entities.

3. TOOLS
Serious or Continuing Noncompliance Process Flowchart
Unanticipated Problems Posing Risk to Subjects or Others Process Flowchart
Guidance: Significant and Nonsignificant Risk Medical Device Studies
Worksheet: Is an IDE Required?

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY
Executive Director
The Executive director will notify the Institutional Official of unanticipated problems posing risks to subjects or others, serious or continuing noncompliance, and terminations by the IRB of ongoing research. The Executive Director will draft the communication to federal and funding agencies.

If the IRB determines that it cannot approve a clinical investigation that is being conducted under an IND or IDE for emergency research conducted under 21 CFR 50.24, send a copy of the Investigator's disapproval letter to the sponsoring company.

If the IRB terminates a study for cause, notify the appropriate Institutional Officials; and prepare draft report to FDA, OHRP (when appropriate) for Institutional Official.

IRB Associate Director or higher
Contact FDA for guidance on SR/NSR device determinations when necessary.

Institutional Official
Where appropriate, The Institutional Official will notify, FDA, OHRP and funding Agency Heads or Sponsors of unanticipated problems posing risks to subjects or others, serious or continuing noncompliance, and terminations by the IRB of ongoing research.

IRB Administrator
Notify the investigator if the IRB determines that a device protocol submitted as a Non-Significant Risk study presents significant risk of harm to study subjects.

Monitor reports of serious and unexpected adverse events from Sponsors to ensure all reportable events are reported to the IRB by the Investigators.

Administrative Assistant
Prepare and distribute all relevant correspondence to other entities in a timely manner.
IC 701
GENERAL REQUIREMENTS FOR INFORMED CONSENT AND DOCUMENTATION

1. PROCESS OVERVIEW
Describe the requirements for obtaining informed consent and documentation of informed consent.

2. RESPONSIBILITY
IRB Administrator is responsible for reviewing all incoming informed consent documents and for communicating with Investigators to bring documents into compliance.

3. TOOLS
Informed Consent Templates

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

IRB Administrator
Conducts pre-review and confirms that all required elements are present. Note any discrepancies on pre-review worksheet. Include pre-review worksheet in IRB member read-ahead packets for studies requiring review by the convened IRB.

Administrative Assistant
Once approval is granted, the Administrative Assistant will insert the date of IRB approval and the date of IRB expiration on all pages of the consent form. The dates of IRB approval and expiration will match the dates indicated in the approval letter.

The Administrative Assistant will stamp amended ICDs, when approved, retaining the original expiration date, unless the review period was changed.

IRB Member Assigned to Review
The Investigator’s plan to obtain informed consent should be assessed by the IRB, the Executive Chair, or her designee to assure the appropriate conditions are met.

The IRB should consider the nature of the proposed subject population, the type of information to be conveyed, and the circumstances under which the consent process will take place (e.g., manner, timing, place, personnel involved). All elements of consent as required by the Federal regulations, as well as any appropriate additional elements are incorporated into the documents.

Provisions have been made if the study is to include non-English speaking participants and the translated documents have been verified to be in a language understandable to the participant.

The IRB Reviewers must assure that provisions for surrogates are reviewed for appropriateness, when applicable.

The reviewers are to verify that the informed consent documents are congruent with the study protocol and IRB application. If not, the Reviewer or IRB will request revisions prior to granting final approval.

The Reviewers will assure that the written language is in lay terms and is understandable.

The IRB must review all modifications to the informed consent process or documentation. If the requested modifications change the risk/benefit ratio, the review must be conducted by the IRB and a determination of the necessity of re-consenting participants must also be rendered.

When the research includes children, the IRB must determine whether assent is required, for what ages assent is required, and how assent is to be documented.
Decisions to waive documentation of informed consent must be clearly documented in the IRB minutes.

**Administrative Assistant**
The Administrative Assistant will copy the date-stamped ICDs and the approval letter and verify the copies are reproducible. The Administrative Assistant will forward a copy of the date-stamped ICD and the approval letter to the Investigator.

The original of the date-stamped ICDs will be maintained in the IRB file.

6. **FURTHER GUIDANCE**

**Certificate of Confidentiality**

**Procedure:**
A Certificate of Confidentiality may be recommended by the IRB when the results of research participation would yield information in one or more of the following categories:

- HIV status, AIDS related complications, or other sexually transmitted diseases (STDs);
- Information relating to sexual attitudes, preferences, or practices;
- Information relating to the use of alcohol, drugs or other addictive products;
- Information pertaining to illegal conduct;
- Information that if released could reasonably be damaging to an individual’s financial standing, employability, or reputation within the community;
- Information that would normally be recorded in a patient’s medical record, and the disclosure of which could reasonably lead to social stigmatization or discrimination;
- Information pertaining to an individual’s psychological well-being or mental health;
- Information collected that may be considered sensitive in connection with behavioral research, interventions and epidemiologic studies; and,
- Genetic information.

