LANCASTER GENERAL HEALTH

HUMAN RESEARCH PROTECTION PROGRAM

POLICY AND PROCEDURE MANUAL

Contents

400 – Institutional Review Board Processes

500 – Ethical Consideration

600 – Research Involving Drugs, Biologics, or Devices

700 – Corrective Actions

Penn Medicine
Lancaster General Hospital

POLICY TITLE: **Human Research Protection Program** **Policy No. 101**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 10/23/15, 02/04/16, 06/22/17, 01/21/19, 01/10/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The Lancaster General Health (LG Health) Human Research Protection Program (HRPP) ensures that all human subject research conducted at LG Health complies with federal and state laws and regulations and ethical standards to safeguard the welfare of human research subjects. In addition, the LG Health HRPP will comply with the International Conference on Harmonization Good Clinical Practices ("ICH-GCP") guidelines when required by protocols conducted under the HRPP.

APPLICABILITY/SCOPE/EXCLUSIONS: This policy applies to all employees, Medical and Dental Staff members, agents, volunteers and students who conduct human subject research under the auspices of LG Health.

POLICY STATEMENTS: LG Health promotes human subject research to advance knowledge and improve patient care. To safeguard the health and welfare of human research subjects, all human subject research conducted under the auspices of LG Health must comply with all applicable federal and state laws and regulations, ethical standards, including, the Declaration of Helsinki, and all other requirements established by the LG Health HRPP. In addition, LG Health is covered by a Federalwide Assurance (FWA), FWA00006038, approved by the Office for Human Research Protections (OHRP). LG Health has designated the Lancaster General Hospital (LGH) Institutional Review Board (IRB), assurance #IRB00000015, to review all human subject research at LG Health. When required or appropriate, LG Health may also choose to rely on another IRB. No human subject research may commence without prior approval of the designated IRB of record.

PROCEDURES

1. **Designation of Institutional Official.** The LG Health Vice President of Research Administration is designated as the LG Health Institutional Official responsible for carrying out the LG Health HRPP. The Institutional Official ensures the LG Health HRPP has the resources and support necessary to effectively safeguard the health and welfare of human research subjects. The Institutional Official is authorized to represent LG Health relating to human subject research conducted at LG Health. The Institutional Official shall be accessible to investigators and employees for purposes of the HRPP. The duties and responsibilities of the Institutional Official shall be further defined in the Institutional Official's Job Description. The Institutional Official has the authority to take action, as necessary, to ensure the protection of human subjects, the integrity of research and the HRPP, the autonomy and authority of the IRB, the proper conduct of research, and to ensure compliance with regulatory and other requirements. This includes the authority to suspend, terminate, or disapprove research, to sanction or restrict research privileges, and to disallow or restrict the use of research data. Such actions will be reported to the HRPP and IRB when appropriate (e.g., so that the HRPP and IRB may take any necessary actions to ensure the protection of human subjects).

2. **Review of Human Subject Research**

   a. All human subject research conducted at LG Health, including research that qualifies for exempt status, must be first approved by the IRB. The investigator must submit a research application to the IRB prior to commencing any human subject research at LG Health. The IRB shall maintain policies and procedures, consistent with federal and state laws and regulations, describing the application and review process of human subject research. The IRB shall approve or disapprove each proposed human subject research project.

b. The IRB also may refer a protocol for which there are particular concerns about risk (e.g., a phase I study of a new chemotherapeutic drug) for further institutional review. In such a case, the protocol would be reviewed first by the LG Medical Executive Committee and then by the Lancaster General Hospital Board of Trustees. Both of these entities would need to approve the project in addition to the IRB.

c. No human subject research project that has been disapproved by the IRB may be approved by any other person, committee, board, or other institutional body. A human subject research project that has been disapproved by the IRB cannot be conducted at LG Health.

d. The IRB or the Chair of the IRB shall have authority to suspend or terminate IRB approval or human subject research, including research that qualifies for exempt status, at any time when the IRB or the Chair of the IRB has reasonably determined that the human subject research poses serious, unexpected harm to human subjects or does not comply with the requirements of the IRB, federal or state laws and regulations, or ethical standards.

e. The IRB may require an investigator to modify the human subject research project to secure approval of the research by the IRB.

f. The LG Health HRPP, including the IRB, is authorized to continuously monitor approved human subject research projects to verify that the research complies with the LG Health HRPP. The LG Health HRPP may also use outside, third parties to observe human subject research, including the consent process, to ensure compliance with the LG Health HRPP.

g. The IRB Office shall provide guidance to individuals to determine whether a proposed activity constitutes human subject research. For example, most peer review activities, quality review activities, and surveillance activities do not constitute human subject research and are not subject to this Policy. Additional information on research determinations can be found in LG Health HRPP Policy 203.

h. In the event an investigator desires to conduct transnational research under the auspices of LG Health, LG Health and the IRB will develop policies and procedures for the proper conduct of the transnational research or designate an appropriate external Institutional Review Board to be the IRB of record. In such circumstances, the investigator desiring to conduct transnational research shall notify the Institutional Official, the CEO of LG Health, the IRB Chair, and LG Health Legal Services.

i. LG Health and investigators are considered engaged in human subjects research, and come under the requirements of the IRB, when LG Health or investigators, as part of the research, obtain: (i) data about subjects of the research through intervention or interaction with them; (ii) identifiable private information about the subjects of the research; or (iii) the informed consent of human subjects for the research. In addition, if LG Health receives an award through a grant, contract, or cooperative agreement directly from the Department of Health and Human Services for non-exempt human subject research, LG Health is considered engaged in research, even if all activities involving human subjects are carried about by investigators, employees, or agents of another institution.

j. When research is not subject to the Common Rule or FDA regulations, LGH ensures that research subjects benefit from equivalent protections by applying the revised Common Rule standards (also known as the 2018 requirements) to the review and oversight of the research. The standards of the revised Common Rule are applied to research both prior to and following the effective date of the revised rule.

3. **Ethical Standards.** All human subject research conducted at LG Health must meet ethical standards adopted by the LG Health HRPP. The IRB Office shall make available to all investigators and research staff all HRPP and IRB policies and procedures, approved ethical standards, and other components of the LG Health HRPP. All investigators have an ongoing duty to maintain an understanding of all current components of the LG Health HRPP. The LG Health HRPP has adopted the following ethical standards, as set forth in the Belmont Report:

a. Respect for Persons: Voluntary participation of human subjects is assured and informed consent is obtained

b. Beneficence: Appropriate balance between benefits of research to the human subject or society and risks assumed by the human subject
c. Justice: Fair procedures exist in the selection of human subjects for research

4. **Prohibition on Undue Influence.** No investigator, researcher, or other staff shall act in such a manner as to unduly influence the IRB or any IRB member regarding any action by the IRB relating to a human subject research project. Any IRB member or other individual who reasonably believes that an investigator, researcher, or other staff engaged in conduct to unduly influence the IRB or an IRB member shall immediately report the conduct to the Chair of the IRB, the Institutional Official, the President of LG Health, or the LG Health Compliance Hotline. The IRB shall immediately investigate the alleged conduct and determine whether the investigator, researcher, or other staff unduly influenced the IRB or an IRB member. The IRB may take any such action as it reasonably determines is appropriate to remedy any alleged undue influence. The IRB is further authorized to notify the Medical Executive Committee or Human Resources, as the IRB deems appropriate.

5. **Education.** The LG Health HRPP shall provide ongoing educational activities for IRB members, investigators, researchers, and other staff regarding human subject research. The educational activities will provide information on ethical standards, criteria for approving human subject research, and other applicable information necessary for the LG Health HRPP to protect the health and welfare of human research subjects. The LG Health IRB Office shall maintain documentation relating to the educational activities, including attendance. The IRB shall develop policies and procedures for educating new members of the IRB. For additional information regarding education of investigators, IRB members, and research staff, please refer to the Duties of the Research Quality Assurance Office Policy.

6. **Conflicts of Interest.** To ensure the integrity of human subject research, no: (i) LG Health director, officer, or employee; (ii) IRB member; or (iii) investigator, researcher, or research staff shall have a non-resolvable conflict of interest, financial or otherwise, in relation to a human subject research project at LG Health. The HRPP shall develop policies and procedures that describe reporting of financial interests and resolution of conflicts of interests of investigators, research staff, and IRB members. Any conflict of interest that cannot be resolved shall be reported to both the President and General Counsel of LG Health. Any conflict of interest reported to the President and General Counsel of LG Health will be evaluated and managed in accordance with the LG Health Conflict of Interest Policy. For the purpose of this Policy, "conflict of interest" shall have the meaning as described in the LG Health Conflict of Interest Policy.

7. **Conflicting Laws.** LG Health will comply with all federal and state laws and regulations applicable to human subject research. In the event of conflict between federal and state, or other laws, LG Health Legal Services must be contacted to advise on resolution of the conflict. LG Health Legal Services shall also serve as a resource for the interpretation and application of state laws as they apply to human subject research.

8. **Subject Outreach.** LG Health is committed to informing prospective research subjects, research subjects, and others about research conducted under the auspices of LG Health. LG Health will maintain a public internet site which will include, at a minimum, the following information:

- Brochure(s) and link(s) on what it means to be a research subject;
- A list of all current research protocols at LG Health;
- Contact information for individuals to ask questions, file complaints, or offer suggestions regarding research at LG Health; and
- Links to other websites, as appropriate, to provide information about research.

As part of LG Health's HRPP evaluation, LG Health will monitor and update, as necessary, its website and subject outreach. LG Health will make changes or updates to its outreach to ensure that prospective research subjects, research subjects, and others have appropriate information and resources to understand research.

ROLES/REPONSIBILITIES

1. The Vice President of Research Administration, as Institutional Official, shall oversee the LG Health HRPP and ensure that all human subject research conducted at LG Health complies with all federal and state laws and regulations and ethical standards to safeguard the health and welfare of human research subjects.

2. The LG Health IRB shall implement policies and procedures, consistent with federal and state laws, establishing the application and review process of proposed human subject research, including research that qualifies for exempt status. The IRB shall approve, require modifications, or disapprove all proposed human subject research projects.

3. The LG Health HRPP shall implement policies and procedures governing research with human subjects to ensure compliance with federal and state laws and regulations and shall review and approve revisions to such policies and procedures. All LG Health HRPP policies and procedures shall be available on the LG Health Research Institute website. The LG Health HRPP will keep IRB members as well as investigators, research staff, and other individuals engaged in human subject research apprised of new information and revisions to applicable policies and procedures. Material revisions to HRPP policies and procedures will be communicated to IRB members during IRB meetings and to investigators and research staff by email, in-person education sessions, or other appropriate communication methods.

4. The LG Health IRB Office is responsible for accepting applications for human subject research projects, communicating substantial revisions of HRPP and IRB policies and procedures to IRB members, investigators, and other research staff, and ensuring the IRB functions in an efficient manner.

5. Investigators and others involved in the conduct of research are responsible for obtaining IRB approval or determination of exempt status before initiating research activities and for conducting research in accordance with LG Health's ethical standards and policies, applicable rules and regulations, and the requirements and determinations of the IRB

DEFINITIONS

Research: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this policy, the following activities are deemed not to be research:

a) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
b) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or

investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

c) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
d) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

The Food and Drug Administration (FDA) defines "Research" as being synonymous with the term "clinical investigation." A clinical investigation is any experiment that involves a test article and one or more human subjects and that either meet the requirements for prior submission to the FDA under Section 505(i) or 520(g) of the Food, Drug, and Cosmetic Act or need not meet the requirements for prior submission to the FDA, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for research or marketing permit.

Human Subject: A living individual about whom an investigator (whether professional or student) who is conducting research:

a) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
b) Obtains, uses, studies, analyzes, or generates identifiable private health information or identifiable biospecimens.

For research covered by the FDA, Human Subject means an individual who is or becomes a subject in a clinical investigation, either as a recipient of the test article or as a control. In the case of a medical device, a Human Subject also includes any individual on whose specimen an investigational device is used or tested or used as a control (regardless of whether the specimens are identifiable).

Intervention: Physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction: Communication or interpersonal contact between investigator and subject.

Private information: Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).

Identifiable private information: Private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

Identifiable biospecimen**:** A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Clinical Trial: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions

on biomedical or behavioral health-related outcomes.

Test Article: Any drug, medical device for human use, human food additive, color additive, electronic product, or other article, subject to regulation by the FDA. Test articles covered by the FDA include, but are not limited to, the following:

- Human Drugs: The primary intended use of the product is achieved through chemical action or by being metabolized by the body. A drug is defined as a substance recognized by an official pharmacopoeia or formulary; a substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; a substance (other than food) intended to affect the structure or any function of the body; a substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device. Biological products are included within this definition and are generally covered by the same laws and regulations, but differences exist regarding their manufacturing processes (chemical process versus biological process.) *http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm*
- Medical Devices: A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes." *http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm*
- Biological Products: A wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available. *http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm*
- Food Additives: A food additive is defined in Section 201(s) of the FD&C Act as any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristic of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use); if such substance is not Generally Recognized As Safe (GRAS) or sanctioned prior to 1958 or otherwise excluded from the definition of food additives. *http://www.fda.gov/Food/IngredientsPackagingLabeling/Definitions/default.htm*
- Color Additives: A color additive is any dye, pigment or substance which when added or applied to a food, drug or cosmetic, or to the human body, is capable (alone or through reactions with other substances) of imparting color. Color additives for use in food, drugs, and cosmetics require premarket approval. Color additives for use in or on a medical device are subject to premarket approval, if the color

additive comes in direct contact with the body for a significant period of time. http://www.fda.gov/Food/IngredientsPackagingLabeling/Definitions/default.htm

- Foods: Foods include dietary supplements that bear a nutrient content claim or a health claim.
- Infant Formulas: Infant formulas are liquid foods intended for infants which substitute for mother's milk.
- Electronic Products: The FDA regulates certain classes of electronic products including radiation-emitting electronic products such as microwaves and x-rays.
- Systematic Investigation: A methodical approach to quantitatively or qualitatively testing a hypothesis or research question by collecting and analyzing data with an intent of drawing a conclusion. Systematic investigations can include, but are not limited to, drug trials, device trials, social/behavioral experiments, surveys, questionnaires, interviews, and observation.
- Generalizable Knowledge: Information or data where the research findings can apply to a population beyond the research subjects themselves and contribute to current academic understanding. Generalizable knowledge refers to dissertation or thesis, oral presentations, poster presentations, publications.

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATION(S)

45 CFR § 46.102
AAHRPP Standards I.1.A, I.1.B, I.1.C, I.1.D, I.1.E, I.1.G, I.2, I.3, I.4.B, III.1.A, and III.2.A

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Evaluation of the Human Research Protection Program Policy No. 102	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 10/23/15, 8/31/17, 09/26/22**
Policy Owner: Edmond K. Kabagambe, DVS, MS, PhD, MBA	

POLICY PURPOSE: To ensure ongoing compliance of the Lancaster General Health (LG Health) Human Research Protection Program (HRPP) with applicable laws, regulations, ethical standards, and accreditation standards and to evaluate the quality, efficiency, and effectiveness of the LG Health HRPP with respect to human subject research conducted at LG Health.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to the LG Hospital Institutional Review Board (IRB), the LG Health Institutional Official, and investigators and other research staff engaged in human subject research at LG Health.

POLICY STATEMENT: Periodically, but not less than annually, the HRPP Leadership Committee shall engage in a review of the LG Health HRPP to ensure the LG Health HRPP complies with all applicable laws, regulations, ethical standards, and accreditation standards and the ensure the LG Health HRPP promotes the health and welfare of human research subjects. The HRPP Leadership Committee shall be composed of the Institutional Official, leadership of the LG Research Institute and its Research Quality Assurance Office, and IRB leadership and counsel.

PROCEDURES

1. The LG Health HRPP Leadership Committee shall conduct an evaluation of the LG Health HRPP. The purpose of the HRPP evaluation is 1) to review specific metrics regarding HRPP resources and regarding the compliance with and the quality, efficiency, and effectiveness of the HRPP, and 2) to identify needs and opportunities and set goals to improve the HRPP.

2. The HRPP evaluation can include audits, surveys, and other methods to monitor and review specific aspects of the LG Health HRPP. Components of an evaluation may include the following:

    - Review of all human subject research policies, procedures, checklists, and other documentation
    - Review of applicable laws, regulations, ethical standards, and accreditation standards
    - Metrics to measure benchmark standards for quality, efficiency, and effectiveness and to assess progress of the HRPP
    - Audit of IRB minutes and documentation
    - Review of IRB member composition and IRB workload
    - Review of human subject research education and outreach activities
    - IRB self-assessment
    - Review of resources allocated to the HRPP (e.g., staffing, space, technology materials, finances)

3. As part of each review, at least one goal for improving the quality, efficiency, and effectiveness of the HRPP will be developed, along with metrics for assessing achievement of the goal(s) at the subsequent evaluation.

4. As part of each review, at least one goal for improving compliance at LG Health will be developed, along with metrics for assessing achievement of the goal(s) at the subsequent evaluation.

5. If needs for education and training are identified, these will be implemented to ensure that all parties engaged in research understand their obligations under the LG Health HRPP.

6. Investigators and research staff shall be requested to offer input on the function and effectiveness of the LG Health HRPP and IRB.

7. To the extent possible, the HRPP leadership should seek input from human research subjects regarding the effectiveness of the LG Health HRPP and IRB.

8. The Administrative Director of the Research Institute shall be responsible for oversight of the evaluation of the HRPP. If opportunities for improvement are identified through the evaluation process, the Administrative Director of the Research Institute will ensure that improvement programs are implemented.

ROLES/REPONSIBILITIES

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATION(S)

AAHRPP Standards I.1.D, I.2, I.4.B, I.5.A, I.5.B, I.5.C, and III.2.A

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Duties of the Research Quality Assurance Office **Policy No. 103**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 09/18/14, 01/01/15, 6/22/17, 10/15/18, 09/26/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy defines the duties of the Research Quality Assurance Office.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at LG Health and to members of the IRB.

POLICY STATEMENTS: The primary function of the Research Quality Assurance Office (RQAO) is to monitor the conduct of clinical research, in order to assure protection of the rights and welfare of research subjects and adherence to federal, state and local laws, institutional policies and the research protocol(s). The RQAO also ensures adequate education and training of the individuals engaged in human subject research and seeks out opportunities for continuous quality improvement within clinical research at LG Health.

PROCEDURES

1. Organizational Reporting
    a. The RQAO reports to the Human Research Protection Program Institutional Official – Vice President of Research Administration.
    b. The activities of the RQAO are governed by the Research Compliance Committee. This committee comprises the Administrative Director of the Lancaster General Research Institute; Vice President of Risk Management and Corporate Compliance; Senior Vice President, General Counsel; Vice President of Research Administration; Medical Director of the LG Research Institute; and Executive Director of the Ann B. Barshinger Cancer Institute.
    c. At any time the RQAO identifies an immediate subject safety concern, the finding(s) will be reported directly to the Human Research Protection Program Institutional Official and the IRB Chair.
    d. Findings by the RQAO will be reviewed by the Research Compliance Committee. The Research Compliance Committee will report cases of non-compliance to the IRB and provide recommendations for corrective action. The IRB reviews cases to make a final determination as to whether non-compliance is serious or continuing and establishes a corrective action plan.
    e. A representative of the RQAO, typically the HRPP / IRB Manager, attends meetings of the IRB and the RCC to address current concerns identified through the monitoring procedures outlined in this Policy.
    f. Findings by the RQAO may be further reported and triaged by the Research Compliance Committee to the Audit and Compliance Committee.
2. Training/Education
    a. The RQAO will administrate use of the CITI Program coursework for training and certification of the IRB Chair, IRB members and LG Health research personnel.

i. A new IRB chair, new IRB member or new researcher identified on an IRB application will be assigned required modules to be completed for certification before commencement of IRB or research duties and responsibilities.

ii. Renewal of all certifications will be required every 3 years.

iii. HRPP Manager shall be responsible for monitoring certifications of researchers by running monthly reports from CITI database.

iv. Failure by researchers to maintain certifications will result in initial approval or continuing review approval being withheld or by cessation of individual research activities, as applicable.

v. Failure by IRB members to maintain certifications will result in recusal from IRB activities.

b. The RQAO will organize education sessions for the IRB, typically in conjunction with scheduled meetings.

c. The RQAO will facilitate educational sessions or seminars to address real-time institutional needs.

3. Routine On-Site Review

a. For studies with ongoing data collection, the RQAO will conduct routine on-site reviews according to the following tiered approach:

Tier 1: Tier 1 studies are defined as investigator-initiated and greater than minimal risk. These studies will be identified at the time of IRB review. The intent is to conduct an on-site review of 100% of these studies within 1 year of the start of subject enrollment.

Tier 2: Tier 2 studies are defined as externally sponsored and greater than minimal risk, not monitored on-site by any Sponsor representative. These studies will be identified at the time of IRB review. The intent is to conduct an on-site review of 100% of these studies within 1 year of the start of subject enrollment.

Tier 3a: Tier 3a studies are defined as externally sponsored and greater than minimal risk, monitored on-site by a Sponsor representative. A sampling of these studies will be chosen for on-site review at the time of IRB review. The focus of the review will be aspects less likely to be monitored by the Sponsor, such as recruitment activities, the consent process, and medical record documentation of research activities. IRB reporting will also be monitored to ensure consistent application of the LG Health IRB policy. Tier 3a studies will not be reviewed more than once without cause.

Tier 3b: Tier 3b studies are defined as low/minimal risk. A sampling of these studies will be chosen for on-site review at the time of IRB review. The focus of the review will be on data security. Tier 3b studies will not be reviewed more than once without cause.

b. On-site review is mandatory for those studies selected; however, the review will be scheduled at a time that is convenient to the Principal Investigator, but must be completed within 3 months of notification.

c. A review template outlining the objectives of the visit will be provided by the RQAO within 30 days prior to the scheduled review.

d. A report outlining the findings, recommendations, and/or corrective actions, as needed, resulting from the routine, on-site review will be completed by the RQAO within 30 days after the scheduled review. The report will be provided to the Principal Investigator and to any other person supervising

study personnel. The report or summary findings also will be shared with the Research Compliance Committee.

4. For-Cause Review

   a. The RQAO will conduct a for-cause review of a study at the request of the IRB or the Research Compliance Committee if:

      i. the investigator and/or research staff have demonstrated poor adherence to IRB policies and/or procedures;

      ii. a credible internal complaint has been reported (i.e., from a research subject or family member, LG Health personnel);

      iii. an external complaint has been reported (i.e., from OHR, the FDA or a Sponsor) of a significant protocol violation involving issues of patient safety, privacy or confidentiality, regulatory non-compliance or Scientific misconduct.

   b. A report outlining the findings, recommendations, and/or corrective actions, as needed, resulting from the for-cause review will be completed by the RQAO within 30 days after the scheduled review. The report will be provided to the Principal Investigator and to the Research Compliance Committee.

5. IRB Review

   a. The RQAO conducts periodic, routine review of the IRB to assess compliance with federal, state and local laws and LG Health policies.

   b. The RQAO examines IRB records for inclusion of required documents such as protocols, investigator brochures, consent documents, recruitment materials, subject injury reports, unanticipated problems, progress reports, data and safety monitoring reports, new findings, and all correspondence between the IRB and researchers.

   c. The RQAO examines IRB minutes for required elements, such as documentation of attendance, recusals, deliberations, controverted issues and resolutions, votes, actions taken, the basis for actions taken, and approval periods.

   d. The RQAO may identify opportunities for improvement and suggest modified processes for adherence to current policies.

6. Research Subject Complaints

   a. The RQAO manages and performs the initial investigation of all research subject complaints reported to the IRB Chair, via the Research Institute website, directly to the Investigator and/or research staff, or via other documented means.

   b. For serious complaints (e.g., complaints of study-related injury, safety concern, violation of subjects' rights, etc.), the RQAO will involve other institutional entities as appropriate (*e.g.*, Legal Services, the IRB, Risk Management, Medical and Dental Staff Office).

   c. The RQAO will report all complaints and resulting actions to the Research Compliance Committee on a quarterly basis.

7. Indirect Monitoring of Clinical Research

   a. The RQAO compiles and assesses Data and Safety Monitoring Board reports. Any immediate subject safety concerns will be reported directly to the Human Research Protection Program

Institutional Official and the IRB Chair. Other pertinent, but non-immediate concerns will be summarized and reported to the IRB for review.

b. The RQAO compiles and assesses reports of external monitors (i.e., typically Sponsor representatives). Any immediate subject safety concerns will be reported directly to the Human Research Protection Program Institutional Official and the IRB Chair. Other pertinent, but non-immediate concerns will be summarized and reported to the IRB for review.

8. Financial Conflict of Interest

a. The RQAO is responsible for gathering Financial Conflict of Interest Forms from the IRB Chair, IRB members and LG Health research personnel.

b. The RQAO will review the Financial Disclosure Forms on record for project personnel at the time of IRB submission and compile Significant Financial Interests for referral to the Research Compliance Committee. The Research Compliance Committee is responsible for determining whether any Significant Financial Interests constitute a Financial Conflict of Interest and for recommending management plans to the IRB as needed (see policy 'Conflicts of Interest in Research').

ROLES/REPONSIBILITIES

DEFINITIONS

REFERENCE DOCUMENTS

Research Quality Assurance On-Site Review Form
Research Quality Assurance IRB Review Form

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standards I.1.E, I.4.A, and I.5.A.

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Responsibilities of Research Investigators Policy No. 104	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 02/04/16, 10/30/17, 03/6/18, 1/29/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: To establish the responsibilities of investigators and research staff conducting research under the auspices of Lancaster General Health (LG Health).

APPLICABILITY/SCOPE/EXCLUSIONS: This policy applies to all investigators and research staff who conduct human subject research under the auspices of LG Health.

POLICY STATEMENTS: In the conduct of research, investigators and research staff will comply with all requirements of this Policy, all applicable policies of the LG Health Human Research Protection Program, all applicable federal and state laws and regulations, and all ethical principles related to the conduct of human subject research.

PROCEDURES

1. **Designation of Principal Investigator and Sub-Investigators.** Each protocol must identify an individual who has primary and ultimate responsibility for the conduct of research activities. This individual may be identified as the Principal Investigator (PI). In the event a research protocol requires skills or experience beyond those held by the PI, the protocol must be modified or an individual who maintains the requisite skills or experience must be identified as a sub-investigator.

   A protocol may also identify any number of sub-investigators who assist the PI in the conduct of the study. The involvement of sub-investigators may include the following activities:
   - Obtaining information about individuals through interactions for research purposes;
   - Obtaining health information or other private information about individuals for research purposes;
   - Obtaining informed consent from individuals to participate in the research, in compliance with the policy Informed Consent and HIPAA Authorization Requirements; and
   - Analyzing data for research purposes.

2. **Responsibilities of Investigators.** Each investigator (i.e., the PI and sub-investigators) must comply with the following requirements during the conduct of research:

   a. Protect the rights, safety, and welfare of research subjects and comply with applicable state and federal regulations and all LG Health policies regarding these protections;

   b. Develop and conduct research that is in accordance with the ethical principles in the Belmont Report;

   c. Develop a research plan that is scientifically sound and minimizes risk to the subjects;

   d. Incorporate into the research a plan to ensure the just, fair, and equitable recruitment and selection of subjects;

   e. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, include additional safeguards in the study to protect the rights and welfare of these subjects;

   f. Ensure that the research includes adequate provisions for the monitoring of subjects and data to ensure the safety of subjects;

g. Ensure that there are adequate provisions to protect the privacy interests of subjects;

h. Ensure that there are adequate provisions to protect the confidentiality interests of subjects, including an information security plan that considers the collection, storage, maintenance, analysis, and transmission of data and other identifiable information;

i. Ensure that there are sufficient resources necessary to protect human subjects, including:

- Access to a population that would allow recruitment of the required number of subjects;
- Sufficient time to conduct and complete the research;
- Adequate numbers of qualified staff;
- Adequate facilities;
- Necessary equipment;
- A plan to ensure proper supervision of the research including a plan for periods of absence or decreased availability; and
- Availability of medical, psychological, or other support that subjects might require during or as a consequence of their participation in the research.

j. Ensure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified and licensed to perform the procedures;

k. Ensure that all study personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles;

l. Ensure that all persons assisting with the research are adequately trained and informed about the protocol and their specific duties and functions;

m. Promptly report any changes in, additions to, or loss of investigators or research staff to the Institutional Review Board (IRB) for evaluation and approval;

n. Ensure that when private health information is used that legally effective HIPAA authorization is obtained for each subject unless the IRB has approved a waiver of the requirement;

o. Ensure that the language in the consent form is consistent with that in the protocol and, when applicable, in the HIPAA authorization;

p. Obtain and document informed consent according to HRPP policies and ensure that no human subject is involved in the research prior to obtaining their consent or consent/permission from their legally authorized representative, unless a waiver of the requirement has been approved by the IRB;

q. Have a procedure to receive questions, complaints, or requests for additional information from subjects and respond appropriately;

r. Ensure that all information provided to the IRB is accurate and complete so that the IRB may fulfill its responsibilities to review the research and make the required determinations;

s. Ensure that all research involving human subjects receives IRB review and approval in writing or a determination of exemption before commencement of the research;

t. Comply with all IRB decisions, conditions, and requirements;

u. Ensure that protocols receive timely continuing IRB review and approval;

v. Report unanticipated problems, deviations, complaints, non-compliance, suspensions, terminations, and any other reportable events to the IRB;

w. Notify the IRB if information becomes available that suggests a change to the potential risks or benefits of the research;

x. Obtain IRB review and approval before changes are made to the research unless a change is necessary to eliminate apparent immediate hazards to the subject(s), in which case the change must be reported to the IRB as soon as possible;

y. Seek organizational or IRB assistance when in doubt about whether proposed research requires IRB review;

z. Ensure that records are retained for the time period and in the manner required by applicable regulations, contractual agreements, and organizational policies;

aa. Ensure that the study procedures that the Principal Investigator delegates to others, such as obtaining consent or performing a protocol required exam or procedure, are prospectively documented in writing; and

ab. During clinical trials conducted in accordance with the International Conference on Harmonisation's Good Clinical Practice (GCP or ICH E6) guidelines, ensure that:

- The clinical trial's randomization procedures, if any, are followed, that the code is broken only in accordance with the protocol, and, when the clinical trial is blinded, that premature unblinding is promptly documented and explained to the sponsor;
- The researcher is familiar with the appropriate use of the investigational product, as described in the protocol, in the current investigator brochure, in the product information, and in other information sources provided by the sponsor;
- A qualified provider (physician or dentist, when appropriate), who is a researcher or a co-researcher for the clinical trial, is responsible for all clinical trial-related medical or dental) decisions.
- Adequate medical care is provided to a subject for any adverse events, including clinical significant laboratory values, related to the clinical trial;
- Researchers inform subjects when medical care is needed for other illnesses of which the researchers become aware;
- The subject's primary physician is informed about the subject's participation in the clinical trial if the subject has a primary physician and if the subject agrees to the primary physician being informed;
- A reasonable effort is made to ascertain the reason when a subject withdraws prematurely from a clinical trial, while fully respecting the subject's rights and understanding that the subject is not obliged to give their reasons for withdrawing;
- If the researcher terminates or suspends a clinical trial without prior agreement of the sponsor, the researcher informs the organization, sponsor, and IRB;
- The researcher reports all serious adverse events (SAEs) to the sponsor except for those SAEs that the protocol or other document (e.g., investigator's brochure) identifies as not needing immediate reporting. The researcher follows regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB;

- The researcher reports adverse events or laboratory abnormalities identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol;
- For reported deaths, the researcher supplies the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports);
- The researcher provides written reports to the sponsor, the IRB, and, where applicable, the organization on any changes significantly affecting the conduct of the clinical trial or increasing the risk to subjects;
- If the IRB terminates or suspends approval of the clinical trial, the researcher promptly notifies the sponsor;
- The researcher ensures the accuracy, completeness, legibility, and timeliness of data reported to the sponsor;
- When required or requested by a sponsor, the IRB, or a regulatory authority (e.g., the FDA), researchers provide evidence of their qualifications such as an up-to-date curriculum vitae, licensure, or other relevant documentation; and
- Upon completion of the clinical trial, the researcher informs the organization, provides the IRB with a summary of the trial's outcome, and provides regulatory authorities with any required reports.

3. **Research Records.** Investigators must maintain and retain research records in accordance with regulatory, sponsor, and LG Health requirements. At a minimum, all research records must be retained for six (6) years from the completion of the research. All research records must be securely maintained and be made available when requested by appropriate oversight organizations or agencies. Research records that must be maintained include, but are not limited to, subject records, recruitment materials, completed consent forms, unanticipated event reports, subject complaints, research results, all versions of protocols, amendment, correspondence to and from the IRB, and continuing review progress reports.

4. **Investigator Concerns.** Investigators may raise concerns or suggestions regarding the LG Health HRPP or the IRB by contacting the LG Health Institutional Official, the IRB Chair, the Administrative Director of the Research Institute, LG Health Legal Services, LG Health Compliance Officer, or other appropriate individual or department. Any concerns or suggestions will be reviewed by the appropriate individual or department, in conjunction with the individual who raised the concern or suggestions, and appropriate changes or improvements implemented as warranted.

ROLES/REPONSIBILITIES

DEFINITIONS

REFERENCE DOCUMENTS

Guidance for Industry: E6 Good Clinical Practice: Consolidated Guidance, Food and Drug Administration, March 2018, Section 4

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standards I.5.C, III.1.C, III.1.D, III.1.E, III.1.F, III.1.G, III.2.A, III.2.B, III.2.C, and III.2.D

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Institutional Conflict of Interest in Research Policy No. 110	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 10/23/15, 11/16/17, 10/06/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy establishes the mechanisms for disclosure of financial interests and identification and management of potential conflicts of interest of Lancaster General Health (LG Health) and its officials and management relating to human subject research.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to LG Health trustees, officers, and senior management, whether or not they are directly involved in human subject research.

POLICY STATEMENTS: The design, conduct, reporting, review, or oversight of human subject research cannot be influenced by, or perceived to be influenced by, any potential conflict of interest of LG Health or its officials and management. Financial interests must be disclosed to appropriate institutional bodies and potential conflicts identified and managed in a way that protects human subjects and maintains the integrity of human subject research.

PROCEDURES

1. Examples of Conflicts of Interest:

a. Institutional Conflict of Interest. Examples of institutional conflicts of interest include, but are not limited to, royalties associated with the investigational product or device that is the subject of research, equity interests in a sponsor of research, and gifts or other items of value from sponsors of research.

b. Individual Conflict of Interest of LG Health Officials and Management. Examples of individual conflicts of interest include, but are not limited to, serving on a board of directors or other management position of a sponsor of research, honoraria, royalties, equity ownership in a sponsor of research, and receipt of gifts or other items of value from sponsors of research.

2. Disclosure of Financial Interests

a. Institutional Financial Investments. On an annual basis, the LG Health Corporate Compliance Officer shall provide a list of research sponsors to the Chief Financial Officer for evaluation with respect to LG financial interests (see section 3).

b. Individual Financial Interests.
In accordance with the LG Health Conflict of Interest Policy, on an annual basis each trustee and officer of LG Health, or a wholly-owned subsidiary of LG Health, must disclose to the Sr. Vice President, Legal Services, any and all personal investments, equity interests, and stock options that individually exceed $50,000.00 and any financial interest related to intellectual property with any publicly or non-publicly traded company providing health-related goods or services. Excluded from the disclosure requirement are mutual funds for which the individual has no control over the investment decisions of the fund and funds that are not actively managed by the individual (*i.e.*, the individual does not participate in any manner in the decisions to purchase or sell individual stocks).

The Sr. Vice President, Legal Services, or their delegate, will review each submission by a trustee and officer and provide the Research Compliance Committee with the list of the pharmaceutical and device

manufacturers with whom trustees and officers have significant financial interests. To the extent possible, the Sr. Vice President, Legal Services will not disclose to the Research Compliance Committee or any other individual the identity of the trustee or officer with the financial interest. The Research Compliance Committee will use this list as a reference in their reviews for potential conflicts of interest (see section 3).

c. Lancaster General Health Foundation. On an annual basis, the Executive Director of the Lancaster General Health Foundation (LGHF), or their designee, shall complete a Financial Interest Statement and submit such statement to the Research Compliance Committee. The LGHF Financial Interest Statement shall require LGHF to disclose to the Research Compliance Committee any entity that provides health-related goods or services or any entity that sponsors health-related research from which LGHF solicited or received gifts, funds, or other items of value.

d. Intellectual Property. On an annual basis, such entity or department that manages LG Health intellectual property shall disclose to the Research Compliance Committee all intellectual property that LG Health owns.

3. Identification and Management of Conflicts of Interest. The LG Health Research Compliance Committee is responsible for reviewing all disclosed institutional financial interests for potential conflict relating to human subject research. The Research Compliance Committee review shall be done in an effort to maintain the highest ethical standards in research, to comply with federal and state laws and regulations, to maintain the integrity in research, and to protect the reputation and credibility of LG Health. As research projects are submitted for initial and continuing IRB review, LG Health Research Compliance Committee shall evaluate the following:

a. Institutional Financial Investments. The Office of the CFO shall determine whether LG Health or any of its affiliates has any financial investments of $50,000 or more in sponsors of research being conducted at LG Health. The Research Compliance Committee is responsible for determining if such interests constitute a potential conflict of interest and, if so, recommending a management plan. Possible management steps include, but are not limited to, external oversight of the research, segregation of funds, use of an unaffiliated IRB, or prohibition on the conduct of a specific research activity. The Research Compliance Committee may consult with the LG Health Audit and Compliance Committee for guidance in resolving or managing conflicts of interest.

b. Individual Financial Interests. If the Research Compliance Committee determines that an officer, trustee, or other individual in management has a financial interest of $50,000.00 or more that poses a potential conflict of interest with a research protocol, the Sr. Vice President, Legal Services, will determine if there is a reasonable presumption that the individual could influence the conduct of the research protocol, and if so, to establish a management plan to reduce or eliminate the individual's ability to influence the conduct of the research protocol. Oversight of the research may be reassigned as needed to reduce or eliminate the potential for conflict of interest. It is the responsibility of the Sr. Vice President, Legal Services, to communicate and document any management plan involving a trustee or officer. Potential financial conflicts with a monetary value less than $50,000.00 will not require a management plan.

c. Lancaster General Health Foundation. If the Research Compliance Committee determines that the Foundation has a financial interest of $50,000.00 or more that poses a potential conflict of interest with

a research protocol, the Research Compliance Committee will determine if there is a reasonable presumption that any individual with knowledge of the financial interest could influence the conduct of the research protocol. If so, the Research Compliance Committee will establish a management plan to reduce or eliminate the individual's ability to influence the conduct of the research protocol. Potential financial conflicts with a monetary value less than $50,000.00 will not require a management plan.

d. Intellectual Property. The Research Compliance Committee shall determine if LG Health holds intellectual property related to any research that it conducts. If so, the Research Compliance Committee and the Institutional Review Board will consider whether compelling circumstances justify overriding the rebuttable presumption against conducting the research. If such compelling circumstances exist, the Research Compliance Committee will develop a management plan with steps that could include, but are not limited to, external oversight of the research, use of an unaffiliated IRB, and segregation of funds. The compelling circumstances that justify the conduct of the research and the details of the intellectual property interest shall be disclosed to the Institutional Review Board (IRB), the University of Pennsylvania Vice Provost for Research, and to any federal sponsoring agency.

e. IRB Review. All management plans will be submitted to the IRB for review and approval.

4. Non-compliance. If an officer, trustee, or other individual in management fails to disclose a Significant Financial Interest, fails to adhere to a management plan, or otherwise fails to comply with this Policy:

a. The Research Compliance Committee will review and evaluate, as soon as reasonably possible, but in no event later than sixty (60) days following identification, an undisclosed Significant Financial Interest to determine whether it constitutes a Financial Conflict of Interest, and if so, will develop a management plan.

b. In any case of non-compliance with this Policy, suitable corrective action may be taken. Such action is described in section 3.14 of the LG Health/Penn Medicine Compliance Program and may include the initiation of proceedings under other LG Health/Penn Medicine policies governing sanctions against individuals, such as the Employee Counseling and Progressive Corrective Action policy, and/or relevant Medical and Dental Staff policies.

ROLES/REPONSIBILITIES

On an annual basis:

1. The LG Health Corporate Compliance Officer shall provide the Research Compliance Committee with a listing of LG Health institutional financial investments.
2. The Sr. Vice President, Legal Services, or their delegate, will provide the Research Compliance Committee with the list of companies providing health-related goods or services with which trustees and officers have significant financial interests.
3. Any entity or department that manages LG Health intellectual property shall disclose to the Research Compliance Committee all intellectual property that LG Health owns.

DEFINITIONS

Institutional Conflict of Interest: A situation in which the financial interests of LG Health, or an affiliate, or of an institutional official with authority to act on behalf of LG Health, might affect, or reasonably appear to affect, institutional processes for the design, conduct, reporting, review, or oversight of human subject research. Institutional financial conflicts of interest include, but are not limited to: i) licensing, technology transfer, patents; ii) investments of the organization; iii) gifts to the organization when the donor has an interest in the research; iv) financial interests of senior administrator; v) other financial interests.

LG Health Officials: LG Health trustees, directors, officers, and management employees who have the authority to act on behalf of LG Health or have the ability to direct, supervise, or oversee human subject research.

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standards I.1.D, I.6.A, and III.2.A

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Conflicts of Interest Involving Researchers Policy No. 111	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/07/09, 04/25/11, 02/10/14, 5/27/14, 01/01/15, 10/23/15, 09/23/16, 04/5/17, 04/10/20, 10/31/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy establishes mechanisms to identify, evaluate, and manage Financial Conflicts of Interest (COI) related to research conducted at Lancaster General Health ("LG Health").

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in research at LG Health.

POLICY STATEMENTS: In the environment of research, transparency and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, Financial Conflicts of Interest involving Investigators conducting research at LG Health must be disclosed and effectively managed or eliminated. It is the policy of LG Health that all Investigators disclose Significant Financial Interests on an annual basis and when new Significant Financial Interests emerge.

PROCEDURES

1. **Disclosure of Significant Financial Interests**

   a. On an annual basis, each Investigator must disclose all Significant Financial Interests, including Fiduciary Roles, on the research portion of the Financial Interest Disclosure Statement that is distributed by the Compliance Department. Disclosure is to include Significant Financial Interests held by the Investigator's spouse and dependent children.

   b. Each investigator also must update their Financial Interest Disclosure Statement within thirty (30) days of discovering or acquiring a new Significant Financial Interest.

   c. Upon submission of a grant proposal, submission of a protocol to the IRB or upon being added as an Investigator on a current research protocol, an investigator must update their Financial Interest Disclosure Statement or attest that it remains accurate.

2. **Review of Significant Financial Interests**

   a. The Research Compliance Committee is responsible for reviewing Significant Financial Interests disclosed by research Investigators. At the time of submission of a protocol to the IRB and annually thereafter, the Research Compliance Committee is responsible for determining whether any Significant Financial Interest constitutes a Financial Conflict of Interest (FCOI).

   b. In reviewing Significant Financial Interests, the Research Compliance Committee may submit any Investigator's Significant Financial Interest to the LG Health Audit and Compliance Committee to obtain guidance as to whether a Significant Financial Interest constitutes a Financial Conflict of Interest.

c. Whenever, in the course of an ongoing protocol, a new investigator discloses a significant financial interest or an existing investigator discloses a new significant financial interest, the following shall occur within 60 days: the Research Compliance Committee shall review the disclosure, determine if it constitutes a Financial Conflict of Interest, and, if so, recommend a management plan, and the IRB shall review and approve the plan. The RCC may implement an interim plan if needed between the date of disclosure and when the review is completed or the management plan is approved.

3. Management and Reporting of Financial Conflicts of Interest

a. If the Research Compliance Committee determines that a Significant Financial Interest constitutes a Financial Conflict of Interest, the Research Compliance Committee may recommend that the Investigator eliminate the Financial Conflict of Interest or that the Financial Conflict of Interest be managed. Factors to consider when determining to manage a Financial Conflict of Interest instead of elimination include:

- The magnitude and nature of the Financial Conflict of Interest
- The uniqueness of the Investigator's position with respect to the study
- The extent to which the Significant Financial Interest could be influenced by research
- The degree of risk to human subjects
- The role of the Investigator in the research such as recruitment, data analysis, or research design

b. If the Research Compliance Committee determines that a Financial Conflict of Interest can be managed, in consultation with the Investigator, the Research Compliance Committee will develop a management plan. Components of the management plan may consist of: (i) public disclosure of the Financial Conflict of Interest; (ii) disclosure of the Financial Conflict of Interest to research subjects; (iii) appointment of an independent monitor to oversee the conduct of the research; (iv) modification of the research plan; or (v) change in personnel responsible for the research; (vi) reduction of elimination of the financial interest; (vii) severance of relationships that create financial conflicts. The management plan must also detail responsibilities and methods to monitor the management plan.

c. The recommendations of the Research Compliance Committee for elimination or management of Financial Conflicts of Interest will be sent to the IRB for review and approval. For Financial Conflicts of Interest identified during the process of initial submission of a protocol to the IRB or at submission for continuing review, the Research Compliance Committee will make reasonable efforts to provide their recommendations for review by the IRB at the same time as the protocol submission.

d. An Investigator must provide written agreement to comply with all terms and conditions of the management plan approved by the IRB. If an Investigator objects to the management plan, the Investigator can request in writing that the Research Compliance Committee reevaluate the management plan. The Investigator's written request must include reasons for objecting to the management plan and, if appropriate, alternative methods to manage the Financial Conflict of Interest. Any revisions to the management plan must then be submitted to the IRB for review.

e. IRB approval (initial or continuing) of a protocol cannot be granted, nor any Federal funds for the project expended, until any Financial Conflicts of Interest have been addressed to the satisfaction of the IRB.

f. Prior to commencing the research and when new Financial Conflicts of Interest are identified during the conduct of research, to the extent required, LG Health will report an Investigator's Financial Conflict of Interest to the applicable research sponsor or government agency.

g. At any time, the Research Compliance Committee may seek the advice and guidance of the LG Health Audit and Compliance Committee with regard to the development of a management plan.

h. Compliance with the approved management plan will be monitored by the Research Quality Assurance Office no less than on an annual basis. Findings from the monitoring will be presented to the IRB each time it conducts a continuing review of a protocol for which a COI management plan was required.

4. Miscellaneous

a. **Training**. All Investigators must receive training relating to this Policy and Financial Conflicts of Interest upon initial commencement of research at LG Health and at least every four (4) years thereafter. Investigators must also receive training within a reasonable period of time following any substantive changes to this Policy or in the event an Investigator is found to be non-compliant with this Policy. The Research Compliance Committee may also require an Investigator to undergo training at any time in the Research Compliance Committee's reasonable discretion.

b. **Public Notice**. This Policy will be posted publically on the LG Health Research Institute website. In addition, as required by law, LG Health will make available to the public, upon written request to the Vice President of Research Administration, certain information regarding Financial Conflicts of Interest of Investigators with respect to research conducted at LG Health. Within five (5) days of a written request, LG Health will provide the following information: (i) Investigator's name, title, and role with respect to research; (ii) the name of the entity in which a Significant Financial Interest is held; (iii) the nature of the Significant Financial Interest; and (iv) the approximate value of the Significant Financial Interest. LG Health may choose to disclose the approximate value of the Significant Financial Interest in the following ranges ($0-$4,999; $5,000-$9,999; $10,000-$19,999; amounts between $20,000-$100,000 by increments of $20,000; and amounts above $100,000 by increments of $50,000).

c. **Non-Compliance**. In the event LG Health becomes aware of instance in which an Investigator failed to disclose a Significant Financial Interest or otherwise failed to comply with this Policy, the Research Compliance Committee:

- Will review and evaluate, as soon as reasonably possible, but in no event later than sixty (60) days following identification of non-compliance with this Policy, the Significant Financial Interest and determine whether it constitutes a Financial Conflict of Interest;
- Will develop a management plan if the Significant Financial Interest constitutes a Financial Conflict of Interest.

If it is determined that a Financial Conflict of Interest exists, the Research Compliance Committee will perform a retrospective review of the research to determine if, during the period of non-compliance, the research was biased in the design, conduct, or reporting of such research. Such retrospective review must be documented and performed within 120 days of the identification of non-compliance. The retrospective review shall include: (i) project number; (ii) project title; (iii) principal or contact investigator; (iv) investigator with the FCOI; (v) entity with which the investigator has the FCOI; (vi) reasons for the retrospective review; (vii) detailed methodology used for the retrospective review; (viii) finding of the review; and (ix) conclusions of the view. LG Health will update any Financial Conflict of Interest report previously submitted to the sponsor or applicable government agency.

d. **Remedies**. If bias from non-compliance with this policy is found, LG Health will immediately notify the sponsor or appropriate government agency and develop a mitigation plan as required by the sponsor or government agency. If it is determined that a Federally funded project of clinical research whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment has been designed, conducted, or reported by an investigator with a financial conflict of interest that was not managed or reported by the LG Health as required by this policy, LG Health shall require the investigator to disclose the financial conflict of interest in each public presentation of the results of the research and to request an addendum to previously published presentations.

e. **Corrective Action.** If an Investigator is found to have failed to disclose a Significant Financial Interest, failed to adhere to a management plan, or otherwise failed to comply with this Policy, suitable corrective action may be taken. Such action is described in section 3.14 of the LG Health/Penn Medicine Compliance Program and may include the initiation of proceedings under other LG Health/Penn Medicine policies governing sanctions against individuals, such as the Employee Counseling and Progressive Corrective Action policy, and/or relevant Medical and Dental Staff policies.

f. **Subrecipients**. To the extent applicable, if any research is conducted by another party through a subaward or subcontract, the written agreement between LG Health and the subrecipient must require the subrecipient to maintain a Financial Conflict of Interest Policy that meets the requirements of the applicable sponsor or government agency. The written agreement will require the subrecipient to certify that its established policy complies with the requirements of the applicable sponsor or government agency. The written agreement will also contain appropriate timeframes for the subrecipient to disclose to LG Health any sub-investigator Financial Conflicts of Interest to allow LG Health to comply with any applicable reporting requirements.

g. **Retention of Records**. All Financial Interest Disclosure Statements, management plans, and other documents related to potential Financial Conflicts of Interest will be retained for the longer of: (i) three (3) years following the date that the final research expenditure report has been submitted to the research sponsor; (ii) as specified by any government agency; or (iii) as required by LG Health policy.

h. **Reporting Requirements.** The Administrative Director of the LG Research Institute or Designee will report to the University of Pennsylvania (UPenn) Office of the Vice Provost for Research when any of the following circumstances occur:

i. Need to submit an FCOI Report to the National Institutes of Health or an FCOI Report to a prime awardee when LG Health is a subrecipient;
ii. Receipt of any inquiries from the public regarding information related to an FCOI;
iii. Need to initiate a retrospective review because an FCOI was not identified and/or managed within the permissible timeframe or because of investigator noncompliance with a management plan; and
iv. Awareness from any source of an investigator with an inventorship interest in intellectual property that is being tested in a trial.

Additionally, the Administrative Director of the LG Research Institute or Designee will, annually each July, report Financial Conflict of Interest metrics to the UPenn Vice Provost for Research as determined by the Vice Provost.

ROLES/REPONSIBILITIES

Investigators shall be responsible to report any Significant Financial Interests to the Research Compliance Committee at time of initial submission of a research project, at time of annual review; or at any time new interests are obtained during the conduct of the research.

Research Compliance Committee members shall be responsible to determine whether a Financial Conflict of Interest exists and whether this Financial Conflict of Interest will impact the rights and welfare of research subjects. The Research Compliance Committee may submit a disclosed Significant Financial Interest or Financial Conflict of Interest to the LG Health Audit and Compliance Committee for review and guidance when deemed appropriate by the Research Compliance Committee.

DEFINITIONS

Investigator: The principal investigator, co- investigator, collaborator, project director, and any other person who is involved in or responsible for the design, conduct, reporting of the protocol, or are otherwise involved in accomplishing protocol objectives.

Remuneration: Salary and any payment for services such as consulting fees, honoraria, or paid authorship.

Equity: Financial interest in an entity such as stock, stock options, or other ownership interest. The value of equity interest is determined through reference to public prices or other reasonable measures of fair market value.

Intellectual property: Rights and interests such as patents and copyrights.

Financial Conflict of Interest: A Significant Financial Interest that could directly and significantly affect the design, conduct, or reporting of research.

Fiduciary Role: Membership on the governing board of an entity, including service on its board of directors, or having a position of authority or responsibility to act in the best interest of the entity, including being an office, manager, partner, or limited liability company member with management responsibility.

Significant Financial Interest: Any financial interest that an Investigator or an Investigator's spouse or dependent children might have that would reasonably appear to be related to the Investigator's institutional responsibilities (*i.e.*, an Investigator's responsibilities on behalf of LG Health, such as research, professional practice, teaching, and LG Health committee membership). It is further defined by the below as to what is and is not a Significant Financial Interest.

1. Significant Financial Interest includes the following:

    a. With regard to any publicly traded entity, remuneration of the Investigator or Investigator's spouse or dependent children that was received from the entity in the 12 months prior to disclosure and equity interest of these persons in the entity as of the date of disclosure that, when aggregated, exceeds $5,000.
    b. With regard to any non-publicly traded entity, remuneration of the Investigator or Investigator's spouse or dependent children that was received from the entity in the 12 months prior to disclosure that, when aggregated, exceeds $5,000.
    c. Also with regard to any non-publicly traded entity, equity interests of any amount held by the Investigator or Investigator's spouse or dependent children.
    d. Intellectual property rights and interests that generated income in the 12 months prior to disclosure, or the right to receive future royalties under a patent license, copyright, or other agreement, for the Investigator or Investigator's spouse or children.
    e. Any reimbursed or sponsored travel (*i.e.*, travel which is paid on behalf of an Investigator or the Investigator's spouse or dependent children and not reimbursed to the Investigator so that the exact monetary value may not be readily known) during the previous twelve (12) months, excluding sponsored or reimbursed travel from a federal, state, or local government agency, an institution of higher education, an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education.
    f. The holding of Fiduciary Roles by the Investigator or the Investigator's spouse or dependent children.

2. Significant Financial Interests ***do not*** include the following:

    a. Income from investment vehicles, such as mutual funds and retirement accounts, as long as the investigator does not directly control the investment decisions made in these vehicles;
    b. Payments to LG Health or the Investigator that are directly related to reasonable costs incurred in the conduct of research as specified in the research agreement(s) between the sponsor and the institution;
    c. Income from seminars, lectures, or teaching engagements sponsored by a federal, state, or local government agency, an institution of higher education, an academic teaching hospital, a medical center, or a research institute affiliated with an institution of higher education;

d. Income from service on advisory committees or review panels for a federal, state, or local government agency, an institution of higher education, an academic teaching hospital, a medical center, or a research institute affiliated with an institution of higher education; and
e. Salary, royalties, or other remuneration paid by LG Health to the Investigator if the Investigator is employed by LG Health.

REFERENCE DOCUMENTS

LGH Institutional Review Board Disclosure of Significant Financial Interest in Research

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

Public Health Service Regulations: 42 CFR §50.601 *et. seq.*

AAHRPP Standards I.1.D, I.6.B, III.1.B, and III.2.A

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Authority and Purpose of the Institutional Review Board Policy No. 201	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 02/19/14, 01/01/15, 02/04/16, 10/12/17, 11/02/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of the Policy is to:

1. State the institutional authority under which the Institutional Review Board (IRB) is established and empowered.
2. Define the purpose of the IRB.
3. State the purview of the IRB and the actions it may take to assure that the rights and welfare of subjects are protected.
4. Define the relationship of the IRB to other committees and to officials within Lancaster General Hospital (LGH).

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at LG Health and IRB members.

POLICY STATEMENT: It is the policy of LG Health that the LGH IRB oversee all research conducted in the LG Health system involving human subjects or human material. All human research activities must be reviewed and approved by the IRB prior to initiation, or the IRB must agree to defer such review to another IRB. The IRB also has the authority to review certain activities, described herein, that may not meet the definition of human subjects research but nevertheless involve use of protected health information (PHI) of LGH patients.

PROCEDURES

1. **Statement of Institutional Authority**. The LGH IRB is established and empowered under the authority of the Board of Trustees of Lancaster General Hospital. All research involving humans as subjects or human material must be reviewed and approved by LGH's IRB prior to initiation of any research related activities, or the IRB must agree to defer such review to another IRB (see policy Reliance on Another IRB). The IRB has the authority to determine whether an activity meets the definition of human subject research or otherwise requires IRB review when such determination is in question, and can also decide whether a research activity submitted for determination of status is exempt from the regulations governing human subject research (see policy Exempt Research).,

2. **Purpose of the IRB**. The purpose of the IRB is to protect the rights and welfare of human subjects participating in biomedical and behavioral research conducted at LGH. The IRB oversees and reviews such research to assure that it meets ethical principles and that it complies with federal regulations that pertain to human subject protection at 45 CFR Parts 46 and 21 CFR Parts 50 and 56, and other pertinent regulations and guidance.

3. **IRB Purview and Actions**

   a. The IRB is established to review biomedical and behavioral research involving human subjects that is conducted by members of the LGH Medical and Dental Staff and employees, volunteers, or agents of LGH regardless of the source of funding and location of the study if:

i. The research is conducted by or under the direction of any member of the LGH Medical and Dental Staff, or employees, volunteers, or agent of LGH in connection with their institutional responsibilities;
ii. The research is conducted by or under the direction of any member of the LGH Medical and Dental Staff or an employee, volunteer, or agent of LGH using any property or facility of LGH;
iii. The research involves the use of LGH's nonpublic information to identify or contact human research subjects; and/or
iv. The research involves the use or disclosure of PHI of patients of LGH, living or deceased.

b. The IRB also has the authority to review activities that may not meet the definition of human subjects research but nevertheless involve use of protected health information of LGH patients, living or deceased, if:

i. The activity is preparatory to research, which includes the screening of medical records to identify people who may be eligible for a research project.
ii. The activity is a scholarly requirement of a student's academic program.
iii. The activity, including a case study or series or a performance improvement activity, results in a manuscript to be submitted to a professional journal or a presentation to be given at a professional meeting.

c. The IRB has the authority to ensure that research, including research that qualifies for exempt status, is designed and conducted in such a manner that protects the rights, welfare, and privacy of research subjects. Specifically:

i. The IRB may disapprove, modify, or approve studies based upon any aspect of human subject protection.
ii. The IRB reviews, and has the authority to approve, require modification in, or disapprove all research activities that fall within its jurisdiction.
iii. The IRB has the authority to conduct continuing review as it deems necessary to protect the rights, welfare and privacy of research subjects, including requiring progress reports from the investigators and review of the conduct of the study, and observe the informed consent process and/or audit the progress of any study under its jurisdiction as it deems necessary to protect the rights and welfare of human subjects.
iv. The IRB may suspend or terminate approval of a study.
v. The IRB may place restrictions on a study.

5. **Federally Funded Research**. If the study is part of an application to a federal sponsoring agency, the human subject research protocol must be reviewed by the IRB before initiation of any research project work and prior to expenditure of any grant funds.

6. **Relationship of the IRB to other LG Entities**. Research that has been reviewed and approved by the IRB may be subject to review by other LG entities (see the Human Research Protection Program, Policy Number 101). If so, these entities may disapprove research that has been approved by the IRB. However, no LG official, committee, or other entity has the authority to approve research if it has not been approved by the IRB.

ROLES/REPONSIBILITIES

Research investigators and LG Health employees, agents, and volunteers shall be responsible to submit any project or activity which may meet the definition of Research, as defined in the LG Health Human Research Protection Program Policy, to the IRB prior to initiating any associated project activity, including recruitment and screening activities.

IRB members shall be responsible to review all research activities to protect the rights and welfare of human subjects participating in biomedical and behavioral research conducted under the auspices of LG Health.

DEFINITIONS

REFERENCE DOCUMENTS

The Belmont Report

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR Part 46 and 21 CFR parts 50 and 56
AAHRPP Standards I.1.A, I.1.C., and III.1.A

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Composition of the Institutional Review Board **Policy No. 202**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 03/20/14, 01/01/15, 02/04/16, 08/31/17, 01/21/19, 12/20/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to identify the requirements for the composition of the Institutional Review Board (IRB).

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to the Vice President of Research Administration, the IRB Chair, and IRB Members.

POLICY STATEMENTS: The IRB shall be able to ascertain the acceptability of proposed research in terms of the commitments of Lancaster General Health (LG Health) and regulations, applicable law, and standards of professional conduct and practice. The IRB should also be able to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The IRB shall, therefore, consist of at least five regular, voting members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by LG Health.

PROCEDURES

1. **Membership Selection Criteria.** IRB members are to be sufficiently qualified through experience and expertise to review research proposals in terms of regulations, applicable law and standards of professional conduct and practice and institutional commitments (including policies and resources). The IRB shall, therefore, include persons knowledgeable in these areas. The membership shall be diverse, so selection shall include consideration of race, gender, cultural backgrounds, research, healthcare or professional experience and sensitivity to such issues as community attitudes to assess the research submitted for review and to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

   There shall be at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. There shall be at least one member who has no direct affiliation with LG Health or affiliation through a family member. There shall be at least one member who represents the general perspective of research subjects.

   Membership shall represent multiple professions. It shall not consist entirely of men or of women.

   Employees of, or individuals in, the Lancaster General Health Foundation or other department or entity who have a substantial role in bringing funds to LG Health may not serve as members of the IRB or be involved in the day-to-day operations of the IRB review process. These individuals may serve as guests at IRB meetings or provide other information to the IRB.

2. **Composition of the IRB**

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

      i. Nonaffiliated member(s). The nonaffiliated member(s) (that is, those members who are not affiliated with LG Health), who can be either scientific or nonscientific reviewers, should be

knowledgeable about the local community and be willing to discuss issues and research from that perspective. Consideration should be given to recruiting individuals who speak for the communities from which research subjects will be drawn. The nonaffiliated member(s) should not be vulnerable to intimidation by the professionals on the IRB.

ii. Scientific members. The IRB may include physicians and doctoral level physical, behavioral, social or biological scientists. Such members satisfy the requirement for at least one scientist. When an IRB encounters studies involving science beyond the expertise of the members, the IRB may use a consultant to assist in the review, as provided by 21 CFR § 56.107(f) and 45CFR § 46.107(f). When FDA regulated products are reviewed, the convened meeting must include a licensed physician member; therefore, at least one member of the IRB must be a physician licensed to practice medicine in the Commonwealth of Pennsylvania.

iii. Nonscientific members. The intent of the requirement for diversity of disciplines is to include members whose main concerns are not in scientific areas. Therefore, nonscientific members are individuals whose education, work, or interests are not in medical, behavioral or social science areas.

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

v. Chair. The IRB Chair should be a highly respected individual from within or outside LG Health and be fully capable of managing the IRB and the matters brought before it with fairness and impartiality. The IRB Chair will be appointed by the Vice President of Research Administration.

vi. Vice Chair. The IRB Vice Chair will be appointed by the Vice President of Research Administration in consultation with the IRB Chair. In the absence of the IRB Chair, the Vice Chair will have the same authority as the Chair. The Vice Chair, as an experienced IRB member, will be designated by the Chair to perform expedited reviews.

b. Alternate Members. Alternate members are qualified voting members who serve as designated alternates for regular members, but they are not expected to attend each meeting. The Chair or their designee, or a designated member of the IRB staff, may ask an alternate member to attend a meeting in order to either draw on their expertise in an area that may be relevant to that meeting's deliberations and/or to establish a quorum for that meeting in the absence of the designated regular member.

An alternate member's presence at an IRB meeting in the place of an absent regular member may be used in establishing a quorum.

c. Special Consultants. Per the process outlined in Policy 305, 2a. the Chair may invite individuals with competence in special areas or knowledge to assist in the initial or continuing review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the regular and alternate members of the IRB, and their presence or absence will not be used in establishing a quorum for an IRB meeting.

i. A consultant may be an individual who is either internal or external to LG Health. A consultant may be asked to review a protocol or provide education on a topic of specific concern to the IRB; a consultant may provide information to the IRB by written report and/or by attending one or more meeting(s).

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

iii. The HRPP & IRB Manager or the IRB Chair or designee will contact the consultant and will determine how the information will be conveyed to the IRB (*i.e.*, attendance at the meeting or written report).

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

v. Use of consultants will be documented in the minutes, as this will be presented to the convened IRB during the discussion of the protocol.

3. **Membership Terms.** Members, including the Chair, will serve on the IRB for a term of three years. Reappointment for additional terms may occur, by mutual agreement of the IRB member, the IRB Chair, and the Vice President of Research Administration. Members appointed during the three year term will be appointed for the remainder of the three year term to allow reappointment of all members at one time. Reappointment will occur in the spring.

4. **Appointments.** The Vice President of Research Administration in consultation with the IRB Chair has the authority to appoint members to the IRB. Members will be solicited from Medical and Dental Staff, LG Health employees and the Lancaster County community.

5. **Resignations and Removals.** A member may resign before the conclusion of their term. The vacancy will be filled as quickly as possible. The Vice President of Research Administration may remove a member at any time.

6. **IRB Roster.** An IRB roster will be maintained by the Institutional Review Board Office and will include:

a. Names of IRB members;

b. Earned degrees;

c. The representative capacity of IRB members:

i. Scientist and non-scientist;

ii. Affiliated or nonaffiliated;

iii. Knowledge of vulnerable populations;

d. Indications of IRB members' experience;

e. Employment, affiliation, or other relationship between the IRB member and the organization;

f. Office (e.g., Chair, Vice Chair);

g. Membership status; and

h. Identification of member's alternate member.

ROLES/REPONSIBILITIES

The Vice President of Research Administration and the IRB Chair shall be responsible for appointing qualified individuals to the IRB.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.107; 45 CFR § 46.107(e); 45 CFR § 46.108
21 CFR § 56.107; FDA 21 CFR § 56.107(f); FDA 21 CFR § 56.115(a)(5);
FDA Information sheets, FAQ, Section II, Quest, 14, 15 (January 1998)
AAHRPP Standards II.1.A, II.1.B, II.1.C, and II.1.E

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Activities Requiring IRB Review Policy No. 203	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 02/10/14, 01/01/15, 8/31/17, 12/17/20, 09/26/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to describe specific activities that require Institutional Review Board (IRB) review as well as those activities that do not require IRB review.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health).

POLICY STATEMENTS: All research involving human subjects (as defined below), and all other activities which even in part, involve such research, regardless of sponsorship, must be reviewed and approved by the Lancaster General Hospital (LGH) IRB.[1] No intervention or interaction with human subjects in research, including recruitment, may begin until the IRB has reviewed and approved the research protocol. Specific determinations as to the definition of "research" or "human subjects", and their implications for the jurisdiction of the IRB are determined by the IRB.

PROCEDURES

1. **Activities That Require IRB Review.** Activities involving the collection of data, for the purpose of contributing to generalizable knowledge, through intervention or interaction with a living individual, or involving identifiable private information including protected health information of a living individual or a decedent, must be reviewed by the IRB. Specific activities that require IRB review include, but are not necessarily limited to:

   a. Any clinical investigation that is regulated by the U.S. Food and Drug Administration (FDA) or that will support an application for research or marketing permit for a product regulated by the FDA.

   b. Systematic investigation of an innovative preventative strategy, screening procedure, diagnostic procedure, treatment, or alteration of a standard procedure or treatment, to evaluate feasibility, efficacy, or safety for scientific purposes, including comparison to an accepted standard.

   c. The assignment of subjects to any social or behavioral intervention for research purposes.

   d. Systematic collection and evaluation of data such as patient demographics, health history, treatments, and outcomes, including studies of approved or standard procedures or treatments to provide additional evidence on feasibility, efficacy, or safety or to compare procedures or treatments.

   e. Collection of data for educational research, including evaluation of instructional strategies, curricula, or classroom management methods, or analysis of educational test results. (These projects may qualify for exemption from further IRB review; see policy on Exempt Research.)

   f. Analysis of an existing data set or a data set abstracted or extracted from existing records. (These projects may qualify for exemption from further IRB review if the data are de-identified and publicly available; see policy on Exempt Research.)

[1] LGH Federal Wide Assurance 00006038

g. Collection, storage, distribution, or analysis of specimens of human cells or tissues for research purposes. (Human cell or tissue repository activities **do not** require IRB review under certain circumstances, discussed in section 4.)

2. **Special Categories of Activities Requiring IRB Review.** Some activities do not follow all of the usual research review processes but are required by regulation to follow a specialized IRB review process.

a. Emergency use of an investigational drug or device to treat a life-threatening or serious condition with no available, standard, acceptable treatment. Such treatment could be initiated with or without prior IRB notification, depending on the timing and urgency of the situation, but must be submitted to the IRB no later than 5 days following the emergency use. Refer to the policy Emergency Use of an Investigational or Unlicensed Test Article.

b. Use of a device under a Humanitarian Device Exemption given by the U.S. Food and Drug Administration. The use of humanitarian use devices must be reviewed by the IRB. Refer to the policy Humanitarian Use Devices.

3. **Activities That Require IRB Review for Privacy Concerns.** The LGH IRB is authorized to review activities that may not meet the definition of research but that involve the use of protected health information or that might reasonably identify subjects by the specificity of the information disclosed.

a. Use of individual patients' protected health information preparatory to research, including use to identify patients who may be eligible for the research. (See section 2 for the circumstances when activities preparatory to research to do not require IRB review.) The investigator must provide assurance that 1) the use or disclosure is requested solely to review PHI as necessary to prepare a research protocol or for similar purposes preparatory to research; 2) the PHI will not be removed from the covered entity in the course of review; and 3) the PHI for which use or access is requested is necessary for the research.

b. Secondary research uses of identifiable private information or identifiable biospecimens that, though meeting criteria for exemption from IRB review are still subject to regulation under HIPAA (see policy on Exempt Research).

c. Student scholarly activities for academic programs. These activities may not meet the definition of research that will contribute to generalizable knowledge. However, if the student uses protected health information of LG patients, living or deceased, the LGH IRB must review the project. The LGH IRB has the authority to require consent when determined to be warranted.

d. Case report, case series, or other publication in a professional journal or presentation to a professional society. If such activities involve the use or disclosure of protected health information, or if there is a reasonable chance that subjects could be identified by the specificity of the information, the LGH IRB should review the activity. The LGH IRB is authorized to require consent when determined to be warranted.

e. Any other research activities that LG Health is engaged in per OHRP guidance: Engagement of Institutions in Human Subjects Research.

4. **Activities Not Subject to IRB Review.** Activities that do not meet the definition of research because they do not involve intervention or interaction with a living individual or use protected health information of a living

individual or decedent, or they do not contribute to generalizable knowledge, do not need to be reviewed by the IRB. Investigators may request documentation from the IRB that the activity is not subject to IRB review. An Initial Application must be submitted in IRBManager for human research determination. Research status will be determined by the IRB Chair or designee under the revised Common Rule, and the definition of research and human subjects set forth by the FDA. The determination that the submission does not constitute research with human subjects will be documented by the IRB Chair or designee on the Initial Application Form in IRBManager. The determination documentation will be maintained by the IRB office in the protocol file. The researcher will be informed of the determination by written correspondence by letter sent via email and may not begin the research until correspondence is received. Notification of approval of the project will be provided to IRB members via the agenda of the next convened meeting.

Specific activities that do not require IRB review include, but are not necessarily limited to:

a. Proposals that lack definite plans for involvement of human subjects.

b. Activities such as quality assurance or quality control, program and fiscal audits, and certain disease monitoring as prescribed by the Pennsylvania Department of Health.

c. Collection for, storage in, or distribution from a repository of specimens of human cells or tissues, if the material satisfies both of the following conditions:

   i. The material, in its entirety, was collected for purposes other than submission to the repository (*e.g.*, the material was collected solely for clinical purposes, or for legitimate but unrelated research purposes, with no "extra" material collected for submission to the repository); and

   ii. The material is submitted to the repository without any identifiable private data or information (i.e., no codes or links of any sort may be maintained, either by the submitter or by the repository that would permit access to identifiable private data or information about the living individual from whom the material was obtained).

d. Use of health information preparatory to research if:

   i. A provider accesses health information of their patients only; or

   ii. An investigator obtains only aggregate data (e.g., number of patients meeting certain criteria) or de-identified data through an LGH data broker.

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

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

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

h. Operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

5. **Failure to Submit Project for IRB Review.** The implications of engaging in activities that qualify as research that are subject to IRB review without obtaining such review are significant. If an investigator begins a project without prospective IRB review and approval and later learns of the review requirement, the investigator should promptly notify the IRB. The IRB, under rare circumstances, may allow use of the data.

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

ROLES/REPONSIBILITIES

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.109
AAHRPP Standards I.1.A and III.1.A

Penn Medicine
Lancaster General Health

POLICY TITLE: Exempt Research Policy No. 204	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09; 04/25//11; 03/19/14, 01/01/15, 08/31/17, 01/21/19, 10/07/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes and outlines the process to determine if a human subject research protocol is subject to categories of research that are exempt from the regulations governing human subject research.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research under the auspices of Lancaster General Health (LG Health) and to Institutional Review Board (IRB) Members.

POLICY STATEMENTS: Research activities in which the only involvement of human subjects will be in one or more specific categories, which are listed below in this Policy, are exempt from the regulations governing human subject research, but are still subject to institutional review for a determination of exempt status and for ethical considerations. Determination of exemption must be based on regulatory and LG Health criteria and documented. Investigators and others may not solely determine whether research qualifies for exempt status. Exempt status will be determined by the IRB Chair or designee.

PROCEDURES

1. **Exempt Research Activities Under the Revised Common Rule, Excluding FDA-Regulated Research.** As determined by the IRB Chair or designee, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from IRB review[1]:

    a. Research conducted in established or commonly accepted educational settings, involving normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction, such as:

        - research on regular and special education instructional strategies, and
        - research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

    b. Research that only includes interactions involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior (including visual or auditory recording), if at least one of the following criteria is met:

        - information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
        - any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; OR

[1] 45 CFR § 46.101(b).

- information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

c. Research involving benign behavioral interventions. Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else. The research must involve benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

- the information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
- any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, educational advancement, or reputation; OR
- the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

d. Secondary research for which consent is not required, involving secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

- the identifiable private information or identifiable biospecimens are publicly available;
- information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;
- research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164 ['HIPAA'], subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.512(b); OR
- the research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information that is or will be maintained on

information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

e. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including:

- procedures for obtaining benefits or services under those programs;
- possible changes in or alternatives to those programs or procedures; or
- possible changes in methods or levels of payment for benefits or services under those programs.

Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

Each Federal department or agency conducting or supporting the research and demonstration projects must establish, or a publicly accessible Federal website or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

2. **Research Activities Exempt Under the Revised Common Rule and FDA Regulations.** Taste and food quality evaluation and consumer acceptance studies are exempt:

- if wholesome foods without additives are consumed; or
- if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

3. **Ethical Standards for Exempt Research.** When making a determination that research is exempt, the IRB Chair or designee will determine that the following criteria are met where applicable:

a. The research presents no more than minimal risk to subjects.

b. Selection of subjects is equitable.

c. If the research involves interactions with subjects, the circumstances of consent minimize coercion and undue influence.

d. Subjects will be informed that the study involves research, will be provided with information about the study procedures, that the research is voluntary, and will be provided with information about whom to contact with questions.

e. Provisions for protecting the privacy interests of subjects are adequate.

f. If private identifying data are recorded, provisions for maintaining the confidentiality of data are adequate.

4. **Limitations on Exemptions.** The exempt category described in 1.b. cannot be used for research involving children other than research involving educational tests or the observation of public behavior when the researchers do not participate in the activities being observed. The exempt category described in 1.c. cannot be used for research involving children. Research involving prisoners is NOT exempt, except for research that is aimed at involving a broader subject population and only incidentally includes prisoners.

5. **Application.** An IRB application must be submitted before the study can be determined to be exempt. The application must include any additional, relevant information such as a proposed informed consent form, survey introduction, data collection tools, and any other subject-facing materials (e.g. advertisements). The IRB reviewer will examine all documents and determine if the study qualifies as exempt research.

6. **Consent Forms.** Exempt research may still require an informed consent form. Such determination will be made by the IRB Chair or designee if they determine informed consent is appropriate for ethical considerations.

7. **Tracking of Exempt Research.** Exempt research is not subject to continuing review by the IRB. However, investigators will be required to provide a status update no less frequently than every 3 years. Investigators must also report any changes in the research protocol to the IRB as they occur. They also must submit a form to close the project when the research is completed and provide the IRB with a final report.

8. **Documentation**

a. The determination that research is exempt will be documented by the IRB Chair or designee on the Exempt Research Determination Form in the IRB electronic system. The determination documentation will be maintained by the IRB office in the protocol file.

b. The researcher will be informed of the determination by written correspondence and may not begin the research until correspondence is received.

c. Notification of approval of the exempt research project will be provided to IRB members via the agenda of the next convened meeting.

d. No IRB member designated to determine exemption status may participate in any exempt review in which the member has a conflict of interest.

ROLES/REPONSIBILITIES

The principal investigator shall be responsible to submit an application to the IRB for determination of exempt status.

DEFINITIONS

REFERENCE DOCUMENTS

The Office for Protection from Research Risk (OPRR) Guidance 45 CFR 46.104 Exempt Research

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.104(d)
AAHRPP Standards II.2.A and II.2.B

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Reliance on another IRB **Policy No. 205**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/1/2016, 08/31/17, 03/6/18, 01/29/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: To set forth the mechanism for the Lancaster General Hospital (LGH) Institutional Review Board (IRB) to rely on the review provided by another IRB.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to the LGH IRB, and investigators and other research staff engaged in human subject research at any entity under the purview of the LGH IRB. **Unless the circumstances are reviewed by the Lancaster General Health (LG Health) Human Research Protection Program (HRPP) and permission is granted, this Policy does not apply to phase I, first in human studies, or studies with safety or tolerance as a primary objective; more than minimal risk studies that do not have the potential for therapeutic benefit; studies with vulnerable populations; or more than minimal risk planned emergency studies exempted from informed consent.** Circumstances when LGH might agree to rely on another IRB for the review of such research include when the research is subject to a single IRB mandate, when the LGH IRB does not have the necessary expertise, and other compelling circumstances. If this policy does not apply or the mechanism to rely on another IRB is not used, the LGH IRB retains the authority to review all studies conducted under its purview.

POLICY STATEMENT: LGH IRB may enter into an agreement to rely on an IRB other than the LGH IRB (external IRB) for review of specific research projects or categories of research. Such research conducted under the auspices of LGH IRB but reviewed by an external IRB remains subject to LG Health HRPP policies and procedures, and the LG Health HRPP retains the authority to issue the final clearance for initiation of the research. The LG HRPP is responsible to verify compliance with contract requirements (if applicable), with requirements regarding education and training, and with conflict of interest disclosure, and to conduct local quality assurance monitoring and local investigation of unanticipated problems, deviations, complaints, or allegations of non-compliance. The LGH IRB retains the authority to observe or investigate any aspect of the research process, and the IRB of record has the authority to direct this to be done when deemed necessary.

This policy does not apply to reliance on the National Cancer Institute Central IRB, which is a special instance that is governed by the policy "Reliance on the National Cancer Institute Central IRB".

PROCEDURES

1. Requirements for Reliance on an External IRB

a. The LG Health HRPP considers the following factors, and others as appropriate, when considering a request to rely upon an external IRB:
   i. The accreditation status of the proposed IRB;
   ii. The compliance history of the IRB (e.g., outcomes of prior audits or inspections, corrective actions);
   iii. Prior experience with the IRB;
   iv. The federal IRB registration and organizational FWA, as applicable; and
   v. The proposed reliance terms and procedures.

b. When reliance on a non-accredited IRB is proposed, the evaluation may also take into consideration one or more of the following based upon the risks of the research, the research activities that LG Health will be involved in, and LG Health's familiarity with the IRB:

i. When the research is minimal risk (or the activities that LG Health is involved with are minimal risk), a statement of assurance from the proposed IRB that its review will be consistent with applicable ethical and regulatory standards, and that it will report any regulatory investigations, citations, or actions taken regarding the reviewing IRB, and, when applicable, to the organization's FWA;
ii. An attestation about, or summary of, any quality assessment of the reviewing IRB such as evaluation by an external consultant or internal evaluation of compliance using the FDA's self-evaluation checklist or AAHRPP's self-evaluation instrument; and
iii. An assessment of the external IRB's policies and procedures.

c. The IRB must be a central IRB specifically for a network in which LG Health is participating or the IRB for an institution with which LG Health is cooperating in the conduct of the particular research for which reliance on the external IRB is being sought.

d. An IRB Authorization Agreement with the external IRB must be executed to allow it to become the IRB of record for the research.
i. An IRB Authorization Agreement may cover only one study or multiple studies, but the agreement must clearly cover the particular study for which reliance on the external IRB is being sought.
ii. The IRB Authorization Agreement must describe the roles and responsibilities of each organization, including a plan for the communication of important information. This plan should address the communication from the IRB of record regarding the actions it takes affecting LG Health investigators or subjects, or unanticipated problems, deviations, or other information requiring investigation by the LGH IRB or LG Health HRPP; and the communication from the LGH IRB or LG Health HRPP regarding results of quality assurance monitoring or investigations of complaints or allegations of non-compliance that are relevant to review by the IRB of record.

e. The LG Health researchers are responsible:
i. to comply with LG Health policies regarding human research protections certification and conflict of interest disclosure;
ii. to provide information to the LGH IRB as in sections 2, 3 and 4 below;
iii. to provide local context information to the IRB of record for review (such local context information is to include, at a minimum, a description of the recruitment and informed consent process and the privacy and confidentiality measures to be taken at LG Health);
iv. to commence research activities only after final clearance from the LG Health HRPP;
v. to obtain and maintain all necessary reviews and approvals for the research (e.g., radiation safety);
vi. to comply with the determinations and requirements of the reviewing IRB; and
vii. to cooperate with the reviewing IRB's responsibilities for initial review and that all information requested by the reviewing IRB must be provided in a timely manner.

2. Submission of Request for Reliance on Another IRB

a. Prior to submitting an application to an external IRB, the LG Health investigator must submit to the LGH IRB a request for reliance on the external IRB. The request is to include a brief study description and the consent form.

b. The LGH IRB will verify that:
i. an IRB Authorization Agreement is in effect that covers the study for which the LGH IRB will rely on the review of the external IRB;

ii. as appropriate, the consent form contains LG Health HRPP contact information and LG Health subject injury language and addresses confidentiality of research data collected by LG Health research staff;
iii. human subject protections certifications have been completed by research personnel, in accordance with LG Health policies;
iv. research staff possess relevant qualifications and expertise to conduct the research; and
v. financial disclosures have been completed by research personnel, in accordance with LG Health policies. Any organizational conflicts of interest will be managed by LG Health and reported, as appropriate, to the IRB of record.

c. The LGH IRB will provide written acknowledgment to the LG Health investigator that the above requirements are met. This acknowledgment may be submitted to the external IRB.

3. Clearance to Begin Research

a. The LG Health investigator (or designated study staff member) is to update the LGH IRB after approval by the external IRB. The LG Health investigator must supply:
i. the approved research protocol;
ii. the approved research consent;
iii. the executed contract or grant award to fund the study, if applicable;
iv. approved recruitment materials, as applicable; and
v. written documentation from the external IRB confirming that it is the IRB of record and as such has approved the research.

b. The LG Health HRPP is to verify that the contract or grant award, if applicable, is consistent with the approved research consent.

c. The LG Health HRPP then issues notice to the Principal Investigator of clearance to begin the research.

d. The LG Health investigator is responsible for:
i. complying with the determinations and requirements of the reviewing IRB;
ii. cooperating with the reviewing IRB's responsibilities for continuing review, review of changes to approved research, review of reportable information, and that all information requested by the reviewing IRB must be provided in a timely manner;
iii. promptly reporting any proposed changes to the research to the reviewing IRB in accordance with the reviewing IRB's policies and procedures. Not implementing changes without IRB approval unless necessary to eliminate apparent immediate hazards to subjects and for informing the reviewing IRB of any such changes in accordance with their policies and procedures;
iv. promptly reporting issues (e.g., complaints, unanticipated problems, noncompliance, etc.) or other reportable information (e.g., DSMB reports) to the reviewing IRB in accordance with their policies and procedures;
v. notifying the reviewing IRB when local policies that may impact IRB review are updated (e.g., who may serve as a legally-authorized representative); and
vi. when enrolling subjects, obtaining, documenting, and maintaining records of consent in compliance with the reviewing IRB's and LGH's requirements.

4. Responsibilities During Study Conduct

a. During the conduct of the study, the LG Health investigator (or designated study staff member) is to supply to the LGH IRB:

i. updates to disclosures of conflicts of interest when new conflicts of interest or changes to existing conflicts of interest are identified, or certification that there are no changes, in advance of continuing review by the IRB of record;
ii. local changes in research status, key personnel, and other administrative changes on an ongoing basis;
iii. documentation of continuing reviews, along with a summary of research conduct including information such as: number of enrollees, study status, and local complaints;
iv. approved amended protocols, consents, and recruitment materials;
v. documentation of study close-out; and
vi. any other communications from the IRB of record that is relevant to the conduct of the research and to the protection of human subjects at LG Health.

b. Investigators and/or study personnel should contact the LGH IRB office if they have any questions, concerns, suggestions, or other input regarding the reviewing IRB or the reliance requirements.

ROLES/REPONSIBILITIES

DEFINITIONS

IRB of record: An IRB other than the LGH IRB that, by mutual agreement, has assumed responsibility for a protocol or multiple protocols to be conducted at LG Health. The IRB of record has the authority to approve, require modification to, or disapprove a protocol before it is conducted at LG Health, as well as to place restrictions on, suspend, or terminate a study at LG Health based on continuing review. The LGH IRB relies on, or defers to, the review of the IRB of record.

Authorization Agreement: An agreement, also called a reliance agreement, which documents respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

REFERENCE DOCUMENTS

LG Health HRPP Policy: Reliance on the National Cancer Institute Central IRB
IRB Authorization Agreement Request Form

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR § 56.114
45 CFR § 46.114
AAHRPP Standards I-.2, II.5.B, and I-9

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Reliance on the National Cancer Institute Central IRB **Policy No. 206**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 07/01/16, 08/31/17, 01/05/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: To set forth the mechanism for the Lancaster General Hospital (LGH) Institutional Review Board (IRB) to rely on the review of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB).

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to the LGH IRB, and to investigators and other research staff engaged in human subject research initiated by the National Cancer Institute Cooperative Groups and conducted at LG Health.

POLICY STATEMENT: LGH IRB has agreed to rely on the National Cancer Institute CIRB for review of Phase III cancer cooperative group trials conducted at LG Health. Such research conducted under the auspices of LG Health but reviewed by the CIRB remains subject to LG Health HRPP policies and procedures regarding education and training, conflict of interest disclosure, quality assurance monitoring, and investigation of complaints or allegations of non-compliance. Further, such research, and the oversight of the research, will also adhere to the reliance agreement with the NCI CIRB and the NCI CIRB Standard Operating Procedures. The LGH IRB retains the authority to observe or investigate any aspect of the research process, and the CIRB has the authority to direct this to be done when deemed necessary.

PROCEDURES

1. General Requirements for Reliance on the CIRB

a. LG Health must have an active registration with the CIRB, which includes an Authorization Agreement and Division of Responsibilities between the NCI Central Institutional Review Board and the Signatory Institution and a current Annual Signatory Institution Worksheet about Local Context.

b. The LG Health investigator must complete or have completed CIRB requirements, including an Annual Principal Investigator Worksheet about Local Context and a Study-Specific Worksheet about Local Context.

c. The LG Health researchers are responsible:
   i. to comply with LG Health policies regarding human research protections certification and conflict of interest disclosure.
   ii. to provide information to the LGH IRB as in sections 2, 3 and 4 below.
   iii. to provide to the CIRB for review for each study a consent addendum that provides information to subjects about costs covered by the study and costs for which they or their insurer will be responsible.
   iv. to obtain and maintain all necessary reviews and approvals for the research (e.g., radiation safety)

2. Study-Specific Submission of Request for Reliance on the CIRB

a. Prior to submitting a study application to the CIRB, the LG Health investigator must submit to the LGH IRB a notice of intent to request review by the CIRB.

b. The LGH IRB will verify that:
   i. human subject protections certifications have been completed by research personnel, in accordance with LG Health policies;

ii. conflict of interest disclosures have been completed by research personnel, in accordance with LG Health policies; and
iii. research staff possess relevant qualifications and expertise to conduct the research.

c. The LGH IRB will provide written acknowledgment to the LG Health investigator that the above requirements are met. This acknowledgment may be submitted to the CIRB.

3. Clearance to Begin Study

a. The LG Health investigator is to update LGH IRB after approval by the CIRB. The LG Health investigator must supply:
i. the approved research protocol;
ii. the approved research consent;
iii. approved recruitment materials, as applicable;
iv. approved conflict of interest management plans, as applicable; and
v. written documentation of CIRB approval.

b. The LG Health HRPP then issues notice to the Principal Investigator of clearance to begin the research.

4. Responsibilities During Conduct of Study Approved by the CIRB

a. During the conduct of the study, the LG Health investigator is to supply to the LGH IRB:
i. updates to disclosures of conflicts of interest when new conflicts of interest or changes to existing conflicts of interest are identified, or certification that there are no changes, in advance of continuing review by the CIRB;
ii. local changes in research status, key personnel, and other administrative changes on an ongoing basis;
iii. documentation of continuing reviews, along with a summary of research conduct including information such as: number of enrollees, study status, and local complaints;
iv. approved amended protocols, consents, and recruitment materials;
v. documentation of study closure; and
vi. any other communications from the CIRB that are relevant to the conduct of the research and the protection of human subjects at LG Health.

ROLES/REPONSIBILITIES

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS
AAHRPP Standard I.9

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Serving as IRB of Record Policy No. 207	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/29/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: To set forth the mechanism for the Lancaster General Hospital (LGH) Institutional Review Board (IRB) to serve as the IRB of record for another organization.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to the LGH IRB, and investigators and other research staff engaged in human subject research at any entity under the purview of the LGH IRB. **Unless the circumstances are reviewed by the LG Health HRPP and permission is granted, LGH IRB will not serve as an IRB of record for phase I studies.**

POLICY STATEMENT: When applicable, LGH IRB complies with federal single IRB (sIRB) requirements and may serve as the IRB of record when appropriate. The LGH IRB must agree to this designation in advance. LGH IRB may enter into an agreement to serve as the IRB of record for an external organization for review of specific research projects or categories of research. Such an agreement shall be documented in a written IRB Authorization Agreement with the external organization. The IRB Authorization Agreement shall describe the roles and responsibilities of each organization, to be maintained by each organization and made available to applicable regulatory bodies, funding agencies, and accrediting organizations upon request. Such research conducted under the auspices of LGH IRB shall be subject to LG Health HRPP policies and procedures, and the LG Health HRPP retains the authority to issue the final clearance for initiation of the research. The LGH IRB retains the authority to observe or investigate any aspect of the research process and has the authority to direct this to be done when deemed necessary.

PROCEDURES

1. **Requirements for Serving as IRB of Record for External Organizations**
    a. An IRB Authorization Agreement with the external organization must be executed to allow the LGH IRB to become the IRB of record for the research.
        i. An IRB Authorization Agreement may cover only one study or multiple studies, but the agreement must clearly cover the particular study for which reliance on the LGH IRB is being sought.
        ii. The IRB Authorization Agreement must stipulate a communication plan. This plan must address the key responsibilities including the communication from LGH IRB regarding the actions it takes, requirements, and determinations; communication from the relying organization about relevant local context, verification of training, conflicts of interest; communication regarding the reporting and determination of events affecting investigators or subjects, or unanticipated problems, deviations, or other information requiring investigation; and the communication from the LGH IRB or LG Health HRPP regarding results of quality assurance monitoring or investigations of complaints or allegations of non-compliance.
    b. The external researchers are responsible:
        i. to comply with LG Health policies regarding human research protections certification and conflict of interest disclosure;
        ii. to provide proof of qualifications, as applicable, to include medical licenses and/or curriculum vitae;
        iii. to provide information to the LGH IRB as in sections 2-5 below;
        iv. to provide information to the LGH IRB or review as described in LG Health HRPP Policy 402; and

v. to commence research activities only after final approval from the LG Health HRPP.

c. When the LGH IRB serves as the IRB of record for another organization, LGH IRB adheres to regulatory requirements and AAHRPP standards as follows:
   i. The LGH IRB composition is appropriate for the research it reviews and complies with applicable regulatory requirements (e.g., DHHS, FDA, HIPAA). When needed, the LGH IRB supplements its expertise through the use of qualified consulting reviewers. Individuals who have a substantial role in bringing funds to LG Health may not serve as members of the IRB or be involved in the IRB's day-to-day operations. See LG Health HRPP Policy 202 for more information.
   ii. The LGH IRB conducts IRB review in accordance with applicable regulatory requirements and AAHRPP standards including initial review, continuing review, review of changes to approved research, and the review of reportable information. The LGH IRB review includes scientific evaluation of the research. When the relying organization conducts scientific review, the results of that review will be provided to the LGH IRB. See LG Health HRPP Policies 402, 403, 405, and 511 for more information.
   iii. The LGH IRB has the authority to observe the consent process or audit the research, or to request that the relying organization do so on its behalf.
   iv. The LGH IRB has the authority to determine that noncompliance is serious or continuing, to determine that an event or issue is an unanticipated problem involving risks to subjects or others, and to require changes to the research, investigators, or study personnel as a result. See LG Health HRPP Policies 511 and 702 for more information.
   v. The LGH IRB has the authority to suspend or terminate IRB approval for any site for which it serves as the reviewing IRB. See LG Health HRPP Policy 701 for more information.
   vi. When applicable, the LGH IRB would draft and submit any federally-mandated reports (i.e., of serious or continuing noncompliance, of unanticipated problems involving risks to subjects or others, any suspension or termination of IRB approval) unless the IRB Authorization Agreement describes another process for such reports. Copies of such reports will be provided to the relying organization.
   vii. When applicable, the LGH IRB will review the addition of new investigative sites to previously approved protocols. The addition of new investigative sites as modifications to approved research may be conducted using expedited review procedures when there is no substantial difference in the protocol activities conducted at the added site or when the activities at the added site are minimal risk and fall within the expedited categories.
   viii. The LGH IRB will make available to the relying organization relevant IRB records, including but not limited to minutes, approved protocols, consent documents and other records that document the LGH IRB's determination.
   ix. The LGH IRB will be responsible for obtaining any additional approvals from DHHS when the research involves pregnant persons, fetuses, and neonates; or children; or prisoners.
   x. The LGH Human Research Protection Program (HRPP) Policy and Procedure Manual is available on the LGH HRPP webpage.

2. External Investigator Responsibilities

a. Investigators are responsible for complying with the requirements of the LGH IRB and must provide information and respond to inquiries and requirements in a timely manner and in accordance with LGH's HRPP Policies and Procedures which are available on the LGH HRPP webpage. See LG Health HRPP Policy 104 for more information.

b. Investigators are responsible for providing the necessary information to the LGH IRB for the IRB to conduct its review. For multi-site research, it is the responsibility of the Lead Principal Investigator, whether from reliant external organization or from LG Health overseeing a multi-site study, to gather the necessary information from participating sites and to submit to the LGH IRB. See LG Health HRPP Policy 402 for more information regarding IRB review.
c. Investigators are responsible for ensuring that any conflicts of interest (COI) of investigators or study team members and associated conflict management plans (CMP) are reported to the LGH IRB. The LGH IRB has the authority to determine whether the COI and CMP, if any, allow the research to be approved. The LGH IRB may add on to, but may not diminish, any existing CMP.
d. Investigators are responsible for providing the LGH IRB with any relevant local requirements or local context information (e.g., who may serve as a legally authorized representative, expected inclusion of persons not fluent in English, etc.) for relying sites.

3. **Submission of Request to Serve as IRB of Record**

a. Prior to submitting an application to the LGH IRB, the external investigator must submit to the LGH IRB a request for reliance either via email or through electronic IRB system, if available. The request is to include a brief study description and the consent form.
b. The LGH IRB will verify that:
    i. an IRB Authorization Agreement is in effect that covers the study for which the LGH IRB will serve as IRB of record;
    ii. as appropriate, the consent form contains LG Health HRPP contact information
c. The LGH IRB will provide written acknowledgment via emailed letter or through electronic IRB system to the investigator that the above requirements are met. This acknowledgment may be submitted to the external organization.

4. **Clearance to Begin Research**

a. The Principal Investigator (or designated study staff member) is to update any additional sites after approval by the LGH IRB, if applicable. The Principal Investigator must supply:
    i. the approved research protocol;
    ii. the approved research consent;
    iii. the executed contract or grant award to fund the study, if applicable;
    iv. approved recruitment materials, as applicable; and
    v. written documentation from the LGH IRB confirming that it is the IRB of record and as such has approved the research.
b. The LG Health HRPP is to verify that the contract or grant award, if applicable, is consistent with the approved research consent.
c. The LG Health HRPP then issues notice to the Principal Investigator of clearance to begin the research.

5. **Responsibilities During Study Conduct**

a. The LGH IRB is responsible for informing relying site PIs of any relevant changes in LGH IRB policies and procedures or other requirements.
b. During the conduct of the study, the investigator (or designated study staff member) is to supply to the LGH IRB:

i. updates to disclosures of conflicts of interest, or certification that there are no changes, in advance of continuing review by the LGH IRB;
ii. any proposed changes to the research (LG Health HRPP Policy 405);
iii. any changes made to protect subjects from apparent immediate hazards (LG Health HRPP Policy 405);
iv. any potential non-compliance or unanticipated problems involving risks to subjects or others (LG Health HRPP Policies 511 and 702);
v. any other reportable information (LG Health HRPP Policy 511);
vi. continuing review information, when applicable (LG Health HRPP Policy 403);
vii. notification of study closure; and
viii. any other communications that are relevant to the conduct of the research and to the protection of human subjects.

ROLES/REPONSIBILITIES

DEFINITIONS

IRB of record: An IRB upon which an external organization or IRB relies that, by mutual agreement, has assigned responsibility for a protocol or multiple protocols to be conducted, whether at an LG Health or external site. The IRB of record has the authority to approve, require modification to, or disapprove a protocol before it is conducted, as well as to place restrictions on, suspend, or terminate a study based on continuing review. The reliant IRB or organization relies on, or defers to, the review of the IRB of record.

Authorization Agreement: An agreement, also called a reliance agreement, which documents respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

Single IRB (sIRB): The IRB of Record, selected on a per study basis, for all domestic sites participating in cooperative or multi-sit research unless an exclusion applies or has been granted. Relying institutions may conduct their own review of the research but are expected to rely upon the designated sIRB for initial and ongoing review of the research.

REFERENCE DOCUMENTS

IRB Authorization Agreement Form LGH IRB of Record

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR § 56.114
45 CFR § 46.114
AAHRPP Standard I-9

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Terms and Duties of IRB Members Policy No. 301	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 02/20/14, 01/01/15, 08/31/17, 10/19/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy defines the duties required of Institutional Review Board (IRB) members.

APPLICABILITY/SCOPE/EXCLUSIONS: IRB Members.

POLICY STATEMENTS: The primary duty of each IRB member is the protection of the rights and welfare of the individual human beings that are serving as the subjects of that research. The IRB member is not serving on the IRB to expedite the approval of research, but to serve as a link between the investigator and the research subjects. In order to fulfill their duties, IRB members are expected to be knowledgeable of the regulations governing human subject protection, biomedical and behavioral research ethics, and the policies of Lancaster General Health (LG Health) governing human subject protection. The IRB must be perceived to be fair and impartial, immune from pressure either by the LG Health administration, the investigators whose protocols are brought before it, or other professional and nonprofessional sources.

PROCEDURES

1. **Term.** Regular IRB members and the Chair are expected to commit to a 3-year term and fulfill certain duties. These duties will be described prior to appointment and each IRB member is expected to fully understand the duties of IRB members prior to accepting appointment as an IRB member. If a member is added during the 3-year term cycle, their reappointment or termination will occur at the time of the completion of that current 3-year cycle.

2. **Specific Duties**[1]

   a. Regular Members

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

      ii. Nonscientific members. Nonscientific members are expected to provide input on areas within their knowledge, expertise, and experience. For example, members who are lawyers should present the legal views of specific areas that may be discussed, such as exculpatory language or state requirements regarding consent. Nonscientific members should advise the IRB if additional expertise in a nonscientific area is required to assess if the protocol adequately protects the rights and welfare of subjects and to comment on the comprehension of the consent document.

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

1 See LGH IRB Policy "Composition of the Institutional Review Board" for a more detailed definition of each category of member.

iv. Alternate Members. The appointment and function of alternate members is the same as that for primary IRB members. An alternate's expertise and perspective should be comparable to those of the primary member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting, in part or in full, or when the regular member has a conflict of interest in regard to a protocol under review. When an alternate member substitutes for a primary member, the alternate member will receive and review the same materials prior to the IRB meeting that the primary member would have received.

The IRB roster identifies the primary member(s) or class of members (e.g., physician scientist) for whom each alternate member may substitute. When both the regular member and the alternate are in attendance at an IRB meeting, only one may be counted towards quorum and vote. The IRB minutes will document when an alternate member replaces a primary member.

Experienced alternate members may be designated by the Chair to conduct expedited reviews.

b. Chair. In addition to the above responsibilities, the Chair shall perform the following duties:

i. Serve in a leadership role in establishing and implementing IRB policy.

ii. Represent the IRB in discussions with LG Health Administration, the Medical and Dental Staff, investigators, federal and state regulators, and others as necessary.

iii. Direct the proceedings and discussions at full meetings of the IRB.

iv. Review all protocols presented to the full IRB. Communicate with the primary and secondary reviewers as necessary to identify and resolve issues related to the protocols before the IRB meeting.

v. Vote on matters at full IRB meetings.

vi. Call special meetings of the IRB when necessary.

vii. Review and identify, as appropriate, protocols meeting criteria for designation as exempt from IRB review. This responsibility may be delegated to the Vice Chair or another experienced IRB member.

viii. Review and approve, as appropriate, protocols meeting criteria for expedited review. This responsibility may be delegated to the Vice Chair or another experienced IRB member.

ix. Review and sign correspondence on behalf of the IRB.

x. Have an in-depth understanding of the ethical issues, state law, institutional policy and federal research regulations that are applicable to human subject protocols reviewed by the IRB.

xi. Recommend to the Vice President of Research Administration committee members for appointment to IRB.

xii. Make decisions in emergency situations to protect subjects and remain in compliance with regulations.

xiii. Suspend the conduct of a research project or clinical trial deemed to place subjects at unacceptable risk pending IRB review.

xiv. Suspend the conduct of a study if the Chair determines that an investigator is not following the IRB's policies or procedures.

xv. Inform IRB and LG Health administration of developing problems.

xvi. Recommend to the Vice President of Research Administration a person to serve as Vice Chair of the IRB.

xvii. Appoint subcommittees of IRB as necessary.

xviii. Relate concerns of IRB staff and members to LG Health administration regarding issues in human research review.

xix. Attend at least one major conference per year on issues related to human subject research protection.

xx. In consultation with LG Health administration, identify education programs for IRB members, investigators and research staff.

c. Vice Chair. In addition to the specific duties listed previously of regular members, the Vice Chair shall perform the following duties:

i. In the absence of the IRB Chair, the Vice Chair will have the same authority as the Chair.

ii. Will be designated by the Chair as an expedited reviewer.

3. Reviewers

a. Primary Reviewers. In addition to the duties described in Section 2.a, above, each regular member of the IRB will serve as a primary reviewer for assigned studies at convened meetings. The primary reviewer presents their findings resulting from review of the application materials and provides an assessment of the soundness and safety of the protocol and recommends specific actions to the IRB. The primary reviewer leads the discussion of the study by the convened IRB. The primary reviewer is to review the entire protocol submission. The primary reviewer will contact the principal investigator regarding any questions or issues with the protocol prior to the IRB meeting at which the protocol will be reviewed.

b. Secondary Reviewers. In addition to the duties described in Section 2.a, above, each regular member of the IRB will serve as a secondary reviewer for assigned studies at convened meetings. The secondary reviewer will serve to supplement the assessment and recommendations provided by the primary reviewer. The secondary reviewer is required to review the entire protocol submission.

c. Expedited Reviewers. The Chair or other experienced IRB member designated in writing by the Chair will serve as an expedited reviewer. The expedited reviewer will meet the following criteria:

i. A minimum of three years' experience as an IRB member.
ii. Complete annual educational activity related to human subject research protection.
iii. Designated by the Chair.
iv. Demonstrate scientific or scholarly expertise.

4. Evaluations of IRB Members and IRB Chair

a. IRB Members and the Chair will be asked to complete a Self-Evaluation Form of the IRB on an annual basis. In addition, on an annual basis, the IRB members will complete an Evaluation Form of the Chair of the IRB. The IRB Self-Evaluation will evaluate the function and operations of the IRB, such as quality of reviews, knowledge of policies and procedures, and preparedness for IRB meetings. The IRB Chair Evaluation Form will evaluate, for example, the Chair's attendance at meetings, the Chair's leadership capabilities, preparedness for meetings, and communication.

b. The Vice President of Research Administration will review the IRB Member and Chair self-assessments and evaluation of the Chair annually and provide feedback to the IRB Chair. The IRB Chair will review the members' self-evaluations and provide the members with feedback. Information gathered in the assessment will also be used to determine education and training needs and to make decisions regarding continuation of IRB membership.

5. Education. Each IRB Member must attend continuing educational sessions, as assigned by the Chair of the IRB. The purpose of the educational program is to ensure IRB Members maintain the competencies required to be effective members of the IRB. The educational sessions may focus on topics such as informed consent, privacy and confidentiality, and scientific validity. In addition each IRB Member must complete the required CITI training on a triennial basis.

ROLES/REPONSIBILITIES

IRB Members and the Chair shall be responsible to carry out the responsibilities outlined in this Policy.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standards I.1.E and II.1.B

SAMPLE SELF-EVALUATION
IRB CHAIR

This assessment tool is designed to help you evaluate your individual service as Chair of the IRB.

	YES	NO	COMMENTS
I direct the proceedings and discussions at full meetings of the IRB efficiently.			
I allow sufficient time for discussion while keeping meetings to defined times.			
I ensure all Board members are given an opportunity for input and treat all opinions with respect.			
I call special meetings of the IRB and appoint subcommittees as necessary			
I communicate regularly to Board members, both as a group and individually			
I have an in-depth understanding of the ethical issues, state law, institutional policy, and federal research regulations that are applicable to human subject protocols reviewed by the IRB.			
I communicate with the primary and secondary reviewers as necessary to identify and resolve issues related to the protocols prior to the meeting.			
I am prepared to lead convened meetings by having general knowledge of all protocols being reviewed.			
I communicate with investigators as needed and can provide guidance in regards to research activities.			
I make decisions in emergency situations to protect subjects and remain in compliance with regulations.			
I identify educational needs for IRB Members, investigators and research staff			

Additional Comments: _____

_____

_____

SAMPLE IRB MEMBER SELF-EVALUATION

This assessment tool is designed to help you evaluate your individual board service. The tool will also provide insight to the IRB Chair and Administrators of any educational needs that may be appropriate for the members of the board.

	YES	NO	COMMENTS
I understand the role of the IRB and my legal and ethical responsibilities as a board member.			
I usually attend regular and special board meetings.			
If I am unable to attend a scheduled meeting I notify the IRB Coordinator in a timely fashion.			
I read all materials I receive prior to the board meetings and come prepared to participate in discussion.			
I complete my assigned reviews in a timely fashion.			
I communicate with investigators as necessary to identify and resolve issues related to protocols prior to the meeting.			
I avoid participation in board issues where it may be perceived I have a conflict of interest.			
I attend educational programs provided by the hospital pertaining to the protection of the rights and welfare of human research subjects.			
I try to be an objective decision maker, considering the impact of issues on individuals, the organization, and the community.			
I actively participate in board meetings by listening, discussing, and presenting complete information as required.			
I am willing to participate in development opportunities including workshops, information sessions, conferences, and taking on new roles.			
I enjoy this service, as a board member in the organization.			

Please provide any suggestions for future educational programs that you believe would be helpful to you in continuing in your role as a member of the IRB.

1. _____

2. _____

3. _____

Name: _____ Date: _____

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Conflicts of Interest Involving IRB members Policy No. 302	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 03/19/14, 01/01/15, 10/12/17, 10/28/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy concerns financial relationships and possible conflicts of interest (COI) for Institutional Review Board (IRB) members and the Chair.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all members of the Lancaster General Hospital (LGH) IRB and their immediate family members.

POLICY STATEMENTS: In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, conflicts should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated.

PROCEDURES

1. **Disclosure and Documentation of Financial Interest and COI.** At a convened meeting, no regular or alternate IRB member may participate in the initial or continuing review of any research project or protocol in which the member has a potential conflict of interest (COI), except to provide information as requested.[1] Potential COIs comprise financial interests related to the research and any role in the research, including a role in monitoring study data on safety or efficacy. It is the responsibility of each voting member or alternate member of the IRB to disclose any potential COI in a study submitted to the IRB and to recuse themselves from deliberations, except as requested to provide information, and from voting. IRB members with a COI will leave the room for the discussion of the protocol and the vote, or be excused to a waiting room if attending virtually, and will not be counted towards a quorum.

   When an IRB member, including the Chair, recuses themselves from deliberating and voting on a protocol, such recusal will be identified in the minutes of the meeting, indicating that a potential conflict of interest was the reason for the recusal.

   No IRB member designated as an expedited reviewer may participate in any expedited review in which the member has a potential COI. This includes review of the initial or continuing application, changes in approved research, and anticipated problems involving risks to subjects or others.

2. **LGH Employees.** LGH employees whose job status or compensation is impacted by research that is reviewed by the IRB must be recused from deliberations, except as requested to provide information, and from voting.

3. **Annual Financial Disclosure.** IRB members shall be required to provide yearly disclosure of their financial interests.

4. **Education and Training in COI.** IRB members are required to participate in education and training activities related to financial conflict of interest issues and requirements for recusal, as specified in this policy.

[1] 45 CFR § 46.107(e); 21 CFR § 56.107(e).

ROLES/REPONSIBILITIES

IRB members shall be responsible for reporting any COI with any research project. IRB members will also be responsible for recusing themselves from any deliberations and voting on any research project in which they have a COI.

DEFINITIONS

Conflict of Interest: IRB member or an Immediate Family Member of the IRB member has: (i) a close personal or professional association with the submitting investigator(s) or sponsoring company, direct participation in the research (*e.g.*, protocol development, principal or sub-investigator); or (ii) any significant financial interest in any sponsoring company defined as greater than $5,000 or 5% ownership interest.

Immediate family member: Spouse; biologic or adoptive parent, child, or sibling; stepparent, stepchild, stepsibling; parent-in-law, child-in-law, sibling-in-law.

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.107(e); 21 CFR § 56.107(e)
AAHRPP Standards II.1.D

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Management of IRB Staff Policy No. 303	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 02/19/14, 01/01/15, 08/31/17, 10/28/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to describe management policies and procedures to ensure the efficient and effective administration and enforcement of Institutional Review Board (IRB) decisions.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to IRB staff and individuals charged with evaluating the staff.

POLICY STATEMENTS: IRB staff shall include administrative personnel to manage the applications to the IRB and to serve as a daily link between the IRB and the research community.

PROCEDURES

1. **Job Descriptions and Performance Evaluations.** Members of the IRB staff should have a description of the responsibilities expected of their positions. The performance of IRB staff will be reviewed according to applicable Lancaster General Health (LG Health) policies.

2. **Staff Positions.** Staffing levels and function allocation will be determined according to LG Health policies, management assessment of support requirements, and budget constraints.

3. **Hiring and Terminating IRB Staff.** The Human Resource policies of the LG Health determine the policies for recruiting and hiring staff. Delegation of specific functions, authorities, or responsibilities may be authorized by the Vice President of Research Administration or IRB Chair to an appropriate staff member.

4. **Documentation.** The Human Resource policies of the LG Health determine the policies for identifying, documenting, and retaining formal staff interactions such as performance reviews, termination procedures.

ROLES/REPONSIBILITIES

The manager of the IRB staff shall be responsible for providing performance review of IRB staff as outlined in applicable LG Health policies.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standard II.1.B

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Electronic Submission of Information to the IRB Policy No. 304	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 02/19/14, 01/01/15, 08/31/17, 03/6/18, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy outlines the process of submitting research information through the electronic Institutional Review Board (IRB) system, IRBManager.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health), IRB Chair and Members, and IRB staff.

POLICY STATEMENTS: The IRB requires investigators to submit all proposed human subjects research applications, continuing review reports, amendments to previously approved research, and unanticipated problems through the electronic IRB application system IRBManager.

PROCEDURES

1. Electronic Submissions

a. IRBManager is an internet-based program. The HRPP & IRB Manager or their designee has full access to the system. Access to the IRBManager is controlled by the IRB Office and is limited to individuals on a need to know basis. Investigators and research staff must contact the IRB Office to gain access to IRBManager. Access to investigators and their research staff is limited to their research studies only. Electronic submissions must contain all material required for the IRB to make the determinations required under OHRP and FDA regulations, and under GCP guidelines, when required by a sponsor.

b. IRB members have access to enable them to review submitted reports and uploaded documents. Information and uploaded documents obtained and reviewed as part of IRB functions are treated as confidential. The information will not be discussed or disclosed outside of the LG Health review process.

c. The submission requirements are outlined on forms built into IRBManager to provide guidance to research staff and investigators. IRBManager also provides checklists with guidance for reviewers to complete reviews.

ROLES/REPONSIBILITIES

The Principal Investigator shall be responsible to submit all required documentation through the electronic IRB system for IRB review.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 108; 21 CFR § 56.108
AAHRPP Standard II.2.E

Penn Medicine
Lancaster General Hospital

POLICY TITLE: IRB Meeting Administration Policy No. 305	
Policy Author: Jonathan B Derr, MS, MBA	**Last Review/Revision Date: 02/19/14, 01/01/15, 08/31/17, 10/28/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy outlines the process to ensure that Institutional Review Board (IRB) meetings are conducted and documented in a consistent manner in order to meet federal and institutional requirements.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to the IRB Chair and Members, and IRB staff.

POLICY STATEMENTS: Except when an expedited review procedure is used, the IRB will review proposed research at convened meetings at which a quorum is present. The IRB will meet monthly.

PROCEDURES

1. IRB Meeting Administration

a. The IRB Chair will direct the proceedings and discussions at the convened meetings. If the Chair is unavailable or is recused due to a conflict of interest the responsibilities will be delegated to the Vice Chair.

b. Quorum

i. A majority of members must be present. Majority is defined as first whole number that exceeds 50%. The IRB Chair will determine when a quorum is established and call the meeting to order.
ii. A quorum consists of regular and/or alternate members and includes at least one member whose primary concerns are in scientific areas, and one member whose primary concerns are in nonscientific areas.
iii. An alternate member may attend in place of a regular member in order to meet the quorum requirements outlined above.
iv. Special consultant(s) will not be used to establish quorum.
v. While not required for quorum, an unaffiliated member and a community representative (who may be the same person) are expected to be in attendance at the majority of meetings.
vi. At the beginning of each IRB meeting, the Chair will ask all IRB members if the IRB member has a conflict of interest related to an agenda item. If a member identifies a conflict with an agenda item, that member will leave the room (or be moved to a waiting room when meeting virtually) during final discussion and vote of the protocol and the member will not be counted towards quorum. The member may participate only to the extent of providing information as requested. This recusal will be documented in the minutes of the meeting.
vii. If a member has not reviewed an agenda item or items, they will be expected to abstain from the discussion and vote for those items. But the member will still count towards the quorum.
viii. In the event the convened IRB reviews research involving a vulnerable population, an individual representing the interests of the group is to be present. When reviewing research involving prisoners, the prisoner representative will be present.

2. Primary Reviewers and Secondary Reviewers

a. Prior to the meeting, the HRPP & IRB Manager or their designee will designate primary and secondary reviewers for each new research protocol and a primary reviewer for each continuing review report and amendment requiring review at the convened meeting. At least one reviewer must have the appropriate scientific or scholarly expertise to conduct an in-depth review of the protocol. The HRPP & IRB Manager or their designee will assign primary and secondary reviewers based on the IRB Member's: (i) scientific or non-scientific background; (ii) particular knowledge and experience in treating or caring for patients who may be recruited for participation in the protocol; (iii) lack of a conflict of interest with the protocol; and (iv) experience on the IRB. The HRPP & IRB Manager or their designee may also consider other factors when assigning primary and secondary reviewers. When the IRB does not have the necessary expertise, for a review available among its members, or when the review could benefit from additional expertise, the HRPP & IRB Manager or their designee will evaluate each protocol and consult with the IRB Chair regarding the need for a Special Consultant in accordance with **Policy 202: Composition of the IRB**. The research will not be scheduled for review at a meeting until the appropriate scientific or scholarly expertise can be obtained. The HRPP & IRB Manager or their designee will inform, in writing, all primary and secondary reviewers of their assignment to review materials. The primary reviewer presents their findings resulting from review of the application materials and provides an assessment of the soundness and safety of the protocol and recommends specific actions to the IRB. The primary reviewer leads the discussion of the study by the convened IRB. The primary reviewer is further to review the entire protocol submission.

b. The secondary reviewer will serve to supplement the assessment and recommendations provided by the primary reviewer. The secondary reviewer is required to review the entire protocol submission.

c. All other members will review materials provided prior to the meeting and will be prepared to participate in the discussion at the convened meeting.

3. Meeting Materials Sent Prior to IRB Meetings. The HRPP & IRB Manager or their designee will send, in writing, to all IRB members study documentation required for review in sufficient time – generally two weeks – prior to the meeting to allow for adequate review. These include:

a. A meeting agenda prepared by the HRPP & IRB Manager or their designee. The agenda will include all reviews to be completed at the convened meeting, all expedited reviews completed since the previous meeting, and all pertinent correspondence to the IRB from researchers.

b. Meeting minutes from the previous IRB meeting will be distributed for final approval at the convened meeting.

c. Research materials (*e.g.*, the protocol, informed consent forms, and recruitment materials) necessary to successfully review the submissions to verify that the approval criteria are met will be provided to the IRB members through IRBManager.

4. Minutes

a. The HRPP & IRB Manager or their designee will prepare IRB minutes and organize the contents of the minutes in accordance with the policy Documenting IRB Discussions and Decisions. Minutes shall be sufficient in detail to show attendance at the meetings, actions taken by the IRB, the vote on these

actions including the number of members voting for, against, and abstaining, the basis for requiring changes in or disapproving research, and a written summary of the discussion of controverted issues and their resolution.

b. Draft minutes will be distributed to the IRB Chair for initial review and approval. The minutes will be distributed to the IRB members prior to the next convened IRB meeting for final approval. Any corrections requested by the IRB will be made by the HRPP & IRB Manager or their designee.

c. The HRPP & IRB Manager or their designee will maintain copies of the agendas and minutes.

5. Voting

a. Members of the IRB vote upon the recommendations made by the primary reviewers according to the criteria for approval. If quorum is lost during a meeting (e.g. through the loss of a required member), the IRB cannot take votes until it is restored. Any loss of quorum is documented in the meeting minutes.

b. Votes may be taken by voice vote, show of hands, or poll response if meeting virtually. Poll responses shall document respondent names.

c. For research to be approved it must receive the approval of a majority of voting members present at the meeting.

ROLES/REPONSIBILITIES

The Principal Investigator shall be responsible to submit all required documentation through the electronic IRB system for IRB review.

IRB members shall be responsible to review their assigned reviews prior to the meeting.

The HRPP & IRB Manager or their designee shall be responsible to document and distribute meeting agendas and minutes to IRB members.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 108; 21 CFR § 56.108
AAHRPP Standards II.1.E, II.2.D, and II.2.E

Penn Medicine
Lancaster General Hospital

POLICY TITLE: **Documenting IRB Discussions and Decisions** **Policy No. 306**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 02/19/14, 01/01/15, 08/31/17, 12/17/20, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to describe documentation of discussions, decisions and actions taken by the IRB at convened meetings through minutes. Minutes of IRB meetings should be clear regarding the actions and exactly what the IRB approved.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to IRB staff and IRB Chair or designee.

POLICY STATEMENT: Discussions and actions performed by the IRB at convened meetings will be documented in minutes.

PROCEDURES

1. The following items should be documented in the minutes:

   a. Attendance at each meeting, including
      i. Each member's (or alternate's) full name;
      ii. Each member's (or alternate's) representative capacity (e.g., scientist, non-scientist, unaffiliated, member who represents the general perspective of research subjects);
      iii. The names of members or alternate members who are participating through videoconference or teleconference;
      iv. Names of alternates attending in lieu of specified (named) absent members;
      v. Names of any consultants present, a brief explanation of their expertise, and notation that the consultant(s) did not vote; and
      vi. The names of non-members and guests in attendance, such as IRB staff, investigators, and study coordinators.

      Note: The minutes will indicate, by name, those members who enter or leave the meeting including notation when the reason for leaving is due to a conflict of interest. The vote on each action will reflect the numbers of members present for the vote on that item.

   b. Notation when alternate member replaces a primary member.
   c. Names of investigators, consultants, or guests at each meeting.
   d. A description of each item reviewed at the meeting, including the type of review (e.g., initial, continuation, modification, interim report).
   e. Actions taken by the IRB.
   f. Separate deliberations for each action.
   g. Votes for each protocol as numbers for, against, or abstaining.
   h. The names of IRB members who leave the meeting due to a conflict of interest as well as documentation that a conflict of interest is the reason for absence.
   i. For initial and continuing review, the approval period (when applicable).
   j. The rationale for requiring continuing review of research that otherwise would not require continuing review (e.g., under the Common Rule)
   k. The basis for requiring changes in the research.
   l. The basis for disapproving research.

m. Risk determination for initial and continuing reviews. When research falls within the expedited categories but has been determined to be more than minimal risk, the rationale for this determination will be noted.
n. A written summary of the discussion of controverted issues and their resolution.
o. Determinations of conflicts of interests and acceptance or modifications of conflict of interest management plans.
p. The rationale for significant risk/non-significant risk device determinations.
q. Required determinations and protocol-specific findings justifying those determinations for:

i. Waiver or alteration of the consent or authorization process.
ii. Research involving pregnant persons, fetuses, and neonates.
iii. Research involving children.
iv. Research involving prisoners.
v. Research involving subjects with diminished capacity to consent.

2. The IRB Chair or designee will review and approve the minutes documented by the HRPP & IRB Manager or their designee prior to distribution to IRB members.

3. Minutes will be distributed to IRB members prior to the next convened board meeting. At the next meeting a vote will be taken whether to approve the minutes as submitted or accept revisions. No additional departments or officials receive the meeting minutes.

4. Written materials reflect the date of approval based upon the type of review that occurred. The IRB letter is dated for the date the letter was written. The IRB letter will include the date of approval determined as follows:
    a. Full Board Review – New Protocol, Continuing Review: Approval date is the date of the IRB meeting at which it is reviewed and approved.
    b. Full Board Review – Amendments: Approval date is the date of the IRB meeting at which it is reviewed and approved.
    c. Expedited – New Protocol, Continuing Review: Approval date is the date the assigned reviewer approves the submission.
    d. Expedited – Amendments: Approval date is the date the assigned reviewer approves the submission.
    e. Exempt Research: Approval date is the date the assigned reviewer approves the submission.
    f. Approval Pending Modifications: If a study is approved pending modifications, the research team receives a letter following the convened IRB meeting or expedited review deferring the study until required modifications are made. The IRB letter with the requested modifications is dated with the date of the IRB meeting at which it was reviewed. After revisions are made and sent to reviewer, the reviewer(s) evaluates if the revisions fulfill the requested modification(s). If the revisions fulfill the requested modification(s), the study is given full approved. The approval date is the date that the full approval was issued after the modifications were made.
    g. Annual Check-In: The HRPP & IRB Manager or their designee administratively reviews and approves the Annual Check-In. The full IRB Board is notified at the next IRB meeting. Approval date is the date the HRPP & IRB Manager or their designee reviews and approves the submission.
    h. Research Closure, Research Completion: The HRPP & IRB Manager or their designee administratively reviews and approves Research Closure and Research Completion submissions. The

full IRB board is notified at the next IRB meeting. Approval date is the date the HRPP & IRB Manager or their designee reviews and approves the submission.

5. Approval periods are documented in the IRB approval letter. The protocol expires after the approval period ends and must be renewed or closed prior to expiration.

6. All IRB actions are communicated to the research team via the publication of a letter through the IRB electronic system within ten (10) working days, whenever possible, of the review. When applicable, a stamped copy of the approved consent form, parental permission form, and/or assent form will also be published. For IRB actions of conditions required for approval or deferral, the notification will include a listing of the conditions or requirements that must be satisfied or responded to. For a disapproval, suspension, or termination, the notification will include the basis for the action and will offer the investigator an opportunity to respond in person or in writing.

ROLES/REPONSIBILITIES

The HRPP & IRB Manager or their designee shall be responsible for documenting actions in the meeting minutes by the IRB at convened meetings.

IRB Chair or designee shall be responsible for reviewing and approving the IRB meeting minutes prior to distribution to other members of the IRB.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR § 56.115(a)(2) & 45 CFR § 46.115(a)(2)
AAHRPP Standards II.2.E,II.5.B, and II.5.C

Penn Medicine
Lancaster General Hospital

POLICY TITLE: **Documentation and Document Management** **Policy No. 307**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 02/19/14, 01/01/15, 02/04/16, 10/12/17, 01/21/19, 12/30/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the requirements for management and retention of research related documents.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to Institutional Review Board (IRB) staff members responsible for coordination and retention of both electronic and paper records of administrative IRB documents and research files.

POLICY STATEMENTS: IRB files must be maintained in a manner that contains a complete history of all IRB actions related to review and approval of a protocol, including scientific reviews, continuing reviews, modifications, reports of unanticipated problems increasing risks to subjects or others, subject complaints, and reports of serious or continuing noncompliance. All records regarding a submitted study (regardless of whether it is approved) must be retained in an appropriate manner as required by regulatory requirements and/or institutional policy.

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

PROCEDURES

1. IRB Administration Documents

a. Rosters of regular and alternate IRB members identified by name; earned degrees; representative capacity; specialty, indicating chief anticipated contribution to IRB deliberations; and association with LG Health.

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

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

iii. The roster of IRB members must be submitted to the Office for Human Research Protections (OHRP). Any changes in membership are reported to OHRP.

b. Current and obsolete copies of the IRB Policies.

c. IRB agendas and minutes will be retained per regulations.

d. Training records.

e. IRB correspondence including reports to regulatory agencies.

f. Documentation of review by another institution's IRB when appropriate.

g. Documentation of cooperative review agreements, e.g. Memoranda of Understanding (MOUs).

h. Federal Wide Assurances.

i. IRB Registrations.

j. Documentation of complaints and any related findings and/or resolution.

2. **Record Retention**. The IRB must retain all records regarding a project or protocol application (regardless of whether it is approved) for at least six (6) years. For all applications that are approved and the research initiated, the IRB must retain all records regarding that research for at least six (6) years after completion of the research or termination of IRB approval.

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

a. Copies of all original research protocols or project descriptions reviewed; scientific evaluations, if any, that accompany the proposals; investigational brochure, if any; recruitment/educational materials; approved consent documents; progress reports submitted by the investigators; data and safety monitoring reports, if any; modifications to previously approved research; reports of unanticipated problems occurring to subjects and reported protocol deviations as submitted; reports of injuries to subjects; records of continuing review activities; documentation of non-compliance; correspondence between the IRB and the investigator; and statements of significant new findings provided to subjects.

b. Reviewer checklists for full board, expedited, and exempt research will be maintained and retained with the corresponding submissions.

c. Records of completed or terminated research projects may be retained off site during the six year mandatory retention period.

3. **Posting of Clinical Trial Consent Forms**. For each clinical trial conducted by LG Health investigators and supported by a Common Rule department or agency, one IRB-approved consent form that was used to enroll a subject must be posted to a publicly available Federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject. This requirement may be satisfied by either LG Health when it is the prime awardee or the Federal department or agency. LG investigators should consult with the grant officer regarding how to satisfy this requirement. The Federal funding department or agency supporting or conducting a clinical trial may determine that they will not make certain information publically available. Additionally, the Federal department or agency may permit or require redactions to information already posted. LG Health has the ability to electronically redact documents and will perform this as requested by the funding department or agency.

ROLES/REPONSIBILITIES

The IRB staff shall be responsible for maintaining and retention of required administrative documents and research projects documentation.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.115, 45 CFR § 46.116h; 21 CFR § 56.115
AAHRPP Standards II.3.F, II.5.A, and III.1.F

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Categories of Action Policy No. 401	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 02/19/14, 01/01/15, 02/04/16, 08/31/17, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the actions the Institutional Review Board (IRB) may take resulting from its review of human subject research.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) and members of the IRB.

POLICY STATEMENTS: As a result of its review, the IRB may determine to approve or disapprove the proposed research activity, or to require modifications to the project/protocol/documents in order to secure IRB approval of the research activity, including exempt research activities as listed in the Exempt Research Policy. For a full board review, any of the below actions will be taken by a vote of a majority of the regular and alternate members present, except for those members present but unable to vote in accordance with the Conflicts of Interest Involving IRB Members Policy. When reviewed via expedited review, the IRB Chair or designee can take any of the actions below except to disapprove a study.[1]

PROCEDURES

1. **Categories of Action.** The IRB may make one of the following determinations as a result of its review of research submitted for initial or for continuing review:

   a. **Approved:** The protocol and accompanying documents are approved as submitted. Final approval will commence on the day the study is approved by an action of the convened IRB or the Chair or their designee, if the review is conducted through the expedited process. The IRB will set the frequency of review of the research that is appropriate to the degree of risk, but in no event will the frequency of review be less than once per year.

   b. **Approved Pending Modifications:** The convened IRB, or the Chair or Chair's designee when conducting a review under an expedited procedure, stipulates specific changes requiring simple concurrence by the investigator. Changes required will be discussed and will be voted upon during the IRB meeting, as well as the terms of approval, duration of approval and risk level. The investigator will be informed in writing of the required changes and requested information and must provide the IRB with the changes or information in writing.

   The Chair or Chair's designee or the person designated by the IRB at a convened meeting to review the changes has the authority to review the information provided by the investigator. If the designated IRB reviewer determines that the investigator has not made the appropriate responses to the IRB's request, they may request additional information or request re-review of the response by the full IRB at a convened meeting. Upon satisfactory review, approval will be issued as of the date that the requested information or materials are approved. However, the expiration date will be based on the date of the initial IRB review. Subjects must not be recruited, nor the project or protocol begun until final approval has been issued.

1 45CFR § 46.109(a); 21CFR § 56.109(a)

c. **Tabled:** Significant questions are raised by the proposal requiring its reconsideration after additional information is received from the sponsor and/or investigator. These requirements shall be transmitted to the investigators by the IRB staff and the modified documents provided to the IRB members at the next appropriate convened meeting.

d. **Disapproved:** The proposal fails to meet one or more of the criteria used by the IRB for approval of research. Disapproval cannot be given through the expedited review mechanism and may only be given by majority vote at a convened meeting of the IRB. Researchers will receive a letter documenting the reasons for the decision to disapprove the research activity and providing the researcher the opportunity to respond in person or writing.

e. **Additional Actions:** In addition to the above actions, the IRB may acknowledge reports and other items that do not involve prospective changes to already approved research. For example, the IRB may acknowledge a Data Safety Monitoring Board report when no issues were identified. The IRB may also acknowledge administrative changes (e.g. adding translated study documents). Further, the IRB may approve an item but include comments noting certain requirements, restrictions, or understandings. For example, with collaborative research, the IRB may note that approval must also be obtained from another IRB with jurisdiction and that the letter documenting that approval must submitted to the appropriate IRB before human research activities involving the collaborating organization or personnel may commence.

ROLES/REPONSIBILITIES

IRB members shall be responsible to determine a category of action as described above when reviewing research projects.

Research investigators shall be responsible to accept the IRB recommendations after review and make modifications if needed.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45CFR § 46.109(a); 21CFR § 56.109(a)

AAHRPP Standard II.2.E.

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Initial Review of Research Policy No. 402	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 08/14/07, 04/25/11, 02/05/14, 01/01/15, 10/23/15, 02/04/16, 08/31/17, 03/6/18, 02/12/19, 01/23/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy outlines the minimum requirements that all non-exempt research proposals that involve human subject participation must meet in order to be approved for conduct at Lancaster General Health (LG Health).

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at LG Health and Institutional Review Board (IRB) members.

POLICY STATEMENTS: All non-exempt research proposals that will enroll human subjects must meet certain criteria before study-related procedures can be initiated at LG Health. The criteria that must be met are based on the principles of justice, beneficence and respect for persons as discussed in the Belmont Report and are specified below. In addition, certain other criteria that are unique to LG Health may apply and must be met as well before any involvement of human subjects may begin. (Note: Exempt research will be reviewed in accordance with the policy Exempt Research.)

PROCEDURES

IRB members will use the Protocol Reviewer Checklist to determine if the research proposal meets approval criteria. All IRB members receive and review all submission materials in IRBManager, including, as applicable: (1) the application form, (2) the protocol, (3) the proposed consent document or request for waiver, (4) data collection forms, (5) recruitment and educational materials, and (6) the investigator's brochure.

1. **Criteria for Approval of Research.** In order for a research project to be approved, the IRB must find that[1]:

   a. Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and (ii) whenever appropriate, by using procedures already performed on the subjects for diagnostic or treatment purposes. See the Assessment of Risks and Benefits Policy for additional information.

   b. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result. In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from the risks and benefits of therapies those subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility. See the Assessment of Risks and Benefits Policy for additional information.

   c. Selection of subjects is equitable. In making this assessment, the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving a category of subjects who are

[1] 45CFR § 46.111; 21CFR § 56.11

vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons. See the Recruitment Methods/Review of Advertisements Policy for additional information.

d. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by appropriate local, state and federal regulations. See the Informed Consent and HIPAA Authorization Policy and the Surrogate Consent and Authorization Policy for additional information.

e. Informed consent will be appropriately documented as required by local, state and federal regulations. See the Documentation of Informed Consent Policy for additional information.

f. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. See the Data Monitoring for Research Activities Involving More Than Minimal Risk Policy for additional information.

g. When appropriate, there is adequate provision to protect the privacy of subjects and to maintain the confidentiality of data. See Uses and Disclosure of Protected Health Information for Research Policy for additional information.

h. When some or all of the subjects, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence or international sites are used, additional safeguards have been included in the study and in the IRB review process to protect the rights and welfare of these subjects. See the Vulnerable Populations Policy for additional information.

2. **Criteria for Approval of Research Qualifying for Limited IRB Review**. Instead of the criteria required in section 1, the criteria required for approval of research deemed to be no more than minimal risk in the below categories that qualify for limited IRB review are:

a. For a limited review of research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) and for which the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, the IRB only needs to determine that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

b. For a limited review of research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording for which the subjects prospectively agree to the intervention and information collection and for which the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, the IRB only needs to determine that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

3. **Requirements for Research Qualifying for Limited IRB Review.** When reviewing studies that qualify for Limited IRB Review, the IRB will ensure the following requirements are adhered to:

   a. The researcher must submit a protocol/application containing the relevant information for the IRB to determine whether the proposed research meets the criteria for approval required under limited IRB review, as well as a consent document, if applicable.
   b. IRB members conducting limited IRB review may not disapprove a research study.
   c. LG Health retains the authority to suspend or terminate IRB approval of research approved with a limited review.

4. **Additional Criteria for Studies Involving Protected Health Information[2].** Studies involving access to or collection of protected health information within the covered entities of Lancaster General Health require consideration of additional items to protect the privacy of the protected health information (see the policy "Uses and Disclosures of Protected health Information for Research". Therefore the IRB must find that:

   a. appropriate authorization is obtained from human subjects or their effective representative for the use or disclosure of their protected health information; OR

   b. the IRB has approved a waiver of such authorization; OR

   c. the use or disclosure of the protected health information is solely preparatory to research; OR

   d. the use or disclosure being sought is solely for research on decedents; OR

   e. the protected health information will be contained in a limited data set governed by a data use agreement; OR

   f. the protected health information will be de-identified.

5. **Scientific Review.** The IRB, in assessing the risks and benefits of proposed research, must find that the research uses procedures that are consistent with sound research design and that the research design can reasonably answer the proposed research question. Also, when a clinical trial of an investigational product requires adherence to the International Conference on Harmonisation's Good Clinical Practice (GCP or ICH E6) guidelines, the IRB must find that the available nonclinical and clinical information on the investigational product is adequate to support the proposed clinical trial. In reviewing the scientific basis of the research, the IRB may use its own knowledge or experience or may utilize outside resources to assist in reviewing the design of the research, such as consultants, medical department review, or funding agencies. In the event the IRB relies on outside resources to review the research design, the IRB will be provided documentation that the scientific and scholarly review was completed, and this documentation will be maintained with the documentation of IRB review.

6. **Other Criteria.** The IRB may require, prospectively or retrospectively, verification of information submitted by an investigator. The need to verify any information will be determined by the IRB at a convened meeting.

[2] 45 CFR 164.508

The purpose of the verification will be to provide necessary protection to subjects when deemed appropriate by the IRB. The criteria to be used to determine verification of information include the following:

- Probability and magnitude of anticipated risks
- Likely medical condition of the proposed subjects
- Probable nature and frequency of changes that may ordinarily be expected in the proposed research
- Research where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports
- Research conducted by investigators who have previously failed to comply with regulations or the requirements or determination of the IRB
- Research subject to internal audit

7. **Determination of Risk.** When reviewing a protocol, the IRB will assign a risk category to each protocol based on the IRB's analysis of the risk to subjects. The categories of risk are as follows:

a. no more than minimal risk; or
b. more than minimal risk.

The criteria for determining when continuing review is required and the continuing review process are addressed in IRB Policy "Continuing Review of Research."

8. **Period of Approval.** Protocols that meet the criteria for continuing review will be subject to such review at least once every twelve months. The IRB may require that a given protocol, based upon its degree of risk, undergo continuing review on a more frequent basis than annually. These studies may involve: more than minimal risk to subjects, a high degree of uncertainty regarding the risks involved with the research being conducted, subjects with greater levels of vulnerability, investigators with limited experience with research or with the specific type of research being conducted, investigators with reported complaints or compliancy issues (either from the EC, IRB, or former research subjects), use of novel therapies, or anticipated rapid enrollment rate. In such cases, the approval for the protocol will be issued for a shorter time frame (e.g., 6 months). Alternatively, the IRB may require that a protocol undergo continuing review after a specified number of subjects are enrolled or within the time frame for which the study was approved, whichever comes first.

The IRB also may refer a protocol for which there are particular concerns about risk (e.g., a phase I study of a new chemotherapeutic drug) to the Medical Executive Committee and the Board of Trustees for further review. In such a case, approval by these entities as well as by the IRB will be required before study-related procedures can be initiated.

9. **Additional Approvals.** Department Heads and Division Chiefs, if applicable, are asked to sign off on applications. This process occurs through secure email. The Regulatory Manager or other designated research personnel provide the Department Head and Division Chief with the IRB application along with the research protocol via email. They are requested to review the documents and reply back via email if they approve the study or if they have questions or concerns. If they express questions or concerns, the PI or other research personnel may be brought into the conversation to answer questions or the sponsor of the research may be brought into the conversation if no one internally can provide the requested information. If they approve, the email approvals are either attached to the IRB application or sent to the HRPP & IRB Manager, depending on

when they are received in the IRB review process. After studies receive final IRB approval, specific appointed individuals receive copies of the approval letters (e.g., Pharmacy, EP Lab, OR).

Potential studies will be subject to review by the Feasibility Committee, comprising of LG Health research leadership, to assess feasibility with regard to investigator time, necessary subject populations, appropriate facilities and resources, qualified staff to carry out responsibilities during the study, and financial feasibility.

ROLES/REPONSIBILITIES

Principal Investigators shall be responsible for submitting research projects meeting the principles of the Belmont Report: justice, beneficence, and respect for persons.

IRB members shall be responsible to ensure all criteria for research are met when reviewing research projects. IRB members shall also be responsible to ensure that special safeguards are in place in the event vulnerable populations will be enrolled in the research project.

DEFINITIONS

REFERENCE DOCUMENTS

OHRP Guidance: Issues to Consider in the Research Use of Stored Data or Tissues, November 7, 1997
Belmont Report
Guidance for Industry: E6 Good Clinical Practice: Consolidated Guidance, Food and Drug Administration, March 2018, Section 2.4

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.111; 21 CFR § 56.111
45 CFR § 164.508
AAHRPP Standards I.1.D, I.1.F, II.2.C, II.2.E.1, II.2.F.1, II.3.A, II.3.C,II.3.D, II.3.E, II.3.F, III.1.C, III.1.D, III.1.E, III.1.F and III.2.A

Penn Medicine
Lancaster General Health

POLICY TITLE: Continuing Review of Research Policy No. 403	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 03/20/14, 01/01/15, 10/12/17, 01/21/19, 07/26/21, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy outlines the process for the renewal of approved research at the expiration of the Institutional Review Board (IRB) approval period.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) as well as IRB members.

POLICY STATEMENTS: The IRB conducts continuing review (renewal) of research at intervals appropriate to the degree of risk involved with the research, but not less than once per year (except as provided in the policy Exempt Research).

PROCEDURES

1. **Determination Whether Continuing Review is Required.** The Lancaster General Hospital (LGH) IRB will determine whether continuing review of a research project is required. Unless the LGH IRB determines otherwise, continuing review of research is not required in the following circumstances:

   a. Research eligible for expedited review in accordance with the LG Health HRPP Policy 404 "Expedited Review of Research";
   b. Research reviewed in accordance with criteria for IRB review (see LG Health HRPP Policy 402 "Initial Review of Research", Section 2);
   c. Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
      i. Data analysis, including analysis of identifiable private information or identifiable biospecimens, and/or
      ii. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

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

   a. It is required by other applicable regulations (e.g., FDA);
   b. The research involves topics, procedures, or data that may be considered sensitive or controversial;
   c. The research involves particularly vulnerable subjects or circumstances that increase subjects' vulnerability;
   d. An investigator has minimal experience in research or the research type, topic, or procedures; and/or
   e. An investigator has a history of noncompliance.

   When the IRB determines that continuing review is required for such research, it will document that rationale in the IRB record and communicate the requirement to the investigator in the IRB determination letter.

2. **Interval for Review for Purpose of Renewal.** When the IRB conducts continuing review of protocols for purposes of renewal of the IRB approval, it must do so at intervals appropriate to the degree of risk involved with the research, which is determined at the time of initial review. For protocols determined to

be more than minimal risk, this interval shall not be less than once per year.[1] The research must be reviewed on or before the expiration date given at the time of the previous IRB review and approval, even though the research activity may not have begun until sometime after the IRB approval was given. Therefore, investigators or qualified designees are required to submit a Continuing Review Progress Report through the electronic IRB system prior to the expiration of the study or as specified by the IRB. All required documentation shall be attached to the Continuing Review Progress Report. The report should normally be filed within 45 days before the study approval period ends.

There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. Extensions beyond the expiration date will not be granted. If the Continuing Review Progress Report is not received as scheduled, the investigator must suspend the study and study enrollment until reports are reviewed and approved.

However, if the investigator is in communication with the IRB, the Continuing Review Progress Report is forthcoming, and, in the opinion of the IRB, subjects participating in such a study would suffer a hardship if medical care were discontinued, appropriate medical care may continue beyond the expiration date of the study approval period for a reasonable amount of time. However, new subjects cannot be enrolled. Prospective research data cannot be collected, and no procedures that are only being performed for the purposes of the protocol may be performed until a Continuing Review Progress Report is reviewed and approved. However, temporarily continuing follow-up of already enrolled subjects in a research project during the period when IRB approval has lapsed may be necessary or appropriate. For example, this would be relevant when the research interventions hold out the prospect of direct benefit to the subjects (e.g., investigational chemotherapy regimen in an oncology trial), or when withholding those interventions poses increased risk to the subjects. If the IRB decides that already enrolled subjects should continue to receive the interventions that were being administered to subjects under the research protocol, data collection (especially safety information) should also continue for such subjects (e.g., implantable device requiring long-term follow-up).

3. Criteria for Renewal

a. When required, continuing review must be substantive and meaningful. When considering whether or not to renew a study, the IRB revisits the same criteria used to grant initial approval as provided in the policy Initial Review of Research. Therefore, the IRB (or the reviewer for protocols reviewed under an expedited procedure) must determine that:

   i. the risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits;
   ii. the selection of subjects continues to be reasonable in relation to anticipated benefits;
   iii. informed consent continues to be sought and appropriately documented;
   iv. there are provisions for safety monitoring of the data, protections to ensure the privacy of subjects and confidentiality of data, and appropriate safeguards for vulnerable populations.

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

[1] 45 CFR §§ 46.103(b)(4) and 46.109(e); 21CFR § 56.109(f); OHRP Guidance on Continuing Review, November 10, 2010.

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

i. Continuing Review Progress Report. All IRB members shall have access to the Continuing Review Progress Report prepared and submitted by the principal investigator through the electronic IRB system. The Continuing Review Progress Report shall include the following information:

a. the number of subjects accrued into the protocol to date;
b. the number or subjects withdrawn from the protocol and the reasons for withdrawal;
c. a summary of adverse events and any unanticipated problems involving risks to subjects or others;
d. a summary of deviations from the protocol;
e. a summary of any complaints about the protocol;
f. a summary of any recent literature, interim findings, and amendments or modifications to the research since the last submission for review;
g. a reassessment of the risk-to-benefit ratio in light of ongoing study findings;
h. any new information relevant to the protocol that has become available to the investigator since the last submission for review by the IRB; and
i. any multi-center trial reports.

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

iii. Current Approved Protocol including any amendments to the protocol since initial review. A copy of the protocol will be available to the primary reviewer of the continuing review through the electronic IRB system. Amendments and addenda to a research protocol should be submitted as generated during the course of the study. They may also be submitted at the time of the continuing review. The amendment and all appropriate documentation (revised informed consent form) must accompany the continuing review application.

d. Continuing Review of DSMB-Monitored Clinical Trials. When a clinical trial is subject to oversight by a Data Safety Monitoring Board (DSMB), whose responsibilities include review of adverse events, interim findings and relevant literature (e.g., DSMBs operating in accordance with the National Cancer Institute Policy for Data and Safety Monitoring of Clinical Trials), the IRB conducting continuing review may rely on a current statement from the DSMB indicating that it has reviewed study-wide adverse events, interim findings and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB. However, the IRB must still receive and review reports of local, on-site unanticipated problems involving risks to subjects or others and any other information needed to ensure that its continuing review is substantive and meaningful.

4. Possible Outcomes of Continuing Review. As an outcome of continuing review, the IRB may authorize continuation of the research, require that the research be modified, or suspend the research. The IRB may need to impose special precautions or relax special requirements it had previously imposed on the research protocol such as frequency of monitoring, requirement for interim reports, or duration of approval period. Any changes required to obtain continued renewal approval shall be provided to the investigators by the IRB

staff. The IRB may also require that any significant new findings that arise from the review process or changes made to the research that might influence subjects' willingness to continue participation (e.g. the expected benefits and risks or the length of participation in the research) be provided to subjects.

5. **Expedited Review for Renewal.** A protocol initially reviewed by the convened IRB may be reviewed using an expedited mechanism if category (8) or category (9) of the expedited review categories is satisfied (See the Expedited Review Policy for additional information). Additionally, a protocol that was determined by the full IRB to qualify for expedited review at the time of initial review (see categories of expedited review in the Expedited Review Policy) may be reviewed and re-approved using an Annual Check-In. If the research qualifies to be reviewed using an Annual Check-In, the research team will receive an email generated from the electronic IRBManager system 28 days prior to the research expiration date. Only critical elements will be collected in this submission including the status of the research and a summary of the research's progress to date. This Annual Check-In submission is reviewed by the HRPP & IRB Manager or their designee and approved administratively without requiring full board review. The full board is notified at the next IRB meeting.

   Further, a protocol that was originally reviewed using expedited review procedures and determined to require continuing review may receive its continuing review on an expedited basis.

   When conducting research under an expedited review procedure, the IRB Chair or their designee conducts the review on behalf of the full IRB using the same criteria for renewal as stated in this Section 3 of this Policy. If the expedited reviewer feels that there has been a change to the risks so that they now are more than minimal as determined previously by the IRB, they may refer the study to the full board for review.

6. **Determination of the Approval Period.** At the time of initial review and at any continuing review, the IRB will determine and inform the investigator in writing of the approval period, including the approval date and expiration date. This determination takes into consideration the following aspects of the research:
   a. The nature of and any risks posed by the clinical investigation.
   b. The degree of uncertainty regarding the risks involved.
   c. The vulnerability of the subjects.
   d. The experience of the clinical investigator in conducting clinical research.
   e. The IRB's or EC's previous experience with that researcher or sponsor (e.g., compliance history, previous problems with the researcher obtaining informed consent, prior complaints from subjects about the researcher).
   f. The projected rate of enrollment.
   g. Whether the study involve novel therapies.
   h. Whether there is more than minimal risk to subjects.

   When continuing review occurs annually and the IRB approves the research within 30 days prior to the date upon which IRB approval expires, the IRB may retain the original anniversary date to determine the next continuing review date.

ROLES/REPONSIBILITIES

Principal Investigator shall be responsible to submit the continuing review progress report in sufficient time for the review to be completed prior to the IRB approval expiration date.

IRB members completing reviews of continuing review reports shall ensure all requirements for continued approval are met.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

HHS 45 CFR §§ 46.103(b)(4), 46.109(e) and 46.109(f);
FDA 21CFR § 56.109(f);
OHRP Guidance on Continuing Review, November 10, 2010
AAHRPP Standard II.2.E.2, II.2.F.2, and II.5.A

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Expedited Review of Research Policy No. 404	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09; 04/25/11; 03/19/14, 01/01/15, 10/12/17, 01/21/19, 07/26/21, 11/02/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the research that can be reviewed by the Institutional Review Board (IRB) Chair or designee and outlines the process to determine if the research meets criteria for expedited review.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) and IRB Members.

POLICY STATEMENTS: Certain categories of research involving human subjects, as identified below, may receive an expedited review procedure by the Chair of the IRB or by one or more experienced reviewers designated in writing by the Chair from among members of the IRB.

PROCEDURES

1. Categories of Research[1]

a. The categories of research that may be reviewed by the IRB through an expedited review procedure include research activities that: (i) present no more than minimal risk to human subjects; **AND** (ii) involve only procedures listed in one or more of the specific categories listed in the regulations at 45 CFR § 46.110 and 21 CFR 56.110. Exhibit A contains a brief description of the categories which may be reviewed through the expedited procedure. The categories listed ***should not*** be deemed to be of minimal risk simply because they are on the list. Inclusion on the list merely means the activity is eligible for review through the expedited review procedure when the specific circumstance of the proposed research involves no more than minimal risk. If the reviewer determines and documents that the research is more than minimal risk, it will be referred for review by the convened IRB.

b. This Policy pertains to both initial and continuing IRB review of the items included in this Policy.

c. Generally, if research did not qualify for expedited review at the time of initial review, it will not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) in Exhibit A attached to this policy. IRB staff may make the determination whether a protocol meets the criteria for category 8 and, if so, move the protocol to expedited review. It is also possible that research activities that previously qualified for expedited review in accordance with this Policy have changed or will change, such that expedited review would no longer be permitted for continuing review.

d. The expedited review process may be used to approve minor changes, as defined in Section 7b, below, in previously approved research during the period (one year or less) for which approval is authorized. Researchers shall submit the same information for expedited review as required at a convened meeting through the electronic IRB system.

e. The expedited review process may be used to conduct a limited IRB review of exempt research for which limited IRB review is required.

[1] 63 Fed Reg 60363-60367 (November 9, 1998)

f. Continuing review of research is not required for research that qualifies for expedited review unless the IRB determines that it is required and documents the rationale within the IRB record. See the policy "Continuing Review of Research".

g. Any protocol revision that entails more than a minimal risk to the subject as determined by the Chair or their designee must be reviewed by the convened IRB at a convened meeting.

h. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects in terms of financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

i. The expedited review process may not be used for classified research involving human subjects.

2. **Expedited Reviewer.** The Chair or other experienced IRB members designated in writing by the Chair will serve as expedited reviewers. The expedited reviewers will meet the following criteria:

a. Have a minimum of three years' experience as an IRB member.
b. Attend educational activities related to human subject research protection.
c. Demonstrate scientific or scholarly expertise.

Additionally, the Chair may appoint an IRB staff member to review specific minor changes to previously approved research through the expedited review process.

3. **Assignment of Expedited Reviews.** The HRPP & IRB Manager or their designee will assign expedited reviews to designated expedited reviewers after reviewing submissions received through the electronic IRB system with consideration to scientific or non-scientific content.

4. **Authority of the Expedited Reviewer**

a. The Chair or other IRB member reviewers, designated in writing by the Chair or by the IRB members voting in a convened meeting may exercise all of the authorities of the IRB, except that he/she may not disapprove the research. A research proposal may be disapproved only after review by the full IRB. The following actions may be taken on new applications that qualify for an expedited review process:

i. The application may be approved as submitted.
ii. The application may be conditionally approved with restrictions, conditions, stipulations, or required modifications including changes to the consent document. Responses to issues raised in an expedited review will be reviewed by the Chair or designee to determine if final action can be taken.
iii. The application may be referred for discussion at a convened meeting of the IRB. The reviewer who conducts the expedited review does not have the authority to disapprove an application. Disapproval is an action that may be taken only at a convened meeting.

b. Consultants may assist the IRB in the review of issues that require expertise beyond that available on the committee, but may not carry out the expedited review.

5. **Notification of the Board.** When the expedited review procedure is used, all regular IRB members shall be informed of research approved by expedited review at the next convened meeting. The IRB's agenda and minutes will include documentation of the studies that were reviewed via expedited review including a brief description of the research, the designated IRB reviewer who approved the research and the approval date. Members at the convened IRB meeting may challenge an action taken through the expedited review process.

6. **Documentation**

a. The information submitted by the investigator and received by the Primary Reviewer for expedited review is the same information provided to the Primary Reviewer at a convened meeting.

b. Standard requirements for informed consent (or its waiver, alteration or exception) apply when the expedited review process is utilized.

c. If the study qualifies for review via expedited review, the designated IRB reviewer will document their determination of the applicable expedited review category on the checklists provided through the electronic IRB system. Similar to a review by a convened IRB, the expedited reviewer will consider and document:

i. all the criteria for approval of research listed in the policy Initial Review of Research, item 1 (from 45 CFR § 46.111 and 21 CFR § 56.111);
ii. all requirements related to research with vulnerable populations (found in 45 CFR Part 46, Subparts B, C, and D), when applicable;
iii. the requirements for informed consent, or for altering or waiving the requirement for consent.

7. **Additional Items that may be Reviewed by Expedited Review**

a. Conditional Approval Pending Minor Revisions or Clarification. Revisions to consent documents and documentation or clarifications submitted as a result of full IRB review and as a condition to final approval may be reviewed by the IRB Chair or designee or any individual designated by the IRB members in a convened meeting. Final approval will be issued provided the revisions, documentation or clarifications do not indicate or result in a change to the study or change the risk/benefit ratio.

b. Minor Changes. The IRB Chair or designee may use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Any protocol revision that entails more than a minimal risk to subjects as determined by the IRB Chair or designee must be reviewed by the full IRB at a convened meeting. Addition of procedures that involve increased risk or discomfort ***may not*** be considered minor changes. The following are examples of the kinds of minor changes that may be eligible for expedited review:

i. Addition of research activity to the protocol that would be considered exempt or expedited if considered independently;

ii. A minor increase or decrease in the number of subjects;

iii. Narrowing the inclusion, or broadening the exclusion criteria;

iv. Change in dose form (caplet to liquid) but not route or dose;

v. Decrease in number of biological sample collections (blood draws);

vi. Increase in number of study visits for safety monitoring;

vii. Decrease in study visits if it does not reduce safety measurements;

viii. Changes in payment for participation (within 50% of original);

ix. Correction of typographical errors or improvement of readability;

x. Addition of qualified investigators;

xi. Addition or deletion of study sites; and

xii. Changes requested by other institutional committee.

c. Revisions to Informed Consent Documents. Minor changes to informed consent documents that do not affect the rights and welfare of study subjects, or do not involve increased risk or significant changes in study procedures may be reviewed and approved by the IRB Chair or designee.

d. Advertisements. The IRB Chair or designee may approve new or revised recruitment advertisements or scripts.

e. Translations. Translations of consent documents will also be submitted for IRB approval and will be reviewed in an expedited manner. There are three options available to obtain approval of translated consent forms.

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

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

iii. The translator will submit a signed statement that the consent document is a true and accurate translation.

ROLES/REPONSIBILITIES

The IRB Chair or designee shall be responsible to complete expedited reviews.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR § 56.102(i); 45 CFR § 46.102(j); 45 CFR § 46.110
63 Federal Register 60363-60367 (November 9, 1998)
AAHRPP Standard II.2.F.1

EXHIBIT A

Expedited Review Research Categories

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

(a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means. (Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.)

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) (Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.)

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this

category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

8. Continuing review of research previously approved by the convened IRB as follows:

(a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

(b) where no subjects have been enrolled and no additional risks have been identified; or

(c) where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

10. Limited IRB review of exempt research involving identifiable private information or identifiable biospecimens as described in Sections 1b, 1c, 2a, and 2b of the policy “Exempt Research”.

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Review of Changes in Approved Research Policy No. 405	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 03/20/14, 01/01/15, 10/12/17, 03/6/18, 01/21/19, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy outlines the process for the review of modifications of previously approved research.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) and members of the Institutional Review Board (IRB).

POLICY STATEMENTS: The IRB requires review and approval of modifications to previously approved research prior to initiation of any changes, with one exception. The exception is a change in research necessary to eliminate apparent immediate hazards to a research subject. In cases where changes were made to eliminate apparent hazards, it is the responsibility of the Principal Investigator (PI) to inform the IRB promptly of the change, and the IRB must determine if the modified research is consistent with ensuring subjects' continued welfare.[1] The requirement for approval of modifications to research includes modifications of exempt research subject to limited IRB review and research for which continuing review is not required.

PROCEDURES

1. **Submissions.** Changes in research may encompass amendments, addenda, deletions, or revisions to either the protocol or consent documents associated with the protocol. The PI shall submit information to allow the IRB to determine if the proposed change may be approved. Materials supporting the changes shall be submitted though the electronic IRB system. The IRB may review the changes in accordance with federal regulations using: (a) an IRB administrative action for administrative or clerical changes that do not otherwise require review as provided in (b) or (c); (b) an expedited review process, which is restricted to review of minor changes in research procedures or the consent document; or (c) a convened meeting to review all changes that are not minor. Changes or modifications reviewed through an expedited review process will be reported to the IRB members through the agenda at the next convened meeting as described in the Expedited Review Policy.

2. **Review.** When changes in research meet criteria for review at a convened meeting, review of the changes will be assigned to a primary reviewer. The primary reviewer will review the changes considering the regulatory criteria for approval and present the changes at the convened IRB meeting. Other IRB members are responsible to review any changes to the consent form. All of the documents will be available to all IRB members through the electronic IRB system. The IRB will determine whether the research with the proposed changes meet the regulatory criteria for approval.

   If the changes or modifications meet criteria for expedited review as described in the Expedited Review Policy, the Chair or a designee will be assigned the review and all information will be available through the electronic IRB system.

3. **IRB Options.** The IRB may retain the original risk determination and approval period granted at the initial review or previous continuing review report or the IRB may change the risk determination and the approval period if warranted by the change in risk. The IRB has the authority to require revisions to the consent

[1] 45 CFR § 46.103 (b)(4); 21 CFR § 56.108(a)

documents and to require that enrolled subjects are notified of the changes or re-consented for participation if it is determined that the changes may affect the subjects' decision to continue in the research.

4. **Documentation.** Whether the changes are reviewed at a convened meeting or through the expedited process, reviewers will complete the reviewer checklists available through the electronic IRB system.

   Researchers will be notified via a letter when the changes to the research have been approved by the IRB. Changes may not be implemented until the researcher receives the approval letter. The only exception to this would be to eliminate apparent immediate hazards to a research subject.

ROLES/REPONSIBILITIES

PIs shall be responsible to submit any changes in approved research prior to implementing the changes unless to eliminate apparent hazards to research subjects.

IRB members shall be responsible to complete a thorough review of any changes to the research study and re-access the risk level.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.108 (a)(3)(iii); 21 CFR § 56.108(a)
AAHRPP Standard II.2.E.3 and II.2.F.3

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Study Completion or Closure Policy No. 406	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 04/01/14, 01/01/15, 02/04/16, 10/12/17, 01/22/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the closure of a research project or protocol.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) and Institutional Review Board (IRB) staff.

POLICY STATEMENTS: The completion of a study, or its closure before its projected completion, is a change in activity and must be reported to the IRB. Although subjects will no longer be "at risk" under the study, a final report/notice to the IRB allows it to close its files and provides information the IRB may use in the evaluation and approval of related studies.[1]

PROCEDURES

1. **Determining When a Project Can Be Closed**

   a. Externally or Internally Funded Protocols. When individually identifiable follow-up data are no longer being collected on subjects enrolled in a protocol or project and any data analysis that could involve identifiable information is complete, the study may be closed.

   b. Multi-Site Protocols. Multi-site industry-supported clinical trials may be closed when data collection and follow-up are complete at the institutional site and the industry monitor has closed the site.

2. **Final Reports.** Final reports should be submitted within 30 days after completion or closure of the study or as soon as possible thereafter. Final reports may be submitted in any format that provides adequate information about the status of the study, such as computer printouts, telephone reports, letters, etc. Final reports may be submitted by the investigator or their designee. The HRPP & IRB Manager or their designee will review all reports of study completion and, if needed, request further information from the investigator to clarify any questions that may arise.

   Notice of the submission of final reports will be presented to the IRB at the next scheduled meeting; and copies of the reports and any supplemental information will be made available for the members upon request.

   Investigators will receive correspondence from the IRB to acknowledge receipt of the final report.

ROLES/REPONSIBILITIES

The investigator or research staff shall be responsible to notify the IRB of the completion or closure of the research study and submission of a “Final Report”.

IRB staff shall be responsible to accept and review the final report and send acknowledgement to the investigator.

DEFINITIONS

[1] 21 CFR § 56.108 (a)(3); 45CFR § 46.103(b)(5).

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR § 56.108(a)(3); 45 CFR § 46.103(a)(5)

Penn Medicine
Lancaster General Hospital

POLICY TITLE: **Management of Information for Multi-Site Research** **Policy No. 407**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 04/23/14, 01/01/15, 10/12/17, 10/09/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the management of multi-site research information and/or communication where the lead principal investigator (PI) is affiliated with Lancaster General Health (LG Health).

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research and Institutional Review Board (IRB) members at LG Health.

POLICY STATEMENTS: When the Lancaster General Hospital (LGH) IRB is serving as the IRB of record for a PI or site who is serving as the lead investigator or lead/coordinating center of a multi-site or collaborative research project, the PI must describe within the protocol and IRB application how the research will be overseen and how issues relevant to the protection of human subjects (e.g., IRB initial and continuing approvals, study modifications, reports of unanticipated problems, interim results, data-safety monitoring, etc.) will be coordinated and communicated among participating sites and investigators. For Food and Drug Administration (FDA)-regulated clinical trials, the plan should address the plan for study monitoring and for the reporting and evaluation of adverse events, significant new risk information, and any other reports mandated by regulation or policy.

The lead PI or lead/coordinating center is responsible for serving as the liaison with other participating sites and investigators and for ensuring that all participating investigators obtain IRB review and approval prior to initiating the research, maintain approval, and obtain IRB approval for modifications to the research. The LGH IRB will evaluate whether the plan for research oversight and management of information that is relevant to the protection of human subjects is adequate.

PROCEDURES

1. The PI shall complete the IRB electronic application with required supporting documentation with the addition of the following elements:

    a. A list of all sites/locations participating in the research study and contact information.
    b. A documented plan for the review of each site's IRB approval notifications and related documents.
    c. A method to ensure that all sites participating in the research have the most current version of the protocol, receive amendments, when applicable, and related communications.
    d. A plan for the collection and management of data from all participating sites.
    e. A process for reporting and evaluating protocol events and deviations from all participating sites.

2. The PI is responsible to submit all reports received from participating sites to the IRB.

3. The IRB will be responsible for initial review of the full protocol (including recruitment materials) and any subsequent continuing reviews, amendments to the protocol or consent documents, unanticipated events or deviations to the research study.

4. Each IRB that reviewed the protocol shall be notified of any protocol changes, unanticipated problems, or other reportable events occurring at any site.

ROLES/REPONSIBILITIES

The PI shall be responsible to inform the IRB and all participating sites of any changes to research study and reportable events.

The IRB shall be responsible to ensure that the PI has appropriate plans in place to disseminate all relevant information to participating sites.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.114
AAHRPP Standards II.2.I and III.2.D

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Review of Sponsored Research Contracts **Policy No 408**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 10/12/17, 10/19/22, 04/13/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the review process for sponsored research agreements.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) that involve a contract with a sponsor of the research.

POLICY STATEMENTS: Research agreements with sponsors of human subject research must be in writing and reviewed by the investigator, LG Health or Penn Office of Clinical Research (OCR) Legal Services , and other LG Health or Penn OCR individuals, as appropriate, to ensure all regulatory requirements and accreditation standards are satisfied.

PROCEDURES

1. Sponsor contracts will be reviewed for the following by LG Health or Penn OCR Legal Services, in consultation with the Institutional Review Board (IRB), the investigator, and others as deemed necessary:
   a. The contract contains provisions that address medical care for research subjects with a research-related injury, when appropriate.
   b. In a study for which a Sponsor conducts research site monitoring visits or conducts monitoring activities remotely, the contract requires that the Sponsor promptly reports to LG Health any findings that could affect the safety of subjects or influence the conduct of the study within thirty (30) days.
   c. When the Sponsor has the responsibility to conduct data monitoring, the contract contains provisions for monitoring the data to ensure the safety of subjects and for providing notice to LG Health of data monitoring committee decisions to continue or stop the study.
   d. Contract contains provisions addressing plans for disseminating findings from the research and the roles that the investigator and sponsor will play in the publication or disclosure of results.
   e. When subject safety could be directly affected by study results after the study has ended, the contract requires the sponsor to notify the investigator and requires reporting of the results to the IRB so that the IRB can consider whether subjects should be informed.
   f. Payment in exchange for referrals of prospective subjects from investigators or physicians ("finder's fees") is not permitted. Similarly payments that are designed to accelerate recruitment that are tied to the rate or timing of enrollment ("bonus payments") are also not permitted.

2. All written agreements with a sponsor will be signed by appropriate LG Health or Trustees of University of Pennsylvania officials in accordance with the LG Health Levels of Authority Policy or the Resolution on the Authority to Execute and Perform Research Contracts and Grants, respectively.

ROLES/REPONSIBILITIES

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standards I.1.D, I.8, II.3.C, III.1.E, and III.2.A

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Certificates of Confidentiality Policy No. 409	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/23/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy outlines the confidentiality protections and maintenance of the confidentiality of identifiable data, when appropriate, preliminary to the research, during the research, and after the conclusion of the research, as outlined by Federal funding regulations.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to Lancaster General Health (LG Health) staff and researchers conducting research under the purview of the LG Health HRPP that is supported in whole or in part by various Federal funding agencies as outlined in the sections below.

POLICY STATEMENTS: Certificates of Confidentiality (CoC) protect research information by prohibiting certain disclosures and conditioning others upon consent from the subject. The protections and requirements of CoCs are outlined in 42 U.S.C. 241(d) and in written policies and requirements of certain Federal agencies such as NIH and CDC and are summarized in this Policy.

PROCEDURES

1. Certificates of Confidentiality

CoC's are obtained as follows:

- CoCs are issued automatically when research is conducted or supported by NIH and falls within the scope of the NIH policy.
- CoCs are issued automatically when research is conducted or supported by the CDC and involves the collection of identifiable, sensitive information.
- CoCs are issued automatically when research is funded by the FDA in whole or in part and involves the collection or use of identifiable, sensitive information as defined in 42 U.S.C. 241(d).
- Research that is not supported by NIH, CDC, or FDA may still benefit from the protections afforded by CoCs through successful application to the NIH, FDA, HRSA, SAMHSA, or other authorized Federal agencies or departments.

Additional information about CoCs and the application process for research not covered by the NIH policy is available on the NIH CoC Website. Information about discretionary CoC's issued by FDA is available in the FDA guidance document: Certificates of Confidentiality.

2. Protections and Requirements

When a CoC is issued, whether automatically or under an approved application, the person(s) engaged in the research must not disclose or provide the name of a subject or any information, document, or biospecimen that contains identifiable, sensitive information about the subject and that was compiled for the purposes of the research:

1. In any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, unless the disclosure is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
2. To any other person not connected with the research, unless:
    a. Required by Federal, State, or local laws (e.g., adverse event reporting to the FDA, transmissible disease reporting required under State law), but excluding proceedings as described in "1" above;

b. Necessary for the medical treatment of the subject to whom the information, document, or biospecimen pertains and made with the consent of the subject;
c. Made with the consent of the individual to whom the information, document, or biospecimens pertains; or
d. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

3. Additional Protections

Identifiable, sensitive information protected under a CoC, and all copies thereof, are immune from the legal process, and shall not, without the consent of the individual to whom the information pertains, be admissible as evidence or used in any action, suit, or other judicial, legislative, or administrative proceeding.

Identifiable, sensitive information that has been collected under a CoC, and all copies thereof, are protected in perpetuity. If identifiable, sensitive information covered by a CoC is shared with other researchers or organizations, the researchers or organizations must be informed that the information is covered by a CoC and of their responsibility to protect the information accordingly.

Nothing in the rule (42 U.S.C. 241(d)) may be construed to limit the access of a subject to information about themselves collected during the research.

When consent is obtained, the consent should inform subjects that a CoC is in place and describe the protections and limitations.

4. NIH and CDC

The NIH Policy on CoCs applies to *"all biomedical, behavioral, clinical, or other research funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts, other transaction awards, or conducted by the NIH Intramural Research Program, that collects or uses identifiable, sensitive information"* that was commenced or ongoing on or after December 13, 2016.

The CDC requirements for CoCs apply to *"CDC supported research commenced or ongoing after December 13, 2016 and in which identifiable, sensitive information is collected, as defined by Section 301(d)."*
CoCs are automatically granted, and the requirements of such must be complied with, whenever a NIH or CDC funded activity falls within the scope of the NIH policy or CDC's requirements. Investigators and institutions are responsible for determining when research with NIH or CDC support are covered by a CoC.
NIH and CDC expand upon 42 U.S.C. 241(d) by explaining that NIH and CDC consider research in which identifiable, sensitive information is collected or used, to include:

- Human subjects research as defined in 45 CFR 46, including research determined to be exempt (except for exempt research when the information obtained is recorded in such a manner that human subjects cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects);
- Research involving the collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual;

- Research that involves the generation of individual level, human genomic data from biospecimens, or the use of such data, **regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained;** or
- Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual, as defined in subsection 301(d) of the Public Health Service Act.

5. FDA

The FDA requires, as a term and condition of all FDA funding and grant awards, compliance with the requirements of 42 U.S.C. 241(d) when research is funded in whole or in part by the FDA and involves the use or collection of identifiable, sensitive information. Certificates are deemed issued through FDA funding/award terms and conditions and are not issued as a separate document.

Investigators and institutions are responsible for determining when research with FDA support is covered by a CoC and for ensuring compliance with the requirements of 42 U.S.C. 241(d). Awardees are expected to ensure that any investigator or institution not funded by FDA who receives a copy of identifiable, sensitive information protected by these requirements, understand they are also subject to the requirements of 42 U.S.C. 241(d). Awardees are also responsible for ensuring that any subrecipient that receives funds to carry out part of the FDA award involving a copy of identifiable, sensitive information protected by these requirements understand they are also subject to subsection 42 U.S.C. 241(d).

When research is not funded by the FDA but involves "the use or study of a product subject to FDA's jurisdiction and subject to FDA's regulatory authority" (e.g., a clinical investigation of a drug, device, or biologic), the sponsor or sponsor-investigator can request a discretionary CoC from the FDA. Information about discretionary CoC's issued by FDA is available in the FDA guidance document: Certificates of Confidentiality.

6. NIH, CDC, and FDA CoC Determination

At LG Health, Grants Department staff will, in consultation with the investigator(s) (or Research Director or designee), determine if the NIH policy or CDC or FDA requirements apply to research with NIH, CDC, or FDA involvement or support. The questions outlined in the NIH policy and CDC requirements will be used to guide the analysis for research conducted or supported by NIH and CDC. The definitions and text of 42 U.S.C. 241(d) will be used to guide the analysis for research supported by FDA funding/awards. When it has been determined that the NIH policy or CDC requirements do not apply, investigators (or Research Director or designee) are responsible for consulting with Grants Department whenever they are proposing changes to the supported activity that may impact or change the analysis.

The NIH policy and CDC requirements include additional responsibilities and requirements for internal controls and for ensuring that recipients of identifiable, sensitive information protected by a CoC understand that they are also subject to the requirements of subsection 301(d) of the Public Health Service Act. Likewise, FDA requires awardees ensure that recipients of identifiable, sensitive information protected by an FDA CoC understand that they are also subject to the requirements of 42 U.S.C. 241(d).

7. Application Procedures for Research Not Automatically Issued a CoC

Any person engaged in human subjects research that collects or uses identifiable, sensitive information may apply for a CoC. For most research, CoCs are obtained from NIH, an investigator may apply for a CoC through the NIH Institute or Center funding research in a scientific area similar to the project.

When a researcher is conducting a research project that is covered by the Agency for Healthcare Research and Quality (AHRQ) confidentiality statute (42 U.S.C. section 299c-3(c)), a CoC is not needed (AHRQ notice NOT-HS-18-012). Investigators should consult with AHRQ when they believe that data might be considered "non-identifiable" or when otherwise uncertain whether a research project falls within the scope of the statute.

When research is not funded by the FDA but involves "the use or study of a product subject to FDA's jurisdiction and subject to FDA's regulatory authority" (e.g., a clinical investigation of a drug, device, or biologic), the sponsor or sponsor-investigator can request a discretionary CoC from the FDA. When FDA funds or conducts research, a CoC is automatically issued.

CoCs may also be issued by other Federal agencies and departments, such as SAMHSA and HRSA.
For more information, see the NIH CoC Website.

8. Institutional Review Board (IRB) Review

Investigators are responsible for clearly representing in the IRB submission that a CoC is in place, or that an application for CoC has been submitted or is pending. When the CoC application is in process or pending, the IRB may condition final approval upon its receipt.

For studies that are already underway, investigators must submit an Amendment request to the IRB, along with updated consent language (if applicable), when a CoC is applied for, or when automatically issued under the NIH policy or CDC requirements.

When reviewing research under a CoC, the LGH IRB will evaluate whether the research plan is consistent with the obligations to protect information and specimens under a CoC and, when consent will be obtained, whether the proposed consent language or other form of notification properly discloses the CoC and appropriately describes the associated protections and limitations. Sample consent language is available on the NIH CoC Website

When research is not under a CoC, the IRB may require an investigator to apply for a CoC if the research includes identifiable, sensitive information and the IRB determines that a CoC is necessary to minimize risks and adequately protect subjects' privacy and the confidentiality of subjects' information or specimens.

ROLES/REPONSIBILITIES

1. Investigator Responsibilities

a. For studies in which informed consent is sought, NIH and CDC expect investigators to inform research subjects of the protections and the limits to protections provided by a Certificate issued by this Policy.

b. When a researcher is issued a Certificate and the researcher will be obtaining informed consent from subjects, NIH expects that the subjects will be told about protections afforded by the Certificate and any exceptions to those protections. The NIH Human Subjects website has suggested consent language that investigators may refer to.

c. For studies that were previously issued a Certificate and notified subjects of the protections provided by that Certificate, NIH does not expect subjects to be notified that the protections afforded by the Certificate have changed, although IRBs may determine whether it is appropriate to inform subjects.

DEFINITIONS

Identifiable, Sensitive Information: Information that is about an individual and that is gathered or used during the course of biomedical, behavioral, clinical, or other research and:

1. Through which an individual is identified; or

2. For which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standard I.4.A

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Assessment of Risks and Benefits Policy No. 501	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 10/12/17, 10/09/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the review process to assess the risks and benefits of research to ensure that the research satisfies the criteria for approval as required by law and regulations.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) and to Institutional Review Board (IRB) Members.

POLICY STATEMENTS: To satisfy the criteria for approval as specified in federal regulations and the Initial Review of Research Policy, the IRB will assess the risks and benefits of proposed research in accordance with the process outlined below.

PROCEDURES

1. The IRB must assess the risks to research subjects arising from their participation in the research. The risks must be justified by the anticipated benefits to subjects or society. In addition, the IRB must ensure that the prospective subjects are fully aware of the risks and benefits of participating in the research. In reviewing the research, the IRB will determine whether the anticipated benefits justify a prospective subject undertaking the risks of the research. If the IRB determines that the risks are unreasonable in relation to the anticipated benefits, the IRB must disapprove the research.

2. The IRB assessment of risks and benefits will include the following:

   a. Identification of Risks. In the documentation submitted to the IRB, the investigator must identify and describe the potential risks to subjects, including an estimate of their frequency and severity. Risks related to participation in the research must be distinguished from risks associated with treatment a patient may receive if not participating in the research.

   b. Ensuring Risks are Minimized. The IRB will review and determine whether the risks will be minimized by analyzing the procedures or methods of the research that expose the subject to risk of harm and determining whether information or data could be obtained by other methods or procedures that expose the subject to less harm. In addition, the IRB will ensure that the research is of sound research design.

   c. Identification of Anticipated Benefits. The IRB will review the anticipated benefits of the research, including the knowledge to be gained from the research. The investigator will submit this information to the IRB during the application process.

   d. Evaluating Whether the Risks are Reasonable in Relation to Anticipated Benefits. The IRB will evaluate whether the risks are reasonable in relation to the anticipated benefits based on the information provided by the investigator and by reviewing the most current information about the risks and anticipated benefits of the procedures or methods involved in the research.

3. In reviewing and evaluating the risks and benefits of the research, the IRB will only consider those risks and benefits that may result from the research and does not consider long-range effects of applying the knowledge

gained in the research or the risks and benefits of treatment that a subject would receive even if not participating in the research.

ROLES/REPONSIBILITIES

The investigator is responsible for providing information about the risks and anticipated benefits of the research to the IRB through the research application process.

The IRB, with assistance from the Primary and Secondary Reviewers, will ensure that the research complies with the criteria for approval as described in federal regulations and the Initial Review of Research Policy.

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR 56.11(a)
45 CFR 46.111 (a)

Penn Medicine
Lancaster General Health

POLICY TITLE: Informed Consent and HIPAA Authorization Requirements Policy No. 502	
Policy Author: Jonathan Derr, MS, MBA.	**Last Review/Revision Date: 01/01/15, 10/23/15, 02/04/16, 11/16/17, 02/02/18, 03/06/18, 01/21/19, 02/12/19, 08/28/19, 02/01/23**
Policy Owner: Edmond Kabagambe, DVM, MS, PhD, MBA.	

POLICY PURPOSE: This Policy describes the general requirements for obtaining informed consent and HIPAA authorization.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research under the auspices of Lancaster General Health (LG Health).

POLICY STATEMENTS: Informed consent must be obtained in advance of subject enrollment in a clinical study and in a legally effective manner. Except as described in this policy, no investigator may involve a human being as a research subject unless legally effective informed consent of the subject or the subject's LAR has been obtained. Consent shall be sought only under circumstances that provide the prospective subject or LAR with sufficient opportunity to consider whether to participate and that minimize the possibility of coercion or undue influence.[1]

Subject HIPAA authorization must be obtained for prospective use or disclosure of protected health information ("PHI") for research conducted under the auspices of LG Health. Except as described in this policy, no investigator may involve a human being as a research subject unless legally effective authorization of the subject or the subject's LAR has been obtained.

Note: Requirements related to the documentation of consent are addressed in the policy Documentation of Informed Consent. Requirements related to (1) determining when a prospective subject is unable to give consent and authorization to participate in research and (2) obtaining consent from a LAR are addressed in the policy Surrogate Consent and Authorization.

PROCEDURES

1. Background and General Requirements for Informed Consent. Informed consent is a process, not just a form. Information must be presented to enable persons to voluntarily decide whether or not to participate as a research subject. It is a fundamental mechanism to ensure respect for persons through the provision of thorough and complete information concerning the study to allow for a voluntary, thoughtful consent to participate.

Information exchange and comprehension are critical to informed consent. The exchange of information between the investigator and the prospective subject or LAR is an ongoing process and can occur in person, virtually, or over the phone. Regardless, the informed consent process must be conducted in a manner that permits the prospective subject to ask questions and receive feedback and, if applicable, allows time to discuss participation with loved ones. The process should emphasize understanding of the information provided and voluntariness of the subject's decision to participate or not participate in the research.

The investigator is ultimately responsible for ensuring that each prospective subject or LAR is adequately informed about all aspects of the research and understands the information provided. The investigator may utilize colleagues or

[1] 45CFR § 46.116; 21CFR § 50.20

staff to assist in the informed consent process, provided the colleagues or staff are competent and have received appropriate training to conduct the informed consent process.

The IRB has the authority to observe or have a third party observe the consent process for adherence to HRPP standards and policies.

The general requirements for consent are:

a. Before involving a human subject in research covered by this policy, legally effective informed consent of the subject or the subject's LAR must be obtained.

b. The informed consent process must provide the prospective subject or LAR with sufficient opportunity to read and understand the consent form, consider its content, discuss it, and determine whether or not to participate in the research. In addition, the informed consent process must be conducted under circumstances that minimize undue influence or coercion

c. The information that is given to the subject or the LAR must be presented in a language and manner that is understandable to the prospective subject or LAR.

d. The procedures used in obtaining informed consent should be designed to provide to the prospective subject or LAR the information that a reasonable person would want to have to make an informed decision about whether to participate, and an opportunity to discuss that information.

e. Except for broad consent obtained in accordance with Sections 3 and 4, informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension. Such key information should include a concise presentation of:

   - The fact that consent is being sought for research and that participation is voluntary;
   - The purposes of the research, expected duration of participation, and a general description of what the research entails;
   - A statement that there may be risks, benefits, and alternatives to participation, and these should be discussed before deciding whether to participate.

   Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate.

f. Informed consent documents may not contain any exculpatory language through which the subject or the LAR is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, LG Health, or its agents from liability for negligence.

2. Elements of Informed Consent

a. Basic Elements.[2] The informed consent process must contain the following elements.

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental or investigational.
- A description of any reasonably foreseeable risks or discomforts to the subject.
- A description of any benefits to the subject or to others which may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- A statement describing the extent to which, if any, the confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration and representatives of the IRB may inspect the records.
- For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained. The informed consent document must not waive or appear to waive the rights of the subject or release or appear to release those conducting the study from liability for negligence.
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights or to register a complaint, and whom to contact in the event that a subject experiences a research-related injury.
- Contact information for an individual or office that is unaffiliated with a specific research study to discuss problems, concerns, questions, obtain information, or to offer input.
- A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may withdraw participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
- For research that involves the collection of identifiable private information or identifiable biospecimens:
  - A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the LAR, if this might be a possibility; OR
  - A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.
- For research regulated by the FDA, a statement that a description of the clinical trial will be available on http://www.clinicaltrials.gov as required by U.S. law. The website will not include information that can identify the participant. At most, the website will include a summary of the results. The participant can reach the website at any time.

[2] 45 CFR § 46.116; 21 CFR § 50.25.

b. Additional Elements.[3] The following elements of information shall also be provided to each subject unless otherwise approved by the IRB:

- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus if the subject is or may become pregnant) which are currently unforeseeable;
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- Any additional costs to the subject that may result from participation in the research;
- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;
- The approximate number of subjects involved in the study;
- A statement that the subjects' biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (*i.e.*, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

3. **Waiver of Informed Consent.** The IRB may waive the requirement to obtain informed consent or approve a consent process that does not include, or alters, some or all of the required elements of informed consent if the IRB determines that:

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

If a waiver is being requested for research involving the use of identifiable private information or identifiable biospecimens, the IRB must determine that the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

FDA regulations do not provide for waivers of informed consent except in certain emergency situations (see the policy Emergency Use of an Investigational or Unlicensed Test Article) and in planned emergency research (see the policy Planned Emergency Research). However, the FDA has indicated that, in light of

[3] 21 CFR § 50.25(b)

recent legislation and until revised regulations are promulgated, it does not intend to object to the waiver of informed consent requirements for a minimal risk clinical investigation meeting the criteria above.

Additionally, the IRB may waive the requirement to obtain informed consent or approve a consent process that does not include, or alters, some or all of the required elements of informed consent if the IRB determines that:

- The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
  - Public benefit or service programs;
  - Procedures for obtaining benefits or services under those programs;
  - Possible changes in or alternatives to those programs or procedures; or
  - Possible changes in methods or levels of payment for benefits or services under those programs;
- The research cannot practicably be carried out without the waiver or alteration of informed consent

The IRB may waive parental or guardian permission for a minor to participate in the research. In order for permission of the parent or guardian to be waived, the research must meet at least one of the following criteria:

- For research not regulated by FDA, that the only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from breach of confidentiality. Each subject must be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; OR
- That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context (this may include minimal risk pre-enrollment screening activities necessary to determine eligibility for research that then requires written consent at the point of enrollment); OR
- If the subject or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

In cases in which the documentation requirement is waived, the IRB may require the principal investigator to provide subjects with a written statement regarding the research. The IRB will document its justification for the waiver if it is approved.

4. **Restrictions on Waivers of Informed Consent**.

a. The IRB cannot waive the requirement for consent for the storage, maintenance, or secondary research use of identifiable private information or identifiable biospecimens if an individual refused to give broad consent for such storage, maintenance, or secondary research use of identifiable private information or identifiable biospecimens.

b. The IRB may not approve a request to alter or omit any of the general requirements for consent. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required in Section 4.

5. **Subjects with Impaired Decision-making Capacity.** If a prospective subject is unable to provide informed consent and authorization to participate in research, consent may be obtained from a LAR (see policy on Surrogate Consent and Authorization).

6. **Elements of HIPAA Authorization.** The following core elements and statements are required for a valid HIPAA authorization, whether obtained as an individual document or combined with the Informed Consent Document as part of a research study:

- A description of the health information to be used and disclosed as part of the research.
- A description of the person or classes of persons authorized to use or disclose the health information.
- A description of the person or classes of persons who may receive the information and the purpose(s) for each disclosure.
- The purpose of the use/disclosure.
- An expiration date or event of the authorization for use or disclosure if any.
- A statement of the subject's right to revoke the authorization and person to contact to revoke it.
- Notice that disclosure of health information may result in loss of protection to subsequent disclosure.
- The consequences to the individual of refusing to provide, or revoking, authorization.
- Signature of the patient and date, or in the case of a designated personal representative, the signature, date, and relationship of the individual.

7. **Waiver of HIPAA Authorization.** The IRB may waive or alter the authorization requirement for the use and disclosure of health information in research that it determines:

a. Involves no more than minimal risk to the privacy of the research subject based upon the presence of the following elements:

- Adequate plan to protect any health information from improper use and disclosures;
- Plan to destroy data identifiers at earliest opportunity consistent with conduct of research; and
- Written assurance that the health information will not be reused or disclosed to any other individual or entity, except as required by law or for other research for which the use or disclosure of the health information would be permitted under the HIPAA Privacy Rule.

b. Could not practicably be conducted without access to and use of the health information.

c. Could not practicably be conducted without the waiver or alteration to the authorization.

8. **Other Requirements for Consents and Authorizations**

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

b. Language Should be Simple. The information provided in the informed consent and HIPAA authorization documents must be in language understandable to the prospective subject. The documents should not include complex language that would not be understandable to all subjects. Technical and scientific terms should be adequately explained using common or lay terminology.

c. Signatures. Requirements regarding signatures on informed consent documents are discussed in the LG HRPP policy "Documentation of Informed Consent".

d. FDA-Regulated Test Articles. For all research involving test articles regulated by the U.S. Food and Drug Administration (FDA), informed consent documents must include a statement that the purpose of

the study includes evaluation of both the safety and the effectiveness of the test article. The consent form must also include a statement that the FDA has access to the subject's medical records.

e. IRB Review of Consent Process. The IRB will take the following into consideration when reviewing the protocol and consent form:

- Who will conduct the consent process.
- Matters of timing of obtaining informed consent and any waiting period between informing the subject and obtaining consent.
- Time required to ensure that the person conducting the consent interview and the prospective subject have had adequate opportunity to exchange information and ask questions.

9. Withdrawal of Consent or Authorization

a. When a subject withdraws consent to participate in a study and/or authorization to use and disclose health information for a study, the data collected on the subject to the point of withdrawal remains part of the study database and may not be removed. The consent or authorization documents cannot give the subject the option of having data removed.

b. An investigator may ask a subject who is withdrawing from a study whether the subject wishes to provide continued follow-up and further data collection subsequent to withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject should distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the continued privacy and confidentiality of the subject's information.

c. If follow-up and data collection after withdrawal from the interventional portion of the study (8b) involves activities that are not covered under the subject's current consent, the investigator must obtain the subject's consent for this limited participation in the study. The IRB must approve the consent document.

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

10. Retention of Original Consent and Authorization Documents. Investigators are to retain the originals of all subject consents and HIPAA authorizations for at least six (6) years from the date of the final notice from the IRB of study completion, closure, or termination.

ROLES/REPONSIBILITIES

DEFINITIONS

REFERENCE DOCUMENTS

Information for Covered Entities and Researchers on Authorizations for Research Uses or Disclosures of Protected Health Information, NIH Publication Number 04-5529, July 2004
IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects: Guidance for Sponsors, Investigators, and Institutional Review Boards, US DHHS, FDA, July 2017

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.116; 21CFR § 50.20
45 CFR § parts 160 and 164
AAHRPP Standards I.4.A, II.3.F, II.3.G, and III.1.F

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Documentation of Informed Consent Policy No. 503	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 02/19/14, 01/01/15, 10/23/15, 11/16/17, 03/06/18, 01/21/19, 08/28/19, 01/30/23**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the requirements for documentation of informed consent and circumstances when the Institutional Review Board (IRB) may waive the requirement to document informed consent.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health).

POLICY STATEMENTS: All subjects, or their legally authorized representatives, must document that they are consenting to participate in any research project that is conducted at LG Health by signing and dating a written consent form approved by the IRB, unless the IRB specifically waives the requirement for written documentation of consent. Authorization for the use or disclosure of health information may be documented by the use of a separate HIPAA authorization form, or combined with an IRB-approved informed consent document.

PROCEDURES

1. **Documentation of Informed Consent[1].** Each subject or the subject's legally authorized representative must sign and date a copy of the current IRB-approved consent form prior to enrollment or any participation in any phase of research, unless the requirement is waived by the IRB. The subject or legally authorized representative must receive a copy of the signed consent document. The IRB may approve procedures for documentation of informed consent that involve: (a) a written consent form signed by the subject; (b) a short form written consent with oral presentation; or (c) in limited circumstances, waiver of documentation of consent (i.e., no signed written consent form). Each of these three options is described in detail below. It is the responsibility of the IRB to determine which of the procedures described below is appropriate for documenting informed consent in protocols that it reviews.

2. **The Informed Consent Form**

   a. Written Consent Form. In most circumstances, the IRB requires that informed consent is documented by the use of a written consent form approved by the IRB and signed (including in an electronic format) by the subject or the subject's legally authorized representative. The investigator should allow the subject or the legally authorized representative adequate opportunity to read the consent document before it is signed. Alternatively, this form may be read to the subject or the subject's legally authorized representative. A written copy of the document must be given to the person signing the consent form.

   b. Language of Consent Form. The written informed consent document should embody, in language understandable to the prospective study subjects, all the elements necessary for legally effective informed consent (see above).[2]

   c. Subjects Who Do Not Speak English. Subjects who do not understand English should be presented with an informed consent document written in a language understandable to them. If it is expected that non-

[1] 46CFR § 46.117
[2] See LGH IRB Policy "Informed Consent and HIPAA Authorization Requirements."

English speaking subjects will be enrolled, a consent document in their language should be submitted at time of initial submission. A certification of the translation must also be submitted with the consent document.

3. Short Form Alternative[3]

a. Oral Presentation Using Short Form. As an alternative to standard written informed consent documents, oral presentation of informed consent information may be used. In such cases, the investigator must provide the prospective subject or legally authorized representative with both:

i. A short form written informed consent document stating that the elements of consent have been presented orally to the subject or the subject's legally authorized representative and that the required key information listed in the policy "Informed Consent and HIPAA Requirements", item 1e, was presented first to the subject or legally authorized representative, before other information, in any, was provided; and

ii. A written summary of the information that is presented orally (the approved full consent document may serve as this summary).

The IRB must review and approve the written summary of the information to be presented orally to the subject or legally authorized representative.

The oral presentation and the short form written document should be in a language understandable to the subject.

b. Witness. A witness to the oral presentation is required. The witness must sign both the short form written consent document and the written summary.

c. Signature of Subject or Legally Authorized Representative. The subject or the legally authorized representative must sign the short form written consent document.

d. Signature of Person Obtaining Consent. The person obtaining consent must sign the written summary of the information that is presented orally. The person obtaining consent may not be the witness to the consent.

e. Subjects Who Do Not Speak English. When informed consent is documented using this short form procedure for non-English speaking subjects: (i) the written summary should embody all the elements necessary for legally effective informed consent (the IRB-approved English language consent document may serve as the summary); (ii) the oral presentation (via a certified translator if necessary) and the short form written informed consent document should be in a language understandable to the subject; and (iii) the witness should be fluent in both English and the language of the subject. The translator may serve as the witness if present in person. Alternatively, the witness may be any adult (18 years of age or older) fluent in both English and the language of the subject, such as a family member, friend, or clinic nurse not involved in the study.

[3] 45CFR § 46.117(b)(2); 21CFR § 50.27(b)(2); FDA Guide to Informed Consent, Information Sheets, 1998, pp.34-35; OHRP Compliance Activities: Common Findings and Guidance #45

The IRB must review and approve the plan to use any foreign language short form consents and to communicate with subjects on an ongoing basis throughout participation in the study.

Expedited review of these versions is acceptable if the protocol, the full English language informed consent document, and the English version of the short form document have already been approved by the convened IRB.

4. Waiver of Documentation

a. The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if the IRB finds any of the following:[4]
   i. For research not regulated by FDA, that the only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from breach of confidentiality. Each subject must be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;
   ii. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context (this may include minimal risk pre-enrollment screening activities necessary to determine eligibility for research that then requires written consent at the point of enrollment); **OR**
   iii. If the subject or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

b. In cases in which the documentation requirement is waived, the IRB may require the principal investigator to provide subjects with an IRB-approved written statement regarding the research.

5. Signatures on Informed Consent Forms. For studies conducted in accordance with GCP guidelines, the person who conducted the informed consent discussion is required to sign and date the consent form along with the subject or legally authorized representative. Furthermore, to provide consistency with LG Health policies on consent and HIPAA authorization in routine clinical care, the LG Health HRPP requires the following for research designated by the IRB to involve more than minimal risk:

- A witness must sign the informed consent form along with the person obtaining consent and the person giving consent.
- The person obtaining consent, the person giving consent (the subject or legally authorized representative), and the witness must provide the date and time of their signature.
- The HIPAA authorization, whether or not it is combined with the consent onto one form, must have its own signature. The person giving consent also must sign and date the HIPAA authorization; no time of signature is required. No signature is required from the person obtaining authorization or from a witness.

6. Use of Mail, Facsimile, Email, or Electronic Signature to Document Informed Consent. The IRB may approve a process that allows the informed consent document to be delivered by mail, email, facsimile, or web-based formats to the prospective subject or legally authorized representative. The IRB also may approve a process involving consent discussion by telephone, provided that the subject or the legally authorized

[4] 45CFR § 46.117(c), 21CFR § 56.109(c)(1).

representative can read the consent document as it is discussed. All other applicable conditions for documentation of informed consent must also be met when using this procedure. That is, unless the IRB has waived documentation of consent, the consent form must be signed and returned in person or by mail, facsimile, email or other electronic format before initiation of study activities. Additionally, the IRB may consider and approve a process that allows electronic signature of the consent form by the subject or the subject's legally authorized representative.

These methods for documenting informed consent do not allow for witnessing of the consent signature as required in section 5 for studies that are more than minimal risk. (The need for remote consenting in studies that are more than minimal risk is most likely to occur when a legally authorized representative is not able to be present in person.) In such studies, the remote consent conversation and the person's verbal consent are to be witnessed by a third party present with the person obtaining consent, and the witness is to record his/her signature and the date and time on the consent along with the person obtaining consent. The IRB at its discretion may allow these exceptions to the documentation of informed consent in studies that are more than minimal risk, except that electronic signature is not allowed for FDA studies unless compliance with 21 CFR Part 11 can be demonstrated.

ROLE(S)/REPONSIBILITIES

DEFINITIONS

Written (or in writing): refers to writing on a tangible medium (e.g., paper) or in an electronic format.

REFERENCE DOCUMENTS

LG Health HRPP Policy "Informed Consent and HIPAA Authorization Requirements."
FDA Guide to Informed Consent, Information Sheets, January 1998, pp.34-35;
OHRP Compliance Activities: Common Findings and Guidance #45

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATION(S)

46 CFR § 46.117
46 CFR § 46.117 (b)(2)
21 CFR § 50.27 (b)(2)
21 CFR § 11.100
45 CFR § 46.117(c)
AAHRPP Standards II.3.F, II.3.G,and II.3.G

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Special Consent Circumstances Involving Communication Barriers **Policy No. 504**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 11/16/17, 02/02/18, 03/6/18, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the processes available for consenting persons with barriers related to limited English proficiency, illiteracy, or sensory deficits for participation in a research protocol, consistent with federal regulations and other policies of Lancaster General Health (LG Health).

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at LG Health and Institutional Review Board (IRB) members.

POLICY STATEMENTS: LG Health is committed to ensuring that persons with barriers to communication have the opportunity to participate in research when appropriate and that, in these circumstances, informed consent is appropriately obtained. Investigators should carefully consider the ethical, legal, subject safety, and scientific ramifications of enrolling subjects when a communication barrier exists, as the communication barrier will affect not only the consent process but also study procedures, such as treatment and outcomes assessment.

PROCEDURES

1. **Persons with Limited English Proficiency.** When enrollment of persons with limited English proficiency is appropriate, the below procedures may be used:

    a. **Expected Enrollment of Persons with Limited English Proficiency.** In some studies, the investigator may be able to anticipate enrollment of persons who do not speak or read, or have limited proficiency in, oral or written English. When the target subject population includes such persons or the investigator and/or the IRB otherwise anticipates that consent will be conducted in a language other than English, the IRB requires a translated consent document, and other subject materials, to be prepared. To ensure that translated documents are accurate, the IRB may choose to require a certified translation, to have an independent back-translation or to have a review of the translated documents by an IRB member or other person who is fluent in that language. The consent discussion should be conducted using an authorized translator, following LG Health policy "Communication with Limited English Proficient Patients and Deaf and Hard of Hearing Patients". A translated consent document must be signed by the subject, and the subject must be given a copy of the signed translated consent document.

    b. **Unexpected Enrollment of Persons with Limited English Proficiency.** If a person who does not speak or read, or has limited proficiency in English presents for possible enrollment, an IRB-approved translated version of the written consent may not be available for use. If an investigator decides to enroll a subject into a study for which there is not an extant IRB-approved consent document in the prospective subject's language, the investigator must receive IRB approval to follow the procedures for a "short form" written consent as described in the policy "Documentation of Informed Consent".

2. **Persons Who Read Braille.** For prospective subjects who are blind and read Braille, the IRB may approve a consent document prepared in Braille. In order to assure itself that a Braille consent document is accurate, the IRB may require a transcription into print text or review of the document by an IRB member or other person

who reads Braille. If possible, the subject will sign the Braille consent; otherwise oral consent will be obtained, witnessed and documented as described in this policy in section 4.

3. **Persons Who Communicate Using American Sign Language (ASL).** For deaf subjects who are fluent in ASL, the consent process may be conducted using ASL and the IRB-approved written consent form. The consent discussion should be conducted using an authorized translator, following LG Health policy "Communication with Limited English Proficient Patients and Deaf and Hard of Hearing Patients". The subject must sign and date the written consent form, and the subject must be given a copy of the signed consent form.

4. **Persons Unable to Read the Consent.** When prospective subjects cannot read the written consent form (for example, people who are blind or illiterate), the IRB may approve an oral consent process, provided the subject (1) retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained orally and (2) is able to indicate approval or disapproval to study entry. For research that is no more than minimal risk, the IRB may approve a waiver of documentation of consent according to the criteria in the policy "Documentation of Informed Consent". For greater than minimal risk research and for research conducted in accordance with the International Conference on Harmonisation's Good Clinical Practice (GCP or ICH E6) guidelines, the consent form and any other written information provided to subjects must be read to the subjects and the subjects must be given an opportunity to ask questions. An audiotape approved by the IRB may also be used. If capable of doing so, the subject signs, or marks an X to signify consent. If that is not possible, the subject may provide oral consent. The person obtaining consent and an impartial witness that was present for the entire informed consent discussion will sign and date the written study consent form with a statement that documents that an oral process was used and, if necessary, that the subject gave oral consent. (Note that the signature of a witness is required in these circumstances, regardless of whether or not a witness signature is required otherwise, as described in the policy "Informed Consent and HIPAA Authorization Requirements", Section 7, item e.) By signing the consent document, the witness is attesting that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally authorized representative, and that consent was freely given by the subject or the subject's legally authorized representative. The consent process will also be documented in the subject's research record. Signed and dated copies of the consent form are given to the subject and, whenever possible, these documents should be provided to the subject in an audio or video format.

ROLES/REPONSIBILITIES

The investigator is responsible to determine when it is appropriate to enroll subject with barriers to communication, and to request approval from the IRB for alternate procedures to be followed and/or materials to be used in the consent process, in accordance with this policy.

DEFINITIONS

REFERENCE DOCUMENTS

LG Health Policy "Communication with Limited English Proficient Patients and Deaf and Hard of Hearing Patients"
LG Health HRPP Policy "Documentation of Informed Consent"

Guidance for Industry: E6 Good Clinical Practice: Consolidated Guidance, Food and Drug Administration, March 2018, Section 4.8.9

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standards II.3.F, II.3.G and III.1.F

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Surrogate Consent and Authorization Policy No. 505	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 02/10/14, 01/01/15, 11/16/17, 02/02/18, 03/06/18, 01/21/19, 10/19/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to set forth guidelines for the Institutional Review Board (IRB) and investigators in proposing, conducting, and reviewing human subject research in subjects with impaired decision-making capacity.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health).

POLICY STATEMENTS: LG Health and the IRB will protect every subject's right to autonomy. LG Health will protect those subjects with diminished autonomy or reduced capacity to consent to research or to provide authorization for the use or disclosure of protected health information ("PHI"). LG Health and the IRB recognize that surrogate consent is necessary in order to offer experimental treatments to a subject with impaired decision-making capacity, when appropriate as outlined in this Policy. Accordingly, the following procedures will be followed when research involves subjects with impaired decision-making capacity or when the investigator determines that an individual subject is unable to give informed consent for participation in research or to authorize use or disclosure of PHI.

PROCEDURES

1. General Information

a. Informed Consent. Federal Regulations and IRB policies require that an investigator obtain the legally effective informed consent of a subject or subject's legally authorized representative prior to participating in research. Federal law defers to state laws to determine who can serve as an individual's legally authorized representative. Pennsylvania law requires the informed consent of the subject or the subject's legally authorized representative before the administration of an experimental medication, the use of an experimental device, or the use of an approved medication or device in an experimental manner. Pennsylvania law permits either the subject's court-appointed guardian or the subject's named health care power of attorney to provide surrogate consent for the performance of any experimental biomedical or behavioral procedure or participation in any biomedical or behavioral experiment, or administration of any medical, therapeutic, or surgical procedures.

For subjects that do not have a court-appointed guardian or a valid health care power of attorney document, Pennsylvania law also authorizes the individuals identified in Section 4, below, as legally authorized representatives who may consent on behalf of a prospective subject who lacks decision-making capacity.

If the research poses no more than minimal risk, the investigator and IRB may consider waiver of the requirement for documentation of informed consent as described in the Documentation of Informed Consent Policy.

b. HIPAA Authorization. In addition to obtaining the subject's informed consent, the Health Insurance Portability and Accountability Act (HIPAA), and its implementing regulations, require entities to obtain a subject's written authorization for uses and disclosures of the subject's PHI. The HIPAA

regulations require the legally authorized representative to sign a HIPAA authorization when the subject lacks decision-making capacity. In such circumstances, the HIPAA authorization must describe the basis of the legally authorized representative's authority to sign on the subject's behalf.

2. <u>Submission and Review of Protocols Involving Subjects Unable to Provide Informed Consent and/or HIPAA Authorization</u>

a. The investigator is responsible for making the determination as to whether the research protocol will or is likely to enroll subjects without capacity to give informed consent or HIPAA authorization. If it is anticipated that the research may involve these individuals, the protocol must describe the process by which the investigator will determine and document the individual's ability to provide consent or HIPAA authorization. The protocol will also describe the process by which the investigator will obtain consent or HIPAA authorization from the legally authorized representative.

b. The IRB will review such protocols and determine and document whether:

i. The risks to the subject are reasonable in relationship to any anticipated benefits to subjects and to the importance of the knowledge that may be reasonably expected to result; and

ii. The description of the informed consent process to be used is appropriate to the risk of the research, as assigned by the IRB; and

iii. The legally authorized representative consent process is appropriate; and

iv. The HIPAA Authorization process, if included as part of the informed consent process, is appropriate; and

v. All other aspects of the proposed research, as provided in other LG Health Human Research Protection Program and IRB policies, are appropriate.

c. If the IRB determines that the risk to the subject is greater than minimal risk, it may require additional protections to ensure that the rights of subjects are protected. Such additional protections may include, but are not limited to:

- Assessment of a subject's ability to assent or legally authorized representative's ability to consent or to provide HIPAA authorization by an independent subject advocate or the subject's primary care physician, consistent with legal requirements
- Independent documentation of the informed consent or HIPAA authorization process (note that a witness to the informed consent is already required under the policy "Informed Consent and HIPAA Authorization Requirements," Section 9, item c).
- Assessment of the appropriateness of the individual serving as the legally authorized representative
- Other safeguards, as appropriate

d. For studies conducted in accordance with the International Conference on Harmonisation's Good Clinical Practice (GCP or ICH E6) guidelines, there are further stipulations on the participation in non-therapeutic clinical trials (trials in which there is no anticipated direct clinical benefit to the subject) of adults who are

unable to consent for themselves. Such trials should be conducted in subjects who personally give consent and sign and date a written consent document; such trials may be conducted in subjects with consent of their legally authorized representatives under the following conditions:

- The objectives of a clinical trial cannot be met by means of a trial in subjects who can give consent personally;
- The foreseeable risks to the subjects are low;
- The negative impact on the subject's wellbeing is minimized and low;
- The clinical trial is not prohibited by law;
- The opinion of the IRB is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect; and
- The trial, unless an exception is justified, is being conducted in patients having a disease or condition for which the investigational product is intended, and the subjects are particularly closely monitored and withdrawn from the trial if they appear to be unduly distressed.

e. Also for studies conducted in accordance with GCP guidelines:

- When a clinical trial (therapeutic or nontherapeutic) includes subjects who can only be enrolled in the trial with the consent of the subject's legal authorized representative, the subject should be informed about the trial to the extent compatible with the subject's understanding and, if capable, the subject should assent, sign and personally date the written informed consent.
- In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally authorized representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally authorized representative is not available, enrollment of the subject should require measures described in the protocol and/or elsewhere, with documented approval by the IRB. The subject or the subject's legally authorized representative should be informed about the trial as soon as possible and consent to continue and other consent should be requested as appropriate.

f. The IRB will not approve any research involving the consent or HIPAA authorization of a legally authorized representative if the IRB determines that the risk to the subject is ***high*** in relationship to the anticipated benefits, if any, to subjects and the importance of the knowledge that may reasonably be expected to result.

3. Determination of an Individual Subject's Ability to Provide Informed Consent or HIPAA Authorization

a. The decision-making capacity of a prospective subject for any research study should be evaluated when there are concerns that the subject may not be capable of making informed and voluntary decisions whether to participate in the research. The investigator and research staff must have procedures in place to evaluate and assess a prospective subject's decision making capacity. At a minimum, the investigator must determine whether the prospective subject understands and comprehends that the activity is research, the nature of the risks and benefits, the requirements to participate in the research, the alternatives available, and that a decision not to participate will not penalize the prospective subject.

b. The investigator is responsible for determining whether the subject can provide informed consent or HIPAA authorization. The investigator will document in the research record, as thoroughly as

possible, the reason for the subject's inability to provide informed consent or HIPAA authorization. The investigator will apply and document any additional safeguards as directed by the IRB.

c. The IRB should consider that research may take place over an extended period of time, and the decision-making capabilities of subjects may change over that time. The IRB may require periodic re-consenting of individuals to ensure that a subject's continued involvement is voluntary. The IRB should take into account the study's anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the IRB should consider whether and when to require a reassessment of decision-making capacity.

4. Individuals Legally Authorized to Provide Effective Surrogate Consent or HIPAA Authorization

a. Adults. A subject's court-appointed guardian or health care agent identified in a Health Care Power of Attorney document may provide informed consent or HIPAA authorization on behalf of a subject who lacks decision-making capacity. If a subject does not have a court-appointed guardian or health care agent, the following individuals, in descending order, may provide consent or HIPAA authorization:

- Spouse, unless a divorce action is pending, and any adult child of the subject from prior relationship
- Adult child
- Parents
- Siblings
- Adult grandchild
- Any adult who has knowledge of the subject's values and beliefs

b. Minors. Generally, a parent or legal guardian is required to provide consent or HIPAA authorization on behalf of a minor (an individual under age eighteen) for health care decisions, including participation in research.

However, Pennsylvania law does, under certain circumstances, allow a minor to consent to certain treatments or procedures. Minors who are permitted under state law and LG Health's Patient Consent Policy to consent to treatment will be permitted to provide their own consent for research.

c. Deceased Individuals. If, under applicable law, an executor, administrator, or other person has authority to act on behalf of a deceased individual or on behalf of the deceased individual's estate, that person may be considered the legally authorized representative.

d. Surrogate in Abuse, Neglect, and Endangerment Situations. Notwithstanding state law or any requirement to the contrary, the investigator or the IRB may elect not to treat a person as the legally authorized representative of a subject if they have a reasonable belief that:

- The subject has been or may be subjected to domestic violence, abuse, or neglect by such person;
- Considering such person as the legally authorized representative could endanger the subject; or
- The investigator, in the exercise of professional judgment, decides that it is not in the best interest of the subject to consider such person as the legally authorized representative.

If such a decision is made not to treat a person as the legally authorized representative for the above reasons, documentation of the factual basis for such decision should be noted in the medical and research record with supporting documentation, if any.

5. Involvement of the Legally Authorized Representative

a. The legally authorized representative should base their decision on the subject's expressed wishes or, if unknown, what the subject would have desired in light of their prognosis, values, and beliefs. The LG Health policy Advance Directives and Surrogate Decision Makers and Pennsylvania law will be followed in the event of a disagreement among legally authorized representatives. When a legally authorized representative provides consent or HIPAA authorization, it is preferable for the legally authorized representative to remain the responsible party for all subsequent research decisions, including the withdrawal of consent or HIPAA authorization.

b. Requirement for Re-consent. If, at any time, a subject is enrolled in research by the consent of a legally authorized representative, and the subject regains capacity to provide consent or HIPAA authorization, the investigator will obtain informed consent and HIPAA authorization from the subject, in accordance with the policy Informed Consent and HIPAA Authorization Requirements, for continued participation in the research.

c. Capacity of Subjects May Fluctuate. The consent process should be ongoing and involve the legally authorized representative if, at any time, the investigator believes the subject is unable to provide informed consent for continued participation in the research in which the subject initially gave informed consent and HIPAA authorization.

ROLES/REPONSIBILITIES

DEFINITIONS

Legally Authorized Representative: An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

REFERENCE DOCUMENTS

Guidance for Industry: E6 Good Clinical Practice: Consolidated Guidance, Food and Drug Administration, March 2018, Sections 4.8.12 and 4.8.14

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

20 Pa.C.S.A. §§ 5421, et. seq.
AAHRPP Accreditation Standards I.1.G, II.4.B and III.1.F

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Uses and Disclosures of Protected Health Information for Research Policy No. 506	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 01/08/13, 03/31/14, 01/01/15, 02/04/16, 10/12/17, 11/02/18, 01/21/19, 01/11/21, 10/11/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the circumstances under which protected health information (PHI) may be used or disclosed for research purposes.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) and Institutional Review Board (IRB) members.

POLICY STATEMENTS: All PHI will be used and disclosed in a manner that respects an individual's right to privacy, and in accordance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and applicable laws. PHI may be disclosed for research without authorization from patients only under specific provisions of HIPAA.

PROCEDURES

1. **Uses of Health Information Related to Research**

   a. General Rule. Except as provided in this Policy and the Policy "Informed Consent and HIPAA Authorization Requirements", the authorization of a research subject must be obtained whenever PHI will be used or disclosed for research. Unless the research meets one of the specific categories where authorization is not required, all investigators must obtain an authorization from all subjects who participate in research. The core elements and required statements for authorization are provided in the Policy "Informed Consent and HIPAA Authorization Requirements", section 9.

   b. Exceptions to Research Authorization Requirement. An investigator may request, and the IRB may consider for approval, an exception to the authorization requirement. Exceptions include the following:

      i. Waiver of Authorization
      ii. Preparatory to Research provision
      iii Research on PHI of Decedents
      iv. De-identified Health Information
      v. Limited Data Set with a Data Use Agreement

      Waiver of Authorization Requirement

      An investigator may apply to the IRB for a partial or total waiver of the authorization requirement in accordance with this Policy. A complete waiver may be approved when the IRB determines that no authorization will be required to use and disclose PHI for a particular research project. A partial waiver of authorization may be approved when the IRB determines that no authorization is required for limited and specific uses and disclosures of PHI, such as screening by phone potential subjects who respond to an advertisement for a research study (see criteria in the policy Informed Consent and HIPAA Authorization Requirements). An investigator may request a waiver and provide supporting information as part of the electronic IRB application.

      Use of PHI Preparatory to Research

The use and disclosure of PHI to develop a research protocol or for similar purposes preparatory to research (e.g., to determine whether the institution has information about prospective research subjects that would meet the eligibility criteria for enrollment in a research study) is permissible with the approval of the IRB. Current interpretation of the HIPAA Privacy Rule stipulates that PHI will not be removed from the institution in the course of review. Due to this limitation, approvals by the IRB will be scrutinized for compliance.

In order to permit a use or disclosure of PHI under this exception, the IRB must obtain representations from the investigator that:

i. the use or disclosure is sought solely to prepare a research protocol or for similar purposes preparatory to research;
ii. no researcher will remove any PHI from the premises of LG Health in the course of the review; and
iii. the PHI for which use or access is sought is necessary for the research purposes.

Researchers must complete an IRB form when seeking access to PHI for preparatory reviews.

Researchers may use this provision when accessing PHI for purposes of identifying and recruiting potential research subjects in accordance with the policy Recruiting Methods and Advertisements. In such circumstances, the above representations must be included with the research application for IRB review.

Research Using the PHI of Decedents

An investigator may use and disclose the PHI of a decedent for research purposes. In order to permit such a use or disclosure, the IRB must obtain representations from the investigator that:

i. the use or disclosure is sought solely for research on the PHI of a decedent (e.g., researchers may not request a decedent's medical history to obtain health information about a decedent's living relative); and
ii. the information for which use or disclosure is sought is necessary for the research purposes.

Moreover, the investigator must provide documentation of the death of any individuals about whom information is sought. A researcher must complete and sign a certification form to engage in research on the PHI of a decedent.

Use of De-Identified Health Information

The IRB may allow completely de-identified information to be used and disclosed for research purposes without authorization. (See Roles/Responsibilities section below for information about how a de-identified data set may be created for research purposes from LG Health electronic health records.) Information may only be considered completely de-identified when either: (i) a qualified statistician documents their determination that the risk of identification is very small; or (ii) the information does not contain any of the following:

1. Name

2. Address (all geographic subdivisions smaller than state, including street address, city county, and zip code)
3. All elements (except years) of dates related to an individual (including birthdate, admission date, discharge date, date of death, and exact age if over 89)
4. Telephone numbers
5. Fax number
6. Email address
7. Social Security Number
8. Medical record number
9. Health plan beneficiary number
10. Account number
11. Certificate or license number
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web URL
15. Internet Protocol (IP) Address
16. Finger or voice print
17. Photographic image - Photographic images are not limited to images of the face.
18. Any other characteristic that could uniquely identify the individual

If the IRB or investigator has any doubts as to whether PHI has been completely de-identified within the meaning of this Policy, the information should be treated as though it were *not* completely de-identified and neither used nor disclosed for research purposes without meeting another exception. Note that information that may be thought to be "de-identified" because direct identifiers are not included and subjects cannot be identified as a practical matter may not meet HIPAA's stricter definition of de-identification. Such information might satisfy the requirements for a limited data set, however (see below).

Limited Data Sets

The IRB may allow the use and disclosure for research purposes of a *limited data set* including a partially de-identified subset of the individual's PHI, provided that the person using or receiving the information has signed a Data Use Agreement through which they agree to protect the privacy of the information received.

A limited data set may be created by removing from the individual's PHI the above list provided under "Use of De-identified Health Information", with the exception that a limited data set may include the following identifiers:

i. Dates related directly to the individual, such as admission, discharge, services, DOB, or DOD
ii. Town, city, state, 5 digit zip code (but no street address)
iii. Age in years, months, or days or hours

2. **Exempt Research.** The Common Rule (45 CFR § 46.104) exempts from IRB approval certain secondary research uses of identifiable private information or identifiable biospecimens (see the policy Exempt Research). Note, however, that research that involves "information collection and analysis involving the investigator's use of identifiable health information" can be exempt under the Common Rule but still

regulated under HIPAA. Note also that the LGH IRB has the authority to review such research for privacy concerns (see the policies on the Authority and Purpose of the IRB and on Activities Requiring IRB Review).

3. **Patient Access to PHI Related to Research.** Individuals generally have a right to access all of their PHI maintained by LG Health or its business associates. Any individual requesting access to PHI obtained in the course of research (including PHI that may be contained in research records) should be directed to submit their request to LG Health's Health Information Management Department for processing in accordance with LG Health's policy regarding patient access to PHI, which provides detailed guidelines for responding to such requests. The HIM Department will determine, with assistance from the investigator and the Privacy Official, whether access to PHI obtained in the course of research should be denied under any of the exceptions described in that policy.

4. **Documentation of PHI Disclosures.** To ensure ability to comply with HIPAA requirements to provide patients, upon their request, with documentation of PHI disclosures, all research records must be retained for six (6) years from the date of study closure.

ROLES/REPONSIBILITIES

Principal Investigators and Research Staff shall obtain approval from the IRB before completing any of the procedures described in this policy.

The IRB shall review all requests regarding the use and disclosure of research subjects' PHI without documented authorization from the research subject.

A data broker may serve as a neutral third party to extract and prepare data from LG systems for use by researchers. The Research Institute biostatistical group serves as the primary data broker for all research data access from electronic health record with backup and other system access provided by Information Services (IS) Business Intelligence (BI) staff.

DEFINITIONS

Protected Health Information (PHI):Individually identifiable health information that relates to past, present, or future health or condition of an individual, provision or care, or payment, and identifies the individual or there is reasonable basis to believe that the information could be used to identify the individual.

REFERENCE DOCUMENTS

Exempt Research Policy
Informed Consent and HIPAA Authorization Requirements Policy
Recruiting Methods and Advertisements Policy

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

Health Insurance Portability and Accountability Act of 1996
45 CFR § parts 160 and 164
AAHRPP Standards II.3.D, and II.3.E

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Vulnerable Populations Policy No. 507	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 08/14/07, 07/07/09, 04/25/11, 02/10/14, 01/01/15, 11/16/17, 10/15/18, 01/21/19, 12/17/20, 10/19/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to set forth guidelines for review of human subject research that could involve individuals who are potentially vulnerable to coercion, present conditions that may affect risk/benefit determinations, or bear an unequal burden in research.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health).

POLICY STATEMENTS: The Institutional Review Board (IRB) will apply additional protections as necessary to protect research subjects that may be vulnerable to coercion or undue influence. Such populations may include, but are not limited to, children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons. The extent of additional protection afforded should depend upon the risk of harm and the likelihood of benefit. In the event that the IRB regularly reviews research involving a vulnerable population, the IRB will consider including one or more individuals who are knowledgeable about and experienced in working with these subjects. Potentially vulnerable groups may include: pregnant persons, fetuses, and neonates; prisoners; children; mentally disabled persons; handicapped persons; and economically or educationally disadvantaged persons.

PROCEDURES

1. Pregnant Persons, Fetuses, and Neonates

a. Subpart B of 45 CFR 46 contains special protections for pregnant persons, fetuses, and neonates while enhancing the participation of pregnant persons in research.

i. Research with pregnant persons may be exempt from these special protections if the research otherwise meets criteria to be exempt from IRB requirements (see the policy Exempt Research).

ii. The LG HRPP may waive the need to meet Subpart B requirements for non-exempt research if it is not federally sponsored, is no more than minimal risk, and includes pregnant persons only incidentally.

iii. Otherwise, the IRB will review research covered by Subpart B and approve only research which satisfies the conditions of all applicable sections of Subpart B as well as other regulatory requirements. Compliance with the provisions of Subpart B will be documented in the electronic IRB system.

b. Pregnant Persons or Fetuses. Pregnant persons may be involved in research if all of the following conditions are met:

i. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant persons, have been conducted and provide data for assessing potential risks to pregnant persons and fetuses;

ii. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the pregnant person, or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means;

iii. Any risk is the least possible for achieving the objectives of the research;

iv. Each individual providing informed consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

v. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

vi. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

vii. Individuals engaged in the research will have no part in determining the viability of a neonate.

Note: The federal regulations also state that for children who are pregnant, assent and permission must be obtained. However, under Pennsylvania law, minors who are pregnant are considered able to give legally effective consent and therefore do not meet the federal definition of "children" (see definitions below).

c. Neonates of Uncertain Viability, and Nonviable Neonates. Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

i. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing risks to neonates;

ii. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate; and

iii. Individuals engaged in the research will have no part in determining the viability of the neonate.

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the IRB determines that: (i) the research holds out the prospect of enhancing the probability of survival or the neonate to the point of viability, and the risk is the least possible for achieving that objective; and (ii) the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research.

After delivery, a nonviable neonate may not be involved in research unless all of the following additional conditions are met: (i) vital functions of the neonate will not be artificially maintained; (ii) the research will not terminate the heartbeat or respiration of the neonate; (iii) there will be no added risk to the neonate resulting from the research; and (iv) the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

d. Viable Neonates. A viable neonate, after delivery, may be included in research only to the extent permitted by and in accordance with the requirements of 45 CFR 46 Subparts A and D.

e. Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material. Research involving, after delivery, the placenta, dead fetus, macerated fetal material, or cells, tissues, or organs excised from the dead fetus, will be conducted only in accordance with applicable federal, state, and local laws and regulations regarding such activities. If information associated with material described in this Subsection is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent Subparts are applicable.

f. Consent Requirements

i. When making determinations about informed consent involving pregnant persons and fetuses, the IRB will determine whether the research is intended to benefit the pregnant person, both the pregnant person and their fetus, or has no prospect of direct benefit.

ii. Only the consent of the pregnant person (or their legally authorized representative) is required if the research:

a. Is intended to solely benefit the pregnant person;

b. Is intended to benefit the pregnant person and their fetus;

c. Has no prospect of benefit, but the risk to the fetus is no greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.

iii. For research involving neonates of uncertain viability, the IRB will accept the consent of either parent or other legally authorized representative, or if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative, except that the consent of the father or their legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

iv. When research involves nonviable neonates, the IRB will require consent of both parents unless one parent is unable to consent due to unavailability, incompetence, or incapacity (and parental consent is not required in cases of incest or rape). Consent by a legally authorized individual for research involving a nonviable neonate is not permitted.

v. For viable neonates, the rules pertaining to research involving children apply.

2. Prisoners. A prisoner is any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. For purposes of this Section 2, the term "minimal risk" shall mean the probability and

magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

a. Subpart C of 45 CFR 46 contains special protections for prisoners while allowing participation in specific categories of research.

b. Research involving prisoners may be exempt from these special protections if the research otherwise meets criteria to be exempt from IRB requirements (see the policy Exempt Research) and only incidentally includes prisoners.

c. The LG Health HRPP may waive the need to meet the Subpart C requirements below for non-exempt research if it is not federally sponsored, is no more than minimal risk, and includes prisoners only incidentally.

d. If an investigator indicates that prisoners will participate in the research, or that subjects may reasonably be expected to be incarcerated at some time point during the study, the following additional requirements will apply to IRB review of the research:

   i. In addition to meeting federal regulations, the research must comply with state requirements for inclusion of prisoners as subjects. LG Health Legal Counsel can assist the IRB with any state requirements.

   ii. A majority of IRB members will have no association with the prison(s) involved, and at least one member shall be a prisoner or prisoner advocate with appropriate background and experience to serve in that capacity.

   iii. The IRB may review research involving prisoners only if it finds that the following conditions are met. Additionally, for research supported by HHS, the IRB must certify to HHS (through the Office of Human Research Protections) that the IRB has reviewed the research under the special conditions required by law and that the research falls into one of the below permissible categories. The research will not begin until HHS (through OHRP) verifies the permissible category.

      a. The research falls into one of the following categories:

         - The research under review involves solely research on practices, either innovative or accepted, which have the intent and reasonable probability of improving the health and well-being of the subjects. For studies supported by HHS and in which prisoners may not benefit from the research because they are assigned to a control group in a manner consistent with the protocol approved by the IRB, the research may proceed only after the Secretary of HHS has consulted with appropriate experts and published notice in the Federal Register of their intent to approve such research.

         - Research on conditions particularly affecting prisoners as a class (e.g., vaccine trials on hepatitis). For studies supported by HHS, the research may proceed only after the Secretary of HHS, or designee, has consulted with appropriate

experts and published notice in the Federal Register of their intent to approve such research.

- Studies of possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subject.

- Studies of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subject.

- Epidemiologic studies that meet the following criteria:

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

b. Any possible advantages accruing to the prisoner through participation in the research, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in prison, are not of such a magnitude that the prisoner's ability to weigh the risks and benefits of the research in the limited choice environment of the prison is impaired.

c. The risks involved in the research are commensurate with the risks that would be accepted by non-prisoner volunteers.

d. Selection procedures within the prison or population are fair to all prisoners and immune from arbitrary intervention by prison authority or prisoners. Unless the investigator provides the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group or eligible prisoners for the research.

e. Any information given to subjects is presented in language that is appropriate for the subject population.

f. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on their parole.

g. Where there is a need for follow-up examination or care of subjects after the end of their participation in the research, adequate provision has been made for such examination or care, taking into account the varying lengths of prisoner sentences, and for informing subjects of this fact.

e. When subjects become prisoners during a research protocol, the below actions are required. This is necessary because it is unlikely that review of the research and the consent document contemplated the constraints imposed by the possible future incarceration of the subject.

i. The investigator is responsible for reporting to the IRB, immediately and in writing, the incarceration of an enrolled.

ii. All research interactions and interventions with, and collection of identifiable private information about, the now-incarcerated prisoner-subject must be suspended immediately, unless the investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated.

iii. At the earliest opportunity after receiving the investigator's written notice (or otherwise becoming aware of the prisoner status of a subject), the IRB should review the protocol again with a prisoner representative as a member of the IRB. The IRB should take special consideration of the conditions of being a prisoner.

iii. Upon this review, the IRB can either: (i) approve the involvement of the prisoner-subject in the research in accordance with this Policy; or (ii) determine that this subject must be withdrawn from the research.

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

If a subject becomes temporarily incarcerated while enrolled in a study, the IRB will determine whether the subject's temporary incarceration has an effect on the study. If the temporary incarceration does not affect the study (e.g., there is no need for study activities to take place during the temporary incarceration), the IRB may determine to keep the subject enrolled. If the temporary incarceration affects the study, the IRB will follow the process described in 2.b.i-iv, above.

3. Children

a. Enrolling children in research presents especially difficult considerations for the IRB. Two factors make a case for research in children:

- Children differ markedly from both animals and adults, and therefore, these models cannot substitute as alternatives to testing in children

- Lack of appropriate research in children will increase their risk of harm from exposure to practices or treatments untested in this population. In addition, new therapies or knowledge could not be developed for diseases or conditions that specifically affect children.

However, research involving children requires the IRB to carefully consider consent, beneficence, and justice. The determination of risk and possible benefit to a child is at the core of the concept of beneficence when considering research in a pediatric population. Therefore, the IRB must consider the

degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the child before it can determine whether or not the IRB has the authority to approve the research.

b. Subpart D of 45 CFR 46 contains special protections for children while enhancing the participation of children in research.

c. When a child is presented that is unable to consent for themselves the parent or legal guardian accompanying them shall provide their name and confirm ability to sign documents and/or be financially responsible, as applicable

d. Research with children may be exempt from these special protections if the research otherwise meets criteria to be exempt from IRB requirements and does not meet any of the exclusions for exemption of research with children (see the policy Exempt Research).

e. IRB approval of a protocol involving children will be documented in the electronic IRB system.

f. When reviewing research conducted on children, risk is defined in terms of minimal and greater than minimal risk, and may only be approved by the IRB as follows:

Category	Risk Determination	Benefit Assessment	IRB Action
404	Minimal Risk	With or without direct benefit	Approvable
405	Greater than Minimal Risk	Potential for direct benefit	Approvable
406	Greater than Minimal Risk	No prospect of direct benefit, but offers general knowledge about the child's condition or disorder	Approvable on a case-by-case basis
407	Greater than Minimal Risk	No direct benefit, but offers potential to "understand, prevent, or alleviate a serious problem affecting the health and welfare of subjects"	Not Approvable *

* Approval to proceed with this category of research must be made by the Secretary of HHS or the Commissioner of the FDA with input from selected experts, and following opportunity for public review and comment.

d. IRB Approvals

i. Category 404. The IRB must find and document that the following three (3) conditions have been met:

- The research is not greater than minimal risk
- Adequate provisions to obtain permission from parents or guardians are in place (IRB may find that permission of one parent is sufficient)
- Adequate provisions for the assent of the child are in place

ii. Category 405. The IRB must find and document that the following four (4) conditions have been met:

- Research greater than minimal risk is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual child
- The risk is justified by the potential benefits to the child
- Adequate provisions to obtain permission from parents or guardians are in place (the IRB may find that permission of one parent is sufficient)
- Adequate provisions for assent of the child are in place

iii. Category 406. The IRB must find and document that the following six (6) conditions have been met:

- Research risk is a minor increase over minimal risk
- There is no prospect of direct benefit to the individual child
- The research is likely to yield generalizable knowledge about the child's disorder or condition
- The research procedure/intervention is reasonably commensurate with experiences that the research subject is exposed to (during actual or expected medical, dental, psychological, social, or educational situations)
- Adequate provisions to obtain permission from the parents or legal guardian are in place (permission from both parents is required, 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)
- Adequate provisions for assent of the child are in place

e. Permission of Parents or Legal Guardian. Children may be subjects of research only if informed consent is obtained from the parents or legal guardian. (Note: see definitions below for clarification regarding minors who are legally able to provide consent in the Commonwealth of Pennsylvania.) For non-FDA regulated studies, consent of the parents may be waived by the IRB in accordance with 45 CFR 46.116 or if parental permission is not a reasonable requirement to protect subjects.

f. Assent of Child. Children over the age of 7 must agree to participate in the research and provide written assent. Separate assent forms should be provided based on reasonable age ranges for comprehension (e.g., 7-10, 11-15, 16-18). Mere failure to object should not, absent affirmative agreement, be construed as consent. The giving of assent should not be assumed by the investigator. Unless waiver of assent is specifically approved, the child may withhold assent, in which case the child may not be enrolled as a research subject.

g. Wards of the State. Children who are wards of the state or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406 or 45 CFR 46.407 only if such research is related to their status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. If the research is approved, the IRB will require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate will be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator, or the guardian organization.

4. **Limitations on Exemptions**. Limitations on research in vulnerable populations that can be considered exempt from IRB review are provided in the policy "Exempt Research".

ROLES/REPONSIBILITIES

DEFINITIONS

Children: Persons who have not attained the legal age for consent, in the jurisdiction where the research is taking place, to treatments or procedures involved in the research. In Pennsylvania, persons under the age of eighteen (18) generally meet this definition of "children". However, there are exceptions in which a person under the age of eighteen (18) does not meet the federal definition of "child" and may provide legally effective consent to participate in research. These exceptions include persons who: 1) have graduated from high school; 2) are married; 3) are or have been pregnant; and 4) are legally emancipated.

Legal Guardian: An individual who is authorized by court order to consent on behalf of a child to general medical care.

Assent: A child's affirmative agreement to participate in research.

Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

Minimal risk (for research involving prisoners): the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives or in the routine medical, dental, or psychological examination of healthy persons.

REFERENCE DOCUMENTS

Prisoner Involvement in Research, OHRP Guidance, last revised June 25, 2004
Secretarial waiver, Federal Register, June 20, 2003 (Vol. 68, No. 119)

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR 46.104
45 CFR 46 Subpart B
45 CFR 46 Subpart C
45 CFR 46 Subpart D
Minor's Consent Act, 35 P.S. § 10102-3
AAHRPP Standards I.1.G, II.4.A, III.1.C, and III.1.F

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Review of Recruiting Methods and Advertisements Policy No. 508	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 02/19/14, 01/01/15, 11/16/17, 10/15/18, 01/21/19, 02/19/21, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to delineate the criteria by which recruitment of subjects will be evaluated and to provide direction for the review and approval of advertisements.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in research involving the recruitment of human subjects at Lancaster General Health (LG Health) and to Lancaster General Hospital (LGH) Institutional Review Board (IRB) members reviewing such research.

POLICY STATEMENTS: The process for recruitment of research subjects must be both ethical and equitable. All research projects involving the recruitment of human subjects must have a recruitment plan that describes the identification and selection of subjects, including all access, use, and storage of protected health information. The IRB must approve a research protocol with an accompanying recruitment plan before any patient screening and enrollment may begin.

All advertising or other recruitment material must be reviewed and approved by the IRB before they are used.

PROCEDURES

The IRB requires that the Principal Investigator (PI) provide the characteristics of the patient population, anticipated accrual, age ranges, health status, gender, and criteria for inclusion or exclusion with the study IRB application. The IRB is authorized to review the purposes of the research, the setting of the research, and whether the population to be recruited is vulnerable to coercion or undue influence. Regulatory determinations will be made if a project proposes to recruit vulnerable populations (see the policy Vulnerable Populations). The IRB will systematically review proposed recruitment processes to judge whether they fulfill the regulatory requirements of informed consent.

1. **General Factors Relating to Recruitment of Research Subjects.** When assessing whether recruitment of subjects is both ethical and equitable and follows federal regulations and IRB policy, the IRB must take the following factors into consideration:

    a. The inclusion/exclusion criteria
    b. Venues in which advertising about the study will appear
    c. The method by which potential subjects are identified, and all details of access to, use of, and storage of protected health information in the process
    d. The setting in which the potential subject is approached for recruitment
    e. The intended populations of potential subjects to be approached for recruitment
    f. Whether potential subjects are vulnerable to coercion or undue influence, by nature of their situation, social status, level of education, health status, cognitive ability, etc.
    g. Whether any payment or non-monetary incentive to subject seems disproportionate to the procedures the subject will undergo
    h. Whether any incentive or remuneration being offered might unduly influence subjects' choice of provider or treatment for their standard medical care, either during or after the study
    i. Whether any payment to the investigator or institution for enrollment might result in undue influence on potential subjects when deciding whether to participate (see policy on Sponsor Contracts)

The IRB may decide that certain recruitment procedures need to be eliminated or modified to avoid the possibility of the subject feeling coerced into participating in the research, or to protect the privacy of the intended population of potential subjects to be screened for eligibility. For example, the IRB may require the use of direct approaches outlined in item 2 below when feasible rather than indirect approaches considered "preparatory to research" as outlined in item 3a(i) below. The IRB may also require changes to the recruitment process to make the recruitment of potential subjects more equitable.

2. **Recruitment of Subjects by a Healthcare Provider or Treatment Staff.** Direct recruitment for a study by a healthcare provider or their treatment personnel is permitted under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and the LGH IRB. These personnel already have a reason to know the patient's PHI and, assuming the study (including the recruitment process) has been approved by the IRB, these personnel may approach the patient about participating in the study without a HIPAA authorization or waiver. The following are permitted direct recruitment methods:

a. A healthcare provider who has a treatment relationship with the patient (the "provider") and who is also the researcher may approach a potential subject about participation in an IRB-approved study in which the provider participates as a researcher. The provider's treatment personnel (those who have a "reason to know" identifiable health information by virtue of the treatment relationship) also may approach a potential subject about their research. The provider or their treatment personnel must note the communication in the patient's medical record.

b. A healthcare provider who is not the researcher (and the provider's treatment personnel) may give the patient a researcher's name and contact information, and the patient may contact the researcher.

c. A provider who is not the researcher (and the provider's treatment personnel) may recruit a patient to participate in a researcher's study. The approach may be in person, by phone, or by written communication. The provider or treatment personnel should provide the name of the researcher, the topic and purpose of the research, a brief description of the PHI that will be shared with the researcher, and what the subject should expect from the researcher.

i. If the approach is in person or by phone, the provider or treatment personnel must request permission to discuss the patient's PHI with the researcher and/or research personnel, such as the coordinator. The patient must give their verbal or written consent to wanting to learn more about the study, and the provider or their staff must note the communication in the patient's medical record. If the patient agrees to a referral to the researcher, suggested documentation language is as follows:

"I discussed the referral of the patient to [team or doctor] for [describe the research]. The patient agreed to the referral, including sharing information about the patient's condition."

ii. If a recruitment letter is used, the following is required:

- Review and approval by the IRB
- An "opt in" or "opt out" mechanism such as a number to call or a postcard to return within a specified time period (*e.g.*, 10 days)
- For an "opt out" mechanism, a statement that if there is no response within the specified time period, a research staff person may call

- Contact of potential subjects only after an "opt in" response has been received or an "opt out" decision has not been received within the specified time period

d. A healthcare provider who is not the researcher (and the provider's treatment personnel) may discuss possible patient eligibility with the research personnel in a de-identified manner (*i.e.*, with all protected health information (PHI) removed). If the research personnel believe the de-identified patient would be eligible for the study, the treatment personnel could then give the patient the researcher's contact information or obtain the patient's permission to give the research personnel the patient's contact information. (See items "b" and "c" above.)

3. **Recruitment by the Researcher.** A researcher may recruit subjects through healthcare providers in the treatment context as described in 2b, c, and d. Alternatively, a researcher may obtain IRB approval to identify and contact potential research subjects outside the treatment context and without their prior consent or authorization.

a. Under regulations regarding research consent, the IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative if:

i. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative; OR

ii. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

b. Under the "preparatory to research" provisions of HIPAA, a researcher who is a workforce member of LG Health may request access to PHI from LG Health patients without their authorization, for the purpose of identifying potential subjects. The researcher must provide proper representations to the IRB, as described in the policy Uses and Disclosures of PHI. The researcher may contact the potential subject to discuss the study and obtain their consent for participation in the research and authorization to use and disclose PHI for purposes of the research. The researcher, under the "preparatory to research" provision and therefore without authorization, may not record and use information in an ongoing manner (e.g., in a pre-screening log) about the status of potential subjects' eligibility, maintain records of people who were found to be ineligible through pre-screening, or maintain information about people who declined.
Under the "preparatory to research" provision of HIPAA, a researcher who is not a workforce member of LG Health also may request, with proper representations to the IRB, to review PHI from LG Health patients for the purposes of identifying potential subjects. This review must be done while within LG Health and without removing PHI from the premises.

c. A researcher who is a workforce member of LG Health may request the IRB to issue a HIPAA waiver to allow the researcher, without authorization from potential subjects, to record and use information in an ongoing manner (e.g., in a pre-screening log) about the status of potential subjects' eligibility, to maintain records of those who were found to be ineligible through pre-screening, or to maintain information about those who declined. The researcher must provide the IRB with information about what data will be recorded, who will have access to the data, and how the "minimum necessary" principle will be met. Furthermore, the request for waiver of authorization must detail how the

regulatory requirements for a HIPAA waiver, which are set forth in the policy Informed Consent and HIPAA Authorization Requirements, will be met.

d. Any of the above activities that are part of a research study's recruitment activities must be described in the application or protocol submitted to the IRB.

4. IRB Review of Advertisements

a. All advertising or other recruitment material should be submitted at time of initial review. If material is obtained following the initial approval, these items should be submitted for expedited review prior to use.

b. When direct advertising is to be used, the IRB must review the information contained in the advertisement and the mode of communication. The IRB must review the final copy of printed advertisements to evaluate the relative size of type used and other visual effects. The IRB may review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording and subsequently review the final taped version prepared from IRB-approved text for final approval.

c. The IRB must review advertising to assure that the advertisements do not:

i. State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent form and protocol.
ii. Include exculpatory language.
iii. Emphasize the payment or the amount to be paid, by such means as larger or bold print.
iv. Promise "free treatment" when the intent is only to say subjects will not be charged for taking part in the investigation.
v. Convey undue coercion.
vi. Make a claim, either explicitly or implicitly, that the drug, biologic, device, or other research procedures are safe or effective for the purposes under investigation, or that the test article or other research procedures are known to be equivalent or superior to any other drug, biologic, device, or procedure.
vii. Use terms such as "new treatment", "new medication", or "new drug" without explaining that the test article or the research procedures are investigational or experimental.

d. Advertisements to recruit subjects should be limited to the information prospective subjects need to determine their eligibility and interest. The following items may be included when appropriately worded:

i. The name and address of the researcher and/or research facility.
ii. The purpose of the research or the condition under study.
iii. In summary form, the criteria that will be used to determine eligibility for the study.
iv. A brief list of benefits to subjects, if any.
v. The time or other commitment required of the subjects.
vi. The location of the research and the person or office to contact for further information.

ROLES/REPONSIBILITIES

The Principal Investigator must submit a recruitment plan that outlines a recruitment process that is compliant with the Health Insurance Portability and Accountability Act and this Policy. The Principal Investigator also must submit all recruitment materials for IRB review.

The IRB will assess the recruitment plan and materials to ensure that it is compliant with all applicable laws and LG Health policies.

DEFINITIONS

Pre-screening: Obtaining and reviewing health information of potential subjects without their knowledge or authorization, for the purpose of further investigating or determining eligibility for research, before contacting them.

REFERENCE DOCUMENTS

Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule, NIH Publication Number 03-5388
LG Health Policy: Uses and Disclosure of PHI

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 164 Subpart E
45 CFR 46.116(g)
AAHRPP Standards II.3.C.1 and III.1.E

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Payment or Remuneration to Subjects Policy No. 509	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 02/19/14, 01/01/15, 11/16/17, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to describe the acceptable parameters for payment or remuneration to research subjects.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to individuals engaged in human subject research at Lancaster General Health (LG Health) and Institutional Review Board (IRB) Members.

POLICY STATEMENTS: LG Health allows payment or remuneration to individuals who participate in human subjects' research. The IRB is authorized to review the amount and schedule of any proposed payment and to determine that it is fair and not an undue inducement to participate.

PROCEDURES

1. Payment or Remuneration to Research Subjects

a. Payment or remuneration to research subjects is intended to compensate them for travel expenses incurred, inconveniences related to the time or effort required, or other expenses associated with the participation in a research study. Payment is not intended to compensate for risks or discomforts.

b. The IRB should consider the below criteria for approval of payment or remuneration to research subjects:

i. Remuneration for participation in research should be reasonable and the amount paid should be comparable to other research projects involving similar time, effort, and inconvenience.
ii. Payment amounts should not be large enough to constitute an undue inducement to participate in a high risk or uncomfortable procedure.
iii. Payment should not be made when research data collection occurs in conjunction with standard medical care, unless the research procedures significantly increase the time required of subjects. That is, payment should not be construed to be an incentive for choosing the provider of the standard medical care.
iv. The IRB may approve studies in which financial remuneration is a major reason for participation as long as the studies represent minimal risk to the subject and the IRB determines that the remuneration will not unduly influence subjects.
v. Credit for payment should accrue as the study progresses and should not be contingent upon the subject completing the entire study.
vi. Any amount paid as a bonus for completion should be reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.
vii. Compensation offered by a sponsor for participation in a trial may not include a coupon good for a discount on the purchase price of the product under investigation after it has been approved for marketing.

c. All information concerning payment, including the amount and schedule for payments, must be set forth in the research consent document. Research subjects may be informed that remuneration is

subject to federal income tax, and any payment over $600 in a calendar year will be reported to the Internal Revenue Service.

2. **Reimbursement to Research Subjects.** Research subjects may receive reimbursement for direct, out-of-pocket costs that a subject may incur as a result of participating in a research study. Reimbursement does not compensate subjects for inconvenience or discomforts. Examples of out-of-pocket costs could include, but are not limited to, mileage, parking, public transportation, and meals. Reimbursement for expenses requires documentation of mileage or receipts. Reimbursement for expenses is not subject to federal income tax.

ROLES/REPONSIBILITIES

It shall be the responsibility of the principal investigator and research staff to provide a description of the payment/remuneration and reimbursement to research subjects within the consent form.

It shall be the responsibility of the IRB to ensure that payment/remuneration and reimbursement are reasonable and not coercive.

DEFINITIONS

Remuneration: The transfer of goods, services, or privileges with monetary or intrinsic value to research subjects in exchange for their participation in research.

REFERENCE DOCUMENTS

26 CFR § 31.3406(b)(3)(1)
Social Security Act, Section 1612(b)

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standards II.3.C.1 and III.1.E

Penn Medicine
Lancaster General Hospital

POLICY TITLE: **Data Monitoring for Research Activities Involving More Than Minimal Risk** **Policy No. 510**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 04/02/14, 01/01/15, 10/12/17, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy outlines the Lancaster General Hospital (LGH) Institutional Review Board (IRB) requirements for a data monitoring plan for more than minimal risk to subjects in research projects.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) and to LGH IRB members.

POLICY STATEMENTS: In research that involves no more than minimal risk, a monitoring plan is usually not required. The IRB requires a data and safety management plan for any research that presents more than minimal risk to research subjects.

PROCEDURES

1. The LGH IRB will determine whether a research activity represents no more than minimal risk or more than minimal risk to subjects and then determine whether a data monitoring plan is required. If one is required, the IRB will review the adequacy of the plan and then monitor that the plan is followed and that appropriate reporting to the IRB occurs.

2. In research that involves more than minimal risk, information regarding the proposed data and safety monitoring plan must be submitted at the time of initial review. The plan should include information such as:

    a. What safety and efficacy data will be collected and monitored.
    b. How the safety information will be collected (e.g. with case report forms, at study visits, by telephone calls with subjects).
    c. The frequency of data collection, including when the safety data collection starts.
    d. Who will monitor the data, their areas of expertise, and their affiliation with the study.
    e. Procedures for analysis and interpretation of data.
    f. Actions the responsible party will take concerning specific events or end points.
    g. Time points for review.
    h. Plan for reporting to the IRB.
    i. Conditions that trigger an immediate suspension of the research, if applicable.
    j. For studies that do not have or are not required to have a data monitoring committee and are blinded, have multiple sites, enter vulnerable populations, or employ high-risk interventions, the IRB needs to carefully review the data and safety monitoring plan and determine whether a data monitoring committee is needed.

3. The IRB will ensure that:

    a. An appropriate monitoring plan is put in place at the start of the research activity that is commensurate with risk, size and complexity of the research activity. Studies that entail more risk, are larger in size, or involve a higher level of complexity may increasingly require representation of more areas of expertise (clinical, statistical, ethical, etc.), more independence of the monitor(s) from the research activity, more formal rules for interpretation of results, and/or increased frequency of monitoring.

b. It receives monitoring reports according to the planned schedule. Monitoring reports should include a description of the data monitored, any recommendations made by the monitor(s), and any actions taken as a result of the monitoring.

4. The IRB may consider a range of monitoring plan options, including:

   a. The principal investigator will have sole responsibility for monitoring and oversight of problems/events.
   b. A group of designated LG Health faculty/staff will have responsibility for monitoring, oversight of adverse events, and other protocol events.
   c. A designated medical monitor, or group of monitors for commercially funded or for not-for-profit sponsored studies, will have responsibility for monitoring, oversight of adverse events, and other events.
   d. A formal Data and Safety Monitoring Board (DSMB) will have responsibility for monitoring, oversight of adverse events, and other problems.

5. In the event that a formal DSMB is to be constituted by a federal funding agency or by a clinical consortium conducting the protocol, or is required by the IRB, the IRB should receive sufficient information to determine that the responsibilities of the formal DSMB represent appropriate data and safety monitoring. The IRB should receive information about individuals who will be selected to serve on the DSMB (names of specific members need not be provided). Also, the IRB should receive a detailed plan for safety and efficacy monitoring to be conducted by the DSMB. The IRB then does not need to receive ongoing safety and efficacy data for the treatment(s) under study but rather a summary of what was reviewed and the DSMB's recommendation regarding continuation of the research after each review that occurs.

6. During the course of a study that does not have a formal DSMB, the IRB may decide that a research activity represents more risk or complexity than originally understood. It may require that the monitoring plan be revised to include representation of more areas of expertise, more independence of the monitor(s) from the research activity, more formal rules for interpretation of results, and/or increased frequency of monitoring.

7. The IRB's decision regarding the need for a monitoring plan and its adequacy if required will be recorded in the checklist for the initial review. At the time of continuing review or review of an interim monitoring report for a study that is more than minimal risk but does not have a formal DSMB, the IRB's decision about the continued adequacy of the current level of monitoring will be recorded.

ROLES/REPONSIBILITIES

The PI shall be responsible to submit the proposed data and safety monitoring plan at the time of initial review. The PI shall also be responsible to submit any data and safety monitoring reports to the IRB when received from the appointed research monitoring body.

The IRB shall be responsible for reviewing a data and safety monitoring plan or making recommendations for a monitoring plan.

DEFINITIONS

REFERENCE DOCUMENTS

NIH Policy for Data and Safety Monitoring, National Institutes of Health, June 1998
Further Guidance on Data and Safety Monitoring for Phase I and Phase II Trials, National Institutes of Health, June 2000.

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

45 CFR § 46.111(a)(6); 21 CFR § 56.111(a)(6)
AAHRPP Standards II.3.B and III.1.C

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Reporting and Review of Events during Research **Policy No. 511**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/20/14, 01/01/15, 02/04/16, 11/16/17, 03/6/18, 10/15/18, 10/29/20, 07/26/21, 10/30/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the requirements for reporting and review of events occurring during research that involve risk to human research subjects.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) or at a site using the Lancaster General Hospital (LGH) Institutional Review Board (IRB) and to IRB Members.

POLICY STATEMENTS: It is the Policy of the IRB that Investigators promptly report any Unanticipated Problems and Unanticipated Adverse Device Effects) to the IRB, appropriate institutional officials and the appropriate federal agencies, such as OHRP and the FDA, in accordance with federal regulations.[1] Investigators also should promptly report certain deviations as defined in this policy. Adverse events and deviations that do not require prompt reporting should be summarized at the time of continuing review.

PROCEDURES

1. Reporting of Adverse Events to the IRB

a. Deaths of Research Subjects.

i. When the death of a research subject meets the definition of an Unanticipated Problem or an Unanticipated Adverse Device Effect (see definitions), and therefore suggests that subjects or others are at increased risk of harm, the investigator is required to report the death within 24 hours of the time the investigator becomes aware of the event.

ii. When a death that does not meet the definition of an Unanticipated Problem or an Unanticipated Adverse Device Effect occurs in an investigator sponsored research study (a study designed and conducted by an LG Health affiliated investigator), the investigator is required to report the death, regardless of whether or not it is thought to be related to the research, within 72 hours.

iii. To meet these reporting requirements for timeliness of reporting, the investigator should complete the electronic event reporting form even if information regarding the death is incomplete. The investigator should make an assessment of the relatedness of the death to the study, the expectedness of the death, and any change in risk to others based on the information available at the time of reporting. A follow-up event report is to be completed as additional information becomes available, and the investigator's assessment of the death can be updated.

1 45 CFR § 46.103(b)(5); 21 § CFR 56.108(b)(1); See also, Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, OHRP, January 15, 2007.

iv. All other deaths can be reported with other adverse events in summary form at the time of IRB continuing review.

b. Non-fatal Unanticipated Problems or Unanticipated Adverse Device Effects. Unanticipated Problems and Unanticipated Adverse Device Effects that are non-fatal are to be reported to the IRB within 10 business days after the Investigator learns of the problem, using the electronic event reporting form.

c. Those problems/events, whether serious or not, that are recorded as part of the study protocol but that the local investigator deems **NOT** to meet the definition of an Unanticipated Problem or Unanticipated Adverse Device Effect (ie, are deemed **unlikely or not related** to the research or **expected or anticipated)** should be reported in summary form (using a table or spreadsheet) at the time of IRB continuing review. There is no requirement to report events that are not recorded as part of the study protocol.

d. Problems/events occurring at other sites that do not meet the definition of an Unanticipated Problem or Unanticipated Adverse Device Effect do not need to be reported to the LGH IRB.

2. **Reporting of Deviations from an Approved Protocol.** A deviation (or group of deviations) from an approved protocol should be reported to the IRB using the electronic event reporting form within 10 business days of its occurrence if any of the following are true:

a. The deviation indicates increased risk for subjects or compromises their rights or welfare;
b. The deviation compromises the scientific integrity of the study or the soundness of the research plan; or
c. The deviation represents serious or ongoing non-compliance (see the policy Allegations of Non-compliance).

Otherwise, all deviations should be reported in summary form at the time of continuing review.

3. **Review by the IRB.** Deaths, Unanticipated Problems, Unanticipated Adverse Device Effects, and any deviations reported in accordance with this policy will be reviewed by the Chair of the IRB or the Chair's designee promptly upon reporting to the IRB office to determine if immediate action is necessary to protect the safety of research subjects due to the nature or frequency of the reported problem. If immediate action is determined to be necessary in order to prevent harm to subjects, the Chair or their designee may take any of the following actions:

a. Request additional information.

b. Recommend review by the full board for possible action.

b. Request modification of the protocol.

c. Monitoring of the research.

d. Monitoring of the consent process.

e. Require information concerning the problem be provided to subjects or others when such information may relate to their willingness to continue to take part in the research. In some cases, this may require changes in the informed consent, protocol, or other study documents, which may require re-consenting currently enrolled subjects.

f. If reviewed at a full IRB meeting, the Board will be provided with all relevant documents to review. The Board may reconsider approval of the study, including suspension and/or termination, if it is determined that the unanticipated problem has resulted in an increased risk to the subjects. In some cases, this could mean modifying the continuing review cycle.

g. Any Death, Unanticipated Problem, or Unanticipated Adverse Device Effect that occurred at LG Health or a site under purview of the LGH IRB and that the IRB Chair or designee determines to involve no more than minimal risk to subjects or others and to require no further action will be reported to all IRB members through the agenda at the next convened IRB meeting.

4. **Protocol Reporting.** Investigators must follow protocol requirements for reporting to sponsors or study coordinating centers. More extensive reporting (i.e., reporting of events that do not meet the definitions of Unanticipated Problems or Unanticipated Adverse Device Effects) may be required.

5. **Reporting to Federal Agencies.** When applicable in accordance with regulations, the IRB will report, or ensure reporting, to the Office for Human Research Protections (OHRP) and/or the Federal Drug Administration (FDA) in a timely manner the following: 1) Unanticipated Problems or Unanticipated Adverse Device Effects; or 2) suspension or termination of IRB approval for a study.

ROLES/REPONSIBILITIES

Principal Investigators shall report unanticipated problems, unanticipated adverse device effects, deaths of research subjects, and other problems/events in accordance with this policy.

The IRB Chair or designee will review any deaths, unanticipated problems or unanticipated adverse device effects submitted and make a determination as described in this policy.

DEFINITIONS

Unanticipated Problems: In general, include any incident, experience, or outcome that meets **all** of the following criteria:

1. Unexpected or unanticipated (in terms of nature, severity, or frequency) given (1) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (2) the characteristics of the subject population being studied;

2. related or possibly related to participation in the research (that is, there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

The following are examples of events that meet the definition of an Unanticipated Problem:

a. Any event (including on-site and off-site adverse events, injuries, side effects, deaths or other problems) which in the opinion of the local investigator was unanticipated, involved increased risk to subjects or others, and was possibly related to the research procedures;

b. Any deviation, whether accidental or intentional, from the IRB-approved protocol that increases risk to subjects;

c. Any publication in the literature, safety monitoring report (including Data and Safety Monitoring Reports), interim result or other finding that indicates an unexpected change to the risk/benefit ratio of the research;

d. Any breach in confidentiality that may involve risk to the subject or others;

e. Any study-related complaint of a subject that indicates an unanticipated risk or that cannot be resolved by the research staff; or

f. Any other possibly related event which in the opinion of the investigator constitutes an unanticipated risk.

For clinical trials being conducted in accordance with the International Conference on Harmonisation's Good Clinical Practice (GCP or ICH E6) guidelines, the following also should be considered an unanticipated problem to be reported to the IRB:

a. New information that might affect adversely the safety of the subjects or the conduct of the clinical trial; or

b. Any change significantly affecting the conduct of the clinical trial or increasing the risk to subjects.

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

Anticipated (expected) Problems and Anticipated Adverse Device Effects: Those that are already described as potential risks in the consent form, listed in the Investigator's Brochure or investigational plan, or part of subjects' underlying disease. Anticipated Problems and Anticipated Adverse Device Effects should be reported in summary form only at the time of IRB continuing review, regardless of whether serious or related. For example, if hospitalization occurs because of expected exacerbation of underlying disease, this event should be reported only at the time of continuing review.

Serious problems or events: Those which in the opinion of the local investigator were life threatening; resulted in death, hospitalization or prolonged hospitalization, disability, or birth defect; or required intervention to prevent one of these outcomes.

REFERENCE DOCUMENTS

Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, OHRP, January 15, 2007.
Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting to IRBs—Improving Human Subject Protection, FDA, January 2009
Guidance for Industry: E6 Good Clinical Practice: Consolidated Guidance, Food and Drug Administration, March 2018, Section 3.3.8

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

HHS 45 CFR § 46.103(b)(5)
FDA 21 § CFR 56.108(b)
FDA 21 § CFR 812.3(s)

AAHRPP Standards II.2.G and III.2.D

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Planned Emergency Research Policy No. 520	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 10/30/17, 10/10/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy establishes the mechanisms for individuals engaged in human subject research at Lancaster General Health (LG Health) to comply with regulatory requirements governing Planned Emergency Research.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at LG Health.

POLICY STATEMENTS: The Institutional Review Board (IRB) may approve an exception to the informed consent requirements for Planned Emergency Research on life-threatening conditions for which available treatments are unsatisfactory and where it is not feasible to obtain informed consent from research subjects or their legally authorized representatives.

PROCEDURES

1. **IRB Review of Planned Emergency Research.** The IRB must initially approve Planned Emergency Research and must continually review Planned Emergency Research thereafter. The IRB must approve both the research and the waiver of informed consent by ensuring that applicable regulatory requirements are met and the requirements of this Policy are satisfied. In addition to IRB approval, a licensed physician who is a member of (or consultant to) the IRB must agree with the determination of the IRB that the criteria for waiver of informed consent are satisfied. The licensed physician cannot be participating in the Planned Emergency Research in any manner. The minutes of the IRB meeting must specifically indicate the licensed physician who reviewed and agreed with the determination of the IRB that the criteria for waiver of informed consent are satisfied as stated in the Informed Consent and HIPAA Authorization Requirements Policy.

2. **Exception From Informed Consent Requirements.** The IRB may approve Planned Emergency Research and grant an exception to the informed consent requirements if the IRB determines that the following criteria have been satisfied:

    a. The research subjects are in a life threatening situation;

    b. Available treatments are unsatisfactory or unproven;

    c. The collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled studies, is necessary to determine the safety and efficacy of the intervention;

    d. Obtaining informed consent is not feasible because:

        i. The research subject will not be able to give their informed consent due to the medical condition;
        ii. The intervention must be administered before consent from the research subject's legally authorized representative can be reasonably be obtained; and
        iii. There is no reasonable way to prospectively identify individuals likely to become eligible for participation in the Planned Emergency Research;

e. Participation in the research holds out the prospect of direct benefit to the research subjects because:

i. Research subjects are facing a life-threatening situation that requires intervention;
ii. Appropriate animal and other pre-clinical studies have been conducted and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the research subjects; and
iii. Risks associated with the Planned Emergency Research are reasonable in relation to what is known about the medical condition of the potential class of research subjects, the risks and benefits of standard treatment, if any, and what is known about the risks and benefits of the proposed intervention;

f. The Planned Emergency Research could not practicably be carried out without waiver of informed consent;

g. The research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each research subject within the therapeutic window and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator must summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review;

h. The IRB has reviewed and approved the informed consent process and an informed consent document that is consistent with regulatory requirement of LG Health policies. The informed consent process and document are to be used with research subjects and legally authorized representatives in situations where use of such process and document is feasible. The IRB must have reviewed procedures to be used when providing an opportunity for a family member to object to a research subject's participation in the research as further described below;

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

i. Consultation with representatives of the communities in which the research will be conducted and from which research subjects will be drawn. The IRB may consider carrying out the consultation with community representatives. Such community consultation may include public meetings, community panels, and community surveys;
ii. Public disclosure to the community of plans for the research and its risks and benefits prior to initiating the research;
iii. Public disclosure of sufficient information following completion of the research to apprise the community of the research, including the demographic characteristics of the research population and the results of the research;
iv. Establishment of an independent data monitoring committee to exercise oversight of the research;
v. If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed to attempting to contact, within the therapeutic window, the research subject's family member and asking whether they object to the research subject's participation in the research. The investigator must summarize efforts

made to contact family members and provide this information to the IRB at time of continuing review.

3. Additional Requirements

a. The IRB must ensure that procedures exist to inform, at the earliest opportunity, each research subject or legally authorized representative (or family member if the legally authorized representative is not available) of the research subject's inclusion in the research, the details of the research and other information contained in the informed consent document. The IRB must also ensure that procedures exist to inform the research subject or legally authorized representative (or family member if the legally authorized representative is not available) that they may discontinue participation in the research at any time without penalty or loss of benefits to which the research subject is entitled. If a legally authorized representative or family member is informed as described above and the research subject's condition improves, the research subject shall be informed of the above information. If a research subject is enrolled in Planned Emergency Research with waived informed consent and the research subject dies before the legally authorized representative (or family member) can be contacted, information is to be provided to the legally authorized representative (or family member).

b. IRB determinations made pursuant to this Policy must be documented and retained by the IRB for at least six (6) years after completion of the research. The IRB shall make the records available for inspection and copying by the FDA.

c. For research subject to FDA regulations, research involving an exception to informed consent under this Policy must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such research as research that may include research subjects who are unable to consent. A separate IND or IDE is required even if an IND for the same drug product or IDE for the same device already exists.

d. For research not subject to FDA regulations, the IRB must document its findings that the research is not subject to FDA regulations. For research subject to DHHS regulations, the IRB will document and report to the Department of Health and Human Services its findings that the requirements of this Policy have been met.

e. If the IRB determines that it cannot approve the research because the research does not meet the criteria in this Policy or applicable regulations or because of other ethical concerns, the IRB must document its findings and promptly provide these findings to the investigator and sponsor, if applicable. The sponsor must promptly disclose this information as applicable to the FDA, to the sponsor's investigators who are participating or are asked to participate in this or substantially equivalent research of the sponsor, and to other IRBs that have been, or are, asked to review this or substantially equivalent research by that sponsor.

ROLE(S)/REPONSIBILITIES

DEFINITIONS

Planned Emergency Research: Research involving human subjects who are in need of emergency medical intervention, but who cannot give informed consent because of their life-threatening medical condition and who do not have a readily available legally authorized representative to provide consent on behalf of the research subject.

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR 50.24;
AAHRPP Standard II.4.C

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Community Based Research Policy No. 521	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 08/31/17, 09/26/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy establishes additional factors investigators and the Institutional Review Board (IRB) may consider when evaluating or reviewing Community Based Research.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to IRB members and investigators conducting research under the auspices of Lancaster General Health (LG Health).

POLICY STATEMENT: LG Health supports research that includes active participation of the community in the design and implementation of research and the analysis of data. Investigators and the IRB, in addition satisfying LG Health policies and procedures and the ethical principles associated with human subject research, will also consider the unique nature of involving the community when evaluating and reviewing Community Based Research.

PROCEDURES

1. **Investigator Responsibilities.** Community Based Research involves interaction with the community that goes beyond the interactions an investigator has with individual research subjects. Community Based Research involves the community in the design and implementation of research, data analyses, and dissemination of findings. Community Based Research should address a community-defined need or problem. In addition to the other requirements of investigators under LG Health policies, regulatory requirements, and ethical principles relating to human subject research, the investigator will consider the following when engaging in Community Based Research:
    - Identify and inform potential community stakeholders in the research, with awareness of the community interests in the research;
    - Encourage feedback and information from the community regarding the research;
    - Respect the community's interest in the research;
    - Disseminate research findings in an appropriate manner to the community; and
    - Maximize collaboration with the community in the conduct of the research.

2. **IRB Review of Community Based Research.** Since Community Based Research may pose different or unique risks and benefits as compared to human subject research, the IRB should consider the following when reviewing Community Based Research:
    - The appropriate community has been identified and the research has appropriate collaboration with the community and community stakeholders;
    - Whether specialized expertise should be consulted to provide input on the local context and other special circumstances;
    - The research appropriately disseminates research results in a way that is understandable to the community;
    - How the community will be involved in the research;
    - Identify and assess the risks and benefits to the community; and
    - How recruitment methods recognize sensitivity and minimize coercion.

ROLES/REPONSIBILITIES

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standard I.4.C

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Research Involving Drugs or Biologics Policy No. 601	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 10/30/17, 10/06/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to describe the process by which the IRB will conduct an initial review of human subject research involving drugs or biologics, whether or not the research requires an Investigational New Drug (IND) application approved by the Food and Drug Administration (FDA).

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to IRB members and all individuals engaged in human subject research at LG Health.

POLICY STATEMENTS: All research conducted at Lancaster General Health (LG Health) involving a drug or biologic must be reviewed by the IRB in accordance with applicable FDA regulations.

PROCEDURES

1. **IRB Review.** For research using drugs, biologics, or other compounds considered drugs by the FDA, the investigator must submit documentation to the IRB on the protocol application whether there is a current IND in place. Examples of appropriate documentation include, but are not limited to, FDA letter, letter from industry sponsor of the research, or other documentation verifying the IND. If the investigator indicates on the protocol application that an IND is not necessary, the investigator must include information substantiating that an IND is not required. If the investigator is applying for an IND or cross-referencing a sponsor's IND files, the IND goes into effect thirty (30) days after the FDA receives the IND, unless the investigator receives earlier notice from the FDA.

   In the protocol application, the investigator must submit information or documentation relating to the management plan for the control and accountability of investigational drug, biologic, or other product associated with the research.

   The IRB will review the protocol application, which will include a determination of whether an appropriate IND is in place or whether an IND is not necessary. The IRB will only grant approval once the IRB determines that an IND is in place or determines that an IND is not necessary. The circumstances in which an IND is not necessary are described in Section 2, below.

2. **Research that Can Be Conducted Without an IND.** An IND is not necessary if the research involves one the following categories:

   A. The drug being used is lawfully marketed in the United States and the following requirements are satisfied:

      - The research is not intended to be reported to the FDA as a well-controlled study in support of a new indication and there is no intent to use it to support any other significant change in the labeling of the drug;
      - If the drug under investigation is lawfully marketed as a prescription drug, the research is

not intended to support a significant change in the advertisement for the drug;

- The research does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks or decreases the acceptability of the risks associated with use of the drug;
- The research is conducted in compliance with the requirements for IRB review and with the requirements for informed consent;
- The research will be conducted in compliance with the requirements that restrict the promotion, commercial distribution, or charging for the drug and prohibit undue prolongation of the research; and
- The research does not intend to make use of the FDA regulations for planned emergency research.

B. The research involves only one or more of the following as an in vitro diagnostic biological product, provided that it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established diagnostic product or procedure and is shipped in compliance with 21 CFR 312.160:

- Blood grouping serum;
- Reagent red blood cells; or
- Anti-human globulin.

C. Research that involves the use of a placebo if the research does not otherwise require submission of an IND.

D. Bioavailability or bioequivalence research using unapproved versions of approved drug products if all of the following conditions are met:

- The drug does not contain a new chemical entity, is not radioactively labeled, and is not cytotoxic;
- The dose does not exceed the dose specified in the labeling of the approved version of the drug;
- The research is conducted in compliance with the requirements for IRB review and the requirements for informed consent; and
- The sponsor satisfies the requirements for retention of test article samples and safety reporting.

E. Research using a radioactive drug or biological product if all of the following requirements are satisfied:

- The research involves basic research not intended for immediate therapeutic, diagnostic, or similar purposes, or otherwise to determine the safety and efficacy of the drug;
- The use in humans is approved by a Radioactive Drug Research Committee approved by the FDA;
- The administered dose is known to not cause any clinically detectable pharmacologic effect in humans; and
- The total amount of radiation to be administered during the research is the smallest radiation dose practical to perform the research without jeopardizing the benefits of the research and is within specified limits.

F. Research using cold isotopes of unapproved drugs if the following requirements are satisfied:

- The research is intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a drug labeled with a cold isotope or regarding physiology, pathophysiology, or biochemistry;
- The research is not intended for immediate therapeutic, diagnostic, or preventive benefit to the subject;
- The administered dose is known not to cause any clinically detectable pharmacologic effect in humans based on clinical date from published literature or other valid human studies;
- The quality of the cold isotope meets relevant quality standards; and
- The research is conducted in compliance with the requirements for IRB review and the requirements for informed consent.

ROLES/REPONSIBILITIES

If the investigator indicates on the IRB application that a study of a drug or biologic does not require an IND, the investigator must provide information substantiating that the study falls into one of the categories of research that do not require an IND.

DEFINITIONS

REFERENCE DOCUMENTS

Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND, DHSS FDA, September 2013.

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR 312, et. seq.
21 CFR 320.31
21 CFR 361.1
AAHRP Standards I.7.A and I.7.B

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Research Involving Devices Policy No. 602	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 07/06/09, 04/25/11, 04/16/14, 01/01/15, 10/30/17, 10/15/18, 10/06/22, 01/17/2023**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: The purpose of this Policy is to describe the process by which the Institutional Review Board (IRB) will conduct an initial review of human subject research involving medical devices and, for devices without an Investigational Device Exemption (IDE) approved by the Food and Drug Administration (FDA), make determinations as to whether a device is exempt from IDE regulations, a "Significant Risk" device or a "Non-Significant Risk" device in accordance with FDA regulations.[1]

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to IRB members and all individuals engaged in human subject research at LG Health.

POLICY STATEMENTS: All research conducted at Lancaster General Health (LG Health) involving a device shall be reviewed by the IRB in accordance with applicable FDA regulations.[2] Use of humanitarian use devices is governed by the Humanitarian Use Devices Policy.

PROCEDURES

1. **Research that can be Conducted without an IDE.** For clinical investigations of devices, an IDE is not necessary if:

   a. The research involves a device legally marketed in the U.S. that is used or investigated in accordance with the indications in the FDA-approved labeling;

   b. The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;

   c. The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence (a "510k" device);

   d. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
      1. Is noninvasive;
      2. Does not require an invasive sampling procedure that presents significant risk;
      3. Does not by design or intention introduce energy into a subject; and

[1] 21 CFR Part 812. See also, *Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Significant Risk and Nonsignificant Risk Medical Device Studies*, US Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health (January 2006).

[2] 21 CFR Parts 50, 56, and 812.

4. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

e. The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;

f. The research involves a device intended solely for veterinary use;

g. The research involves a device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c); or

h. The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

2. **Identification of Device as Significant Risk.** When submitting an application to conduct clinical research involving a medical device, an Investigator is to indicate whether the sponsor has identified the device as Significant Risk (SR) or Non-Significant Risk (NSR) (see definitions). If the sponsor has identified the devices as SR, the Investigator must provide the IRB with the IDE number for the device and submit with the IRB application the IDE letter issued by the FDA. Sponsors are responsible for making the initial risk determination and providing it to the IRB.

3. **Non-Significant Risk Device Studies.** If the FDA has already determined a study to be SR or NSR, then the investigator shall provide documentation of such determination and the FDA's determination is final. If the FDA has not made a device risk determination for the study, the IRB will review any study that the investigator or sponsor has put forth as NSR. If the investigator or sponsor has determined that the device is NSR and has not obtained an IDE, the IRB will determine whether, in the context of the study or by the nature of the device, the study presents a SR or a NSR of harm to study subjects. The IRB's NSR determination is important because the IRB serves as the FDA's surrogate for review, approval, and continuing review of the NSR device studies. If the IRB agrees that the device is NSR and approves the study, the investigation may begin without submission of an IDE application to the FDA but must be conducted in accordance with the abbreviated requirements of IDE regulations which are as follows:

a. An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor (or sponsor-investigator):
   i. Labels the device in accordance with 21 CFR 812.5;
   ii. Obtains IRB approval of the investigation after presenting the reviewing IRB with an explanation of why the device is not a significant risk device, and maintains such approval;
   iii. Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care informed consent under 21 CFR Part 50 and documents it, unless documentation is waived by an IRB under 21 CFR 56.109(c);
   iv. Complies with the requirements of 812.46 with respect to monitoring investigations;
   v. Maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10);
   vi. Ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and
   vii. Complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

If the IRB determines that the device is SR, the IRB will notify the Investigator and, where appropriate, the sponsor. **The investigation may not proceed until both the IRB and FDA approve the investigation.**[3] The sponsor must then notify the FDA that the IRB has deemed the device SR and file an IDE application. The FDA has the ultimate decision in determining if a device protocol is SR or NSR.

To assist the IRB in making the determination of the risk status of the device, the IRB shall review information such as reports of prior investigations conducted with the device, the protocol, a description of the subject selection criteria, and monitoring procedures. The sponsor must provide to the IRB a risk assessment and the rationale used in making its risk determination. The risk determination is based on the proposed use of a device in the investigation, not on the device alone.

In deciding if a study poses a significant risk, the IRB will consider the nature of the harm that may result from use of the device. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR. Also, if the subject must undergo a procedure as part of the investigational study (*e.g.*, a surgical procedure), the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

The IRB will document SR/NSR device determination in the meeting minutes and identify the rationale used by the IRB for the determination.

4. **IRB Review.** Once the SR/NSR decision has been reached, as determined by the convened IRB, the IRB must then determine whether the study should be approved in accordance with the requirements of 21 CFR Part 56.

All SR device studies present more than minimal risk and, therefore, full IRB review of the study is required. In most circumstances, full IRB review will also be required for NSR device studies. Some NSR studies, however, may qualify as minimal risk[4] and the IRB may choose to review those studies under its expedited review procedures.[5]

The criteria for deciding whether SR or NSR device studies should be approved are the same as for any other FDA regulated study.[6] The IRB is to assure: (i) that risks to subjects are minimized and are reasonable in relation to anticipated benefits and knowledge to be gained; (ii) subject selection is equitable; (iii) informed consent materials and procedures are adequate; (iv) adequate provisions for controlling the use of test articles; and (v) provisions for monitoring the study and protecting the privacy of subjects are acceptable. To assure that the risks to the subject are reasonable in relation to the anticipated benefits, the risks and benefits of the investigation should be compared to the risks and benefits of alternative devices or procedures. This differs from the judgment about whether a study poses a SR or NSR which is based solely upon the seriousness of the harm that may result from the use of the device.

In the protocol application, the investigator must submit information or documentation relating to the management plan for the control and accountability of investigational devices or other product associated

[3] 21 CFR § 812.66.
[4] 21 CFR § 56.102(i).
[5] 21 CFR § 56.110; See also, LG Health HRPP Policy 404: "Expedited Review of Research."
[6] 21 CFR § 56.111.

with the research.

ROLES/REPONSIBILITIES

The Principal Investigator shall be responsible when submitting an application to indicate whether the sponsor has identified the device as significant risk or non-significant risk. If the device has been determined a SR, the Principal Investigator shall also submit the IDE number and the IDE letter issued by the FDA.

The IRB shall be responsible to review research projects with investigational devices applying the same criteria as listed on the LG Health HRPP Policy 402 "Initial Review of Research."

If the sponsor of the device determines the device to be NSR the IRB shall be responsible to determine whether, in the context of the study or by nature of the device, the study presents a SR or a NSR of harm to study subjects.

DEFINITIONS

Medical Device: In part, any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized. Medical devices include, among other things, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts, intraocular lenses, and orthopedic pins. Medical devices also include diagnostic aids such as reagents and test kits for in vitro diagnosis of disease and other medical conditions such as pregnancy.

Investigational Device: A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Clinical investigations undertaken to develop safety and effectiveness data for medical devices must be conducted according to the requirements of the Investigation Device Exemption (IDE) regulations.[7] Certain clinical investigations of devices (e.g., certain studies of lawfully marketed devices) may be exempt from the IDE regulations.[8] Unless exempt from the IDE regulations, an investigational device must be categorized as either "significant risk" (SR) or "non-significant risk" (NSR). The determination that a device presents a non-significant or significant risk is initially made by the sponsor. The proposed study is then submitted either to FDA (for SR studies) or to an IRB (for NSR studies).

Significant Risk device[9]: A device that presents a potential serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; (2) is used in supporting or sustaining human life; (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. SR device studies must follow all the IDE regulations at 21 CFR 812. SR device studies must also have an IDE application approved by FDA before they may proceed.

Non-Significant Risk: A device that does not meet the definition for significant risk study. These devices pose minimal risk to subjects. Note that this risk determination should be based not only on the **nature** of the device, but also on the proposed use of the device in the research study. NSR device studies have fewer regulatory requirements than SR device studies. NSR device studies must, however, follow the abbreviated requirements contained in the IDE regulations which address labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion.[10]

[7] 21 CFR Part 812.
[8] 21 CFR § 812.2(c).
[9] 21 CFR § 812.3(m)
[10] 21 CFR § 812.2(b)

NSR device studies should not be confused with the concept of "minimal risk," a term utilized in the IRB regulations[11] to identify certain studies that may be approved through an "expedited review" procedure.

REFERENCE DOCUMENTS

Information Sheet Guidance for IRBs, *Clinical Investigators, and Sponsors, Significant Risk and Nonsignificant Risk Medical Device Studies*, US Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, January 2006.
LG Health HRPP Policy 402: "Initial Review of Research - Criteria for Approval of Research"
LG Health HRPP Policy 404: "Expedited Review of Research"
LG Health HRPP Policy 603: "Humanitarian Use Devices"

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR § Parts 50, 56, & 812
21 CFR § 56.102(i)
21 CFR § 56.110
21 CFR § 56.111
21 CFR § 56.812.2(b)
21 CFR § 56.812.2(c)
21 CFR § 56.812.3(m)
21 CFR § 56.812.62
21 CFR § 56.812.66
Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Significant Risk and Nonsignificant Risk Medical Device Studies, US Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, January 2006.
AAHRPP Standards I.7.A and I.7.B

[11] 21 CFR Part 56

Penn Medicine
Lancaster General Hospital

POLICY TITLE: Humanitarian Use Devices Policy No. 603	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 02/20/14, 01/01/15, 10/3017, 10/06/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the responsibilities of Investigators and the Institutional Review Board (IRB) in the use of Humanitarian Use Devices (HUD).

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals requesting the use of a Humanitarian Use Device at Lancaster General Health (LG Health) and IRB Members.

POLICY STATEMENTS: All Investigators must comply with all applicable regulations pertaining to HUDs and that all uses of HUDs are reviewed and approved by the IRB as defined in Federal regulations.

The HUD is not considered "investigational" nor is the use of the device considered "research". However, the federal statute and implementing regulations require IRB review and approval before a HUD is used.

A HUD is approved for marketing through a Humanitarian Device Exemption (HDE) application. An HDE application is a Pre-marketing Approval application that is not required to contain clinical data demonstrating "effectiveness" (defined under 21 CFR 860(e)(1).) The FDA may grant HUD designation to a device which meets the criteria in 21 CFR 814.102, and marketing approval for an HUD device through an HDE. Only HUDs with approved HDEs may be used at LG Health.

Once IRB approval is granted, use of the HUD within the approved indication(s) is allowed. The IRB does not need to be notified of individual clinical uses.

PROCEDURES

1. Principal Investigator Responsibilities

a. Complete and submit an IRB application that includes the following information:

i. The FDA HDE number and approval order
ii. A description of the device
iii. The product labeling
iv. Patient information packet that may accompany the HUD
v. A summary of how the physician proposes to use the device, including a description of any screening procedures, the HUD procedure, and any follow-up visits, tests, or procedures
vi. A HUD specific consent form (this can be from the device company or the LG Health template for Humanitarian Use Device Informed Consent and Privacy Authorization Form (available from the IRB office).

b. Comply with continuing review requirements at the designated IRB intervals.

c. Submit reports to the IRB whenever the HUD may have caused or contributed to a death or serious injury, or has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

d. Obtain and document clinical informed consent as it would be for similar clinically approved devices. When the use of a HUD is for diagnosis or treatment, and not associated with research or data collection, HIPAA regulations for research are not applicable.

e. When available, provide information packets to patients prior to their receiving the HUD. If no packet is available, the patient should be provided with the following information (this information may be provided in the HUD informed consent document):

i. An explanation that the HUD is designed to diagnose or treat the disease or condition described in the HDE labeling and that no comparable device is available to treat the disease or condition.
ii. A description of any ancillary procedures associated with the use of the HUD.
iii. A description of the use of the HUD.
iv. All known risks or discomforts.
v. Information reflecting the HUD status of the device including a statement indicating that the effectiveness of the device for this use has not been demonstrated.
vi. If the HUD is studied in a clinical investigation, consent must conform to the requirements found in 21 CFR 50.25.

f. Once IRB approval has been obtained, the investigator may use the HUD for its approved indication(s).

2. IRB Responsibilities

a. Conduct the initial review of the HUD application at a convened meeting. The IRB will have among its members (or consultants) the appropriate experience and expertise to perform a complete and adequate review of the use of the HUD at LG Health.

b. Determine, based on the information provided by the Investigator, whether the clinical investigation described in the IRB application is consistent with the indications for which the HDE was approved. If so, the IRB will follow policies based upon 21 CFR Part 50 (protection of human subjects) and 56 (IRB review) regulations. Clinical investigation of an HUD for an indication other than that approved in the HDE must be conducted in compliance with additional Investigational Device Exemption regulations.

c. Follow as much as possible the criteria in the policy Initial Review of Research and other IRB policies when reviewing use of the HUD.

d. Ensure that health care providers are qualified through training and expertise to use the HUD.

e. The IRB may approve the use of the HUD for a period of time, not to exceed one year. With higher risk devices, the IRB may approve the use of the HUD for a specific number of patients and require a summary report before approving use in additional patients.

f. The IRB may refer the continuing review of use of the HUD in accordance with its approved labeling to expedited review procedures as outlined in the policy Expedited Review of Research.

ROLES/REPONSIBILITIES

The principal investigator shall be responsible to submit an application and receive approval from the IRB before using the device at LG Health. The principal investigator shall be responsible to submit continuing review reports as required by the IRB.

The IRB shall be responsible to conduct an initial review of the HUD at a convened meeting and conduct continuing review annually, not to exceed one year from the previous review. The continuing review may be conducted through the expedited process.

DEFINITIONS

Humanitarian Use Device Exemption (HDE): A Food and Drug Administration (FDA) approval for a physician to use a HUD in clinical treatment or as the subject of a clinical investigation.

Humanitarian Use Device (HUD): A device that is intended to benefit patients by treating or diagnosing a disease or condition that affects not more than 8,000 individuals in the United States per year.

REFERENCE DOCUMENTS

Guidance for Industry and Food and Drug Administration Staff, Humanitarian Device Exemption (HDE) Program, FDA, September 2019

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR § Part 50 and 56
21 CFR Part 814
21 CFR § 56.110
21 Century Cure Act 2016 (Pub. L. No. 114-255)
AAHRPP Standard I.7.A

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Lancaster General Hospital

POLICY TITLE: Emergency Use of an Investigational or Unlicensed Test Article Policy No. 604	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 03/16/17, 10/06/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy establishes the mechanism for individuals engaged in human subject research at Lancaster General Health (LG Health) to comply with regulatory requirements governing the emergency use of investigational or unlicensed test articles.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at LG Health.

POLICY STATEMENTS: Any emergency use of an investigational or unlicensed test article by an individual engaged in research at LG Health shall comply with this Policy and the requirements of the Food and Drug Administration (FDA).

PROCEDURES

1. **Criteria for Emergency Use.** An individual engaged in research may only use an investigational or unlicensed test article on an emergency basis if the following criteria are met: (i) the patient has a life-threatening or severely debilitating conditions; (ii) no standard, acceptable treatment is available; and (iii) there is insufficient time to obtain Institutional Review Board (IRB) approval of its use. However the researcher must obtain the informed consent of the subject or the subject's legally authorized representative, except as provided in Section 3, below.

2. **Obligations of Researcher.** Prior to using an investigational or unlicensed test article on an emergency basis, notification and approval from the IRB is not required. However the researcher is required to report the emergency use of an unlicensed test article within 5 working days of utilizing the investigational or unlicensed test article. The following criteria is required in writing: (i) explanation of the life-threatening or severely debilitating condition necessitating the emergency use; (ii) description of standard treatments previously used and explanation of why alternatives are not acceptable; (iii) description of the investigational or unlicensed test article; and (iv) evidence of Investigational Device Exemption (IDE) or Investigation New Drug Application (IND) for the investigational or unlicensed test article. When the emergency use is of an investigational drug or biologic, the informed consent must comply with the requirements of 21 CFR 50. When the emergency use is of a medical device, the informed consent should be consistent with 21 CFR 50, as applicable.

3. **Exceptions to Informed Consent.** Informed consent is not required if the researcher and a physician not otherwise participating in the emergency use certify in writing that:

    a. The subject has a life-threatening condition that necessitates emergency use of an investigational or unlicensed test article;
    b. There is no available alternative, approved therapy that provides equal of greater likelihood of saving the subject's life;
    c. The subject is unable to provide informed consent; and
    d. There is insufficient time or opportunity to obtain informed consent from the subject's legally authorized representative.

4. Additional Requirements

a. The emergency use of an investigational drug or biologic requires an IND. The researcher shall be responsible for obtaining the IND.
b. For emergency use of an unapproved medical device, the researcher shall obtain an IDE, unless an IDE does not exist. If an IDE does not exist, the researcher shall obtain the approval of the manufacturer for emergency use.
c. The researcher is responsible for reporting the emergency use to the drug or device manufacturer or the FDA.
d. The researcher shall report any adverse events or unanticipated problems associated with the emergency use to the IRB.

5. IRB Review. Within five (5) working days of the emergency use, the researcher must notify the IRB. The researcher shall provide the following information:

a. Description of the investigational or unlicensed test article;
b. IND number for an investigational drug or biologic, or IDE number, if an IDE exists, for an investigational device;
c. Documentation required by Section 2;
d. If the researcher did not obtain informed consent, documentation required by Section 3; and
e. Any other information that the IRB may request.

The IRB will review the documentation provided and determine if the emergency use met regulatory requirements and complied with this Policy. If the IRB determines that the researcher did not comply with this Policy or regulatory requirements, the IRB will determine if non-compliance occurred in accordance with the LG Health Reporting and Review of Non-Compliance with Human Research Protection Program Policy. In addition, the IRB shall also review any adverse events or unanticipated problems associated with the emergency use.

6. Limitations. The emergency use exemption described in this Policy may only be used for a single use or course of treatment of the investigational or unlicensed test article. Any subsequent use of the investigational or unlicensed test article must obtain IRB approval.

The FDA considers the emergency use of a test article, other than a medical device, to be a clinical investigation and the patient to be a subject; the FDA may require data from an emergency use to be reported in a marketing application.

Department of Health and Human Services (DHHS) regulations do not permit emergency uses of test articles to be classified as human subjects' research, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.

ROLE(S)/REPONSIBILITIES

DEFINITIONS

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATION(S)

21 CFR 50.23; 21 CFR 56.102; 21 CFR 56.104
AAHRPP Standard I.7.C

Penn Medicine
Lancaster General Hospital

POLICY TITLE: **Management of Investigational Products** **Policy No. 605**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 10/23/15, 10/30/17, 10/06/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This policy describes (1) the procedures study personnel are to follow and (2) the documentation required for the receipt, storage, distribution, transportation, and return of investigational drugs or biologics (active agents and matching placebos, as applicable) and investigational devices used in human research.

APPLICABILITY/SCOPE/EXCLUSIONS: This policy applies to all clinical studies conducted at Lancaster General Health (LG Health) that involve investigational drugs, biologics, or devices. These studies may be conducted under an Investigational New Drug application (IND) or Investigational Device Exemption (IDE), or may be determined to be exempt from the requirement for an IND or IDE.

POLICY STATEMENTS: The management of and accountability for investigational drugs, biologics, and devices will be in accordance with Federal, state and local regulations and sponsor requirements.

PROCEDURES

1. Investigational product accountability documentation is to be completed on arrival of supplies, each time investigational product is distributed or used, and when investigational product is returned to the sponsor or destroyed. (An Investigational Product Accountability Log template is available to investigators on the LG Research Institute website if one is not provided by the study sponsor.)

2. Delivery of investigational product may be accepted by a hospital pharmacist, investigator, or study coordinator. Upon receipt of the study product, the shipment is to be inventoried, verifying that the compound or device, receipt date, lot number, batch or serial number(s), formulation (for a drug or biologic) or version (for a device, such as size), quantity, and randomization codes, if applicable, on the packing slips are the same as what was actually received. If any discrepancies are found, they must be promptly brought to the attention of the Sponsor/supplier of the investigational product. Documentation of receipt (paper and/or electronic) is to be completed and will be provided to the Sponsor if required.

3. The product labeling must clearly identify the product as intended for investigational use and include any applicable warnings or precautions. The label must not be removed, defaced, or modified without permission of the sponsor/manufacturer.

4. Investigational products are to be stored in a secure, locked environment with access limited to essential research personnel and managed according to requirements listed in the protocol or the investigator's brochure. Investigational products should be stored separately from non-investigational products.

5. The temperature of refrigerators or freezers containing investigational drugs or biologics is to be continuously monitored by an electronic device. Temperature ranges are to be set with an alarm system to alert personnel if the temperature goes below or exceeds the set parameters. The temperature may be manually logged on a weekday basis or continuously monitored/documented via the LG Health automated environmental monitoring system. If a temperature excursion occurs that is unexpected (i.e., not planned and explained by temporary movement of investigational product for purposes such as inventory or maintenance of refrigerators or freezers), that drug is to be quarantined until the Sponsor or representative can be contacted for further instructions. It is not to be dispensed to a subject.

6. Each time that investigational product is distributed to a subject or is otherwise released for use at the study site, it must be appropriately recorded. Documentation includes the following:
    a. Subject's study ID code(s)
    b. Amount/quantity distributed/released
    c. Date of distribution/use (and time, if appropriate)
    d. Product identification numbers, such as lot number, batch or serial number, and randomization code, if appropriate
    e. Signature of authorized person dispensing or releasing the product

7. When investigational product is distributed to subjects, the researcher designated by the PI to distribute the product must ensure that the subject understands when and how to take or use the product. When the protocol requires the subject to record the day, times, and methods of taking or using the study product, the researcher must make sure the subject understands how to fulfill the responsibility.

8. Compliance by the subject with the procedures described in the protocol should be monitored by the research team. Any investigational product that is lost or otherwise no longer available but was not used should be documented along with the reason the product is unavailable.

9. Investigational product is to be returned, disposed of, or destroyed in accordance with the protocol or contract when product expires or at the conclusion of the study. The following procedure is followed if study drug is to be destroyed at Lancaster General Hospital (LGH) by the Pharmacy Department.
    a. Drug may be returned to an onsite pharmacy for destruction. Alternatively, upon notification, the LGH Pharmacy may pick up and transport drug from a remote location to the main hospital location for destruction.
    b. Medications are destroyed using a third party Environmental Protection Agency (EPA) compliant pharmaceutical waste program. Medications are segregated, packaged, and shipped by hazard level according to local, state and federal regulation(s) and incinerated for final disposition.

10. During the course of the study, partially used product, opened containers, and ancillary supplies are disposed of in the manner described in the protocol, and, if they are biohazards, in accordance with the LGH biohazard policies.

11. Investigational product may be transported to other locations by research staff or by secured courier service. Appropriate environmental controls and tracking are to be maintained.
    a. Investigational product will be transported only if necessary to implement protocol requirements at the site.
    b. Transportation time shall be kept to a minimum and research staff will be required to travel in the most direct route possible to the new location.
    c. If there is a required storage temperature for the investigational product to be transported, the sponsor must be consulted and the sponsor's specifications followed for the transport container or other environmental conditions of transport.
    d. An investigational product transport log will be completed, including the location of the investigational product storage area, the date and time of leaving the storage area, the name of the new location, and date and time or arrival at the new location.
    e. The investigational product transport log will be kept with the study's investigational product accountability log.

12. A copy of all accountability document(s) are to be maintained in the study's regulatory files.

13. When a study involves an investigational product, the Institutional Review Board (IRB) application must contain specifics regarding the storage and management of and accountability for the investigational product.

ROLES/REPONSIBILITIES

Principal Investigator (PI): The Principal Investigator is responsible and accountable for investigational product management in accordance with federal and local law, rules, and regulations. The PI may delegate responsibility for the management of investigational product to another qualified researcher involved in the study, but may not delegate accountability. Examples of qualified researchers to whom the PI may delegate responsibility for investigational product management include Clinical Research Coordinators, Clinical Research Nurses, Research Assistants, and Pharmacy Assistants. The PI must provide specifics regarding the storage and management of and accountability for investigational product to the IRB.

DEFINITIONS

Investigational drug or biologic: A drug or biologic, not FDA approved, which is being tested in a clinical trial for safety and efficacy. Investigational drugs and biologics also include drugs and biologics with marketing approval if they are being tested for a different formulation, strength, route of administration or packaging other than what is approved. An FDA approved drug or biologic could also be investigational if it is being tested for an indication which is not approved or to gain further information about an approved use. An investigational drug or biologic may also be referred to as "study medication" or "study drug."

Placebo**:** An inactive substance used as a control in a randomized clinical trial. The active drug or biologic together with the matching placebo, if applicable, may jointly be referred to as "study medication" or "study drug."

Investigational device**:** A device that is used in a clinical study designed to evaluate the effectiveness and/or safety of the device. Investigational devices also may be modifications of devices with marketing approval, or an approved device may be considered investigational if it is being tested for an indication that is not approved. An investigational device may also be referred to as a "study device".

REFERENCE DOCUMENTS

Investigational Product Accountability Log Template
Investigational Product Transportation Log Template

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

AAHRPP Standards I.1.D, I.7.B, and III.2.A

Penn Medicine
Lancaster General Hospital

POLICY TITLE: **Terminations and Suspensions of IRB Approval and Administrative Holds of Research Activities** **Policy No. 701**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 04/16/14, 01/01/15, 06/22/17, 03/6/18, 10/15/18, 10/30/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy describes the Institutional Review Board (IRB) actions associated with suspending or terminating IRB approval of research.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at Lancaster General Health (LG Health) and IRB Members.

POLICY STATEMENTS: Federal regulations require that the IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unanticipated problems involving risk to subjects or others, serious or continuing non-compliance in the conduct of the study, or problems identified in a monitoring process leading to unexpected serious harm to subjects. Suspensions and terminations represent an action by the IRB to temporarily or permanently withdraw approval for some or all research procedures. An investigator may also voluntarily suspend some or all previously approved research activities to allow reassessment of risks and benefits or evaluation of the conduct of the study, or suspend a study at the direction of a sponsor or regulatory authority. Additionally, the IRB may place an administrative hold on some or all previously approved research activities when the investigator has not met requirements of the Human Research Protection Program (HRPP), as long as there is not immediate risk to subjects or others or to the scientific integrity of the study that would require suspension, termination, or other further action by the HRPP.

PROCEDURES FOR TERMINATIONS AND SUSPENSIONS OF IRB APPROVAL

1. Terminations and Suspensions of IRB Approval

a. The IRB has the authority to suspend or terminate IRB approval of human research studies at a convened meeting. The IRB may make the determination to suspend or terminate IRB approval to protect the safety or integrity of the research subjects, the researchers, the institution, or the research itself.

b. The IRB Chair, or in their absence, the Vice Chair, also has the authority to suspend approval of a human subjects research study (or associated studies) when an event occurs and, in their judgment, taking such action cannot wait until a convened IRB meeting in order to protect the rights and welfare of subjects. An action taken by the IRB Chair to suspend approval will be reviewed by the IRB at the next convened IRB meeting. The IRB will decide whether to continue the suspension, terminate approval, or reinstate approval.

c. The Institutional Official has the authority to suspend or terminate the organization's approval for research. Such actions will be promptly reported to the IRB so that the IRB can review the circumstances and take any necessary actions relevant to IRB review and oversight.

d. Suspension or termination of IRB approval shall be immediately documented in writing to the Principal Investigator (PI). The notice must include the reasons for the suspension or termination, the opportunity to respond in person to the IRB Chair or IRB, and to request the PI to provide a plan for ensuring that the rights and welfare of all currently enrolled or previously enrolled (if appropriate) subjects are protected.

Suspensions or terminations of IRB approval will be promptly reported in accordance with LG Health Policy 511 "Reporting & Review of Events During Research."

e. The IRB will determine and inform the PI of steps to be taken as a result of suspension or termination of the approval of research. Steps could include:

i. Notification of currently enrolled subjects that the study has been suspended or terminated by a written communication. In this case, communication to subjects will explain the rationale for the action taken;

ii. Transferring oversight of the study to another investigator;

iii. Continuation of the study under the oversight of an independent monitor;

iv. Making arrangements for medical care or treatment outside of the research for subjects, if applicable;

ii. Withdrawal of subjects, considering the rights and welfare of those individuals before such a step is taken;

iii. Informing the subjects of any follow-up procedures permitted or required by the IRB for subject safety;

iv. Submission of reports to the IRB and the sponsor of any adverse events or outcomes that occurred during the period when suspension or termination occurred;

v. Notification to the sponsor (if applicable) of the suspension or termination.

f. For a suspension to be lifted:
i. The investigator must explain in writing how the issues leading to the suspension were resolved, provide documentation of all required actions, and submit any modifications of study materials for review.
ii. The convened IRB must agree that the issues regarding safety of subjects or integrity of the study have been adequately addressed and that the study again meets criteria for approval. Any modifications to study materials must be approved.

g. The convened IRB also may decide to move from suspension to termination of a study, in which case the procedures of 1c should again be followed.

2. <u>Suspensions of Research Activities Initiated by an Investigator, Sponsor, or Regulatory Authority</u>

a. An investigator may voluntarily suspend, or place on hold, some or all research activities until additional information can be obtained to determine if a change in the risk and benefit assessment of the research has occurred, or if potential areas of non-compliance exist.

b. An investigator may suspend, or place on hold, some or all research activities in response to a directive from a sponsor, FDA, NIH officials, or other authorized review body.

c. The investigator must:

i. Notify the IRB in writing within five working days of the action that they are voluntarily suspending study activities.

ii. Submit the suspension as an amendment and include:
- Justification for the suspension and any supporting documentation;
- A description of the research activities that will be put on hold; and
- Proposed actions to protect and notify currently enrolled subjects, as applicable.

d. The IRB Chair, or in the Chair's absence, the Vice Chair or Institutional Official, reviews the action and determines whether IRB approval should be suspended pending review by the convened IRB and whether any additional procedures need to be followed to protect the rights, safety and welfare of subjects. The actions taken by the convened IRB should follow procedures for suspensions or terminations of IRB approval.

e. To request to resume research activities following a suspension initiated by an investigator, sponsor, or regulatory authority, the investigator must make this request in writing and explain how the issues leading to the suspension were resolved. Any revisions to previously reviewed materials must be submitted.

f. The convened IRB must review any revised materials resulting from the suspension and may allow the study to return to active status if the reason for suspension was satisfactorily addressed, the study again meets criteria for approval, and all modifications to study materials were approved. If in the judgment of the IRB concerns remain about risks to subjects or others or about non-compliance, procedures for further suspension or termination of IRB approval may be followed.

3. Administrative Holds of Research Activities

a. The IRB Chair or designee may place some or all research activities on administrative hold because of a lapse in approval, non-compliance with requirements for human subjects training or financial disclosure, or other administrative reason that does not immediately place subjects or others at risk of harm or compromise the scientific integrity of the study.

b. The IRB Chair or designee may allow the study to return to active status after an administrative hold if the issues leading to the administrative hold have been satisfactorily addressed.

ROLES/REPONSIBILITIES

POLICY TITLE: Terminations and Suspensions of IRB Approval and Administrative Holds of Research Conduct
Policy No. 701

The IRB shall be responsible to determine when approval of a research study should be temporarily suspended or terminated at a convened meeting.

The IRB Chair or Vice Chair shall be responsible to determine when approval of a research study should be temporarily suspended or terminated when in their judgment taking such action cannot wait until a convened meeting.

The IRB shall be responsible to notify the PI immediately of this action as well as the organization official.

The PI shall be responsible to notify subjects and the sponsor (if applicable).

DEFINITIONS

Suspension of research: A temporary halt to some or all research procedures until the IRB determines whether the research may recommence (with or without modifications to the research) or whether the research must be terminated.

Termination: A permanent stop to the research and all research-related activities.

Administrative hold: An action by the IRB to temporarily stop some or all approved research activities when the investigator(s) has/have not met requirements of the HRPP. Administrative