How to apply for the Certificate of Confidentiality.

- It must be noted that the issuance of this certificate is up to the discretion of the NIH. If granted, the Certificate provides indefinite protection from compulsory disclosure, such as subpoena for research data.
- Applications for a Certificate of Confidentiality should be submitted to the NIH at least three (3) months prior to the date on which enrollment is expected to begin.
- The Investigator should notify the IRB that a Certificate of Confidentiality has been requested in the initial IRB submission.
- The Investigator must include language describing the Certificate of Confidentiality, as well as any voluntary disclosures, in the “Unforeseeable Risk” section of the informed consent document template.
- A copy of the IRB approval letter will be forwarded by the Investigator to the agency, in which the certificate was applied, for final review and determination.

**IRB Responsibilities.**

The IRB Reviewer will assure that the proposed research meets regulatory requirements for approval under 45 CFR 46.111, which includes provisions to protect the privacy of participants and confidentiality of data. This IRB determination will include the recommendation of a Certificate of Confidentiality when the proposed research includes sensitive information that may cause harm to the participant as a result of compelling disclosure.

The IRB Reviewer will review the informed consent documents to assure that a description of the Certificate of Confidentiality and any voluntarily, disclosure plans by the Investigator are appropriately described. The Reviewer will verify the appropriate template language is included in the ICD.
If the Investigator has not already applied for a Certificate of Confidentiality, upon its review of the research, the IRB may recommend that an Investigator apply for a Certificate of Confidentiality.

Administrator Responsibilities.

The IRB Administrator will conduct pre-review of the proposed research and consider the potential collection of sensitive information as defined and verify that a request for a Certificate of Confidentiality has been initiated.

The Administrator will consult with the Executive Chair or designee if the study contains sensitive information for guidance on whether the Investigator should be contacted and advised to initiate the request for a certificate, if he or she has not initiated such a request.

The Administrator will pre-review the informed consent documents to verify that a description of the Certificate of Confidentially is included, as well as any planned voluntary disclosures by the Investigator.

The Administrator will proceed with procedures for review and approval at the review level in which the study qualifies.

Calculating the “Date of IRB Approval” on the ICDs.

Approval at a convened meeting. When the convened IRB approves the IRB submission, the date of the convened IRB meeting is the “Date of IRB Approval” stamped on the informed consent document (ICD).

Approval pending changes at a convened IRB meeting. When the IRB application is approved with specific changes requested, pending review and approval by the Chair, the date that the changes are verified by the Chairperson or his or her designee is the “Date of IRB Approval” stamped on the ICDs.

Expeditied Review. When the IRB application is approved through an expedited review process, the date that final approval is extended by the Chairperson or his or her designee is the “Date of IRB Approval” stamped on the ICDs.

Modifications. The “Date of IRB Approval” for amended ICDs is based on the type of review or determination as described above. For example, when a modification is approved pending changes at a convened IRB meeting; the date that the changes are reviewed and approved by the Executive Chair Chair or is the date of IRB approval stamped on the informed consent documents.

Calculating the “Date of IRB Expiration” on the ICDs.

Approval at a convened IRB meeting. Based on the approval period granted, the date of expiration is calculated from the date of the convened IRB. For example, if the IRB meeting date is 12/01/2003, then the “Date of IRB Expiration” is 11/30/2004 for a 12 month review interval.

Approval pending changes at a convened IRB meeting. Based on the approval period granted, the date of expiration is calculated from the date of the convened IRB meeting. It is not calculated from the date the Chair or her designee verifies and grants final approval. For example, if the IRB approves pending changes on 12/01/2003 and the response is verified by the Chair on 3/1/2004, then the “Date of IRB Expiration” for a 12 month review interval and 11/30/2004.

Expeditied review. Since there is no convened meeting in an expedited review, the “Date of IRB Expiration” will be calculated based on the review interval determined by the Chair or his or her designee using the date that the initial submission or most recent Continuing Review was approved by the Executive Chair or her designee.

Modifications. The approval date of a modification does not affect the calculation of the expiration date unless the IRB increases or decreases the review interval.
IC 704

ASSENT

1. PROCESS OVERVIEW

2. RESPONSIBILITY
During the pre-review process, the IRB Administrator is responsible for determining whether assent is indicated and is responsible for communicating assent requirements to the investigator, as appropriate.

3. TOOLS

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Primary Reviewer
When research involves children, ensure that assent process and forms, if any, are appropriate.

5. FURTHER GUIDANCE

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.

These Federal regulations go on to state that "adequate provisions" must be made for soliciting the assent of children, when the IRB determines that they are capable of participating in such a process based on their age, maturity, and state of mind.

Before the process can begin, parents or guardians must give permission for their children to participate. Then, the child or teenager may be provided with a form that explains, in concrete and age-appropriate terms, the purpose of the research, what they will be asked to do, and what procedures they will undergo. For older adolescents (ages 16 or older), this might look very much like the adult informed consent document. For younger children, the terms and explanations will be greatly simplified into words they can understand.

When children or minors are involved in research, the regulations require the assent of the child or minor and the permission of the parent(s), in place of the consent of the subjects.

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 their parents or legally authorized representatives. The IRB must determine whether the permission of both parents is necessary, and the conditions under which one parent may be considered "not reasonably available" [§46.408 and §50.55]. In addition, the regulations require that the IRB 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.

The regulations provide that an IRB may find that the permission of one parent is sufficient for research to be conducted under [§46.404 /§50.51] and (minimal risk research) or §46.405/ §50.52 (research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects).

Where research is covered by §46.406 - 46.407/§50.53 – 50.54 and permission is to be obtained from parents, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child §46.408(b)/ §50.56

While children may be legally incapable of giving informed consent, they nevertheless may possess the ability to assent to or dissent from participation. Out of respect for children as developing persons, children should be asked
whether or not they wish to participate in the research, particularly if the research: (1) does not involve interventions likely to be of benefit to the subjects; and (2) the children can comprehend and appreciate what it means to be a volunteer for the benefit of others.

The IRB must determine for each protocol - depending on such factors as the nature of the research and the age, status, and condition of the proposed subjects - whether all or some of the children are capable of assenting to participation. Where appropriate, IRBs may choose to review on a case-by-case basis whether assent should be sought from given individual subjects. The federal regulations do not require that assent be sought from children starting at a specific age, but that their assent should be sought when, in the judgment of the IRB, the children are capable of providing their assent. IRBs are to take into account the ages, maturity, and psychological state of the children involved.

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 must also determine that the provisions for obtaining and documenting assent are adequate. The child should be given an explanation of the proposed research procedures in a language that is appropriate to the child's age, experience, maturity, and condition. This explanation should include a discussion of any discomforts and inconveniences the child may experience if he or she agrees to participate.

The federal regulations require that all research activities must comply not only with the regulations but also with the law of the state in which they are performed.
RI 801 IRB-REQUIRED INVESTIGATOR ACTIONS

1. PROCESS OVERVIEW

2. RESPONSIBILITY
IRB Administrator (or equivalent) is responsible for tracking Investigator compliance with IRB requirements stipulated during the IRB’s review of the Investigator’s research.

Executive Chair (or designee) is responsible for facilitating Investigator compliance with IRB requirements through his/her management of IRB deliberations.

3. TOOLS

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

IRB Administrator
Provide Investigators with assistance on preparing IRB submissions, securing initial and ongoing approval of research, and providing all required reports.

Contact Investigators as often as needed to assist in the development of submission materials and to secure all necessary information for ongoing IRB review and approval.

Executive Chair and IRB Administrator
Provide Investigators with appropriate guidance in preparing IRB submissions and in conducting the informed consent process and other subject protection activities.

Administrative Assistant
Distribute communications to and from Investigators to appropriate IRB staff and members in a timely manner.
1. PROCESS OVERVIEW
Describe procedures to assist the IRB management in maintaining and ensuring the effectiveness of the human research protection program.

2. RESPONSIBILITY
The Executive Director, Human Research Protection is responsible for implementation of the QA/QI program. All staff and IRB members are responsible for contributing to the effectiveness of the QA/QI program.

3. TOOLS

4. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Executive Director, Associate Director
Determine internal auditing plan and schedule.

Administrative Coordinator for QA and Assigned IRB Administrators and Administrative Assistants
Perform QA monitoring of daily IRB operations and documentation to assess compliance with IRB policies and procedures.

Communicate results to the Associate Director.

Associate Director
Determine root causes and appropriate plans for deficiencies reported at these meetings.

Communicate finding to Executive Director, IRB Executive Chair, and IRB administrative staff.

Develop process and implement process improvement plans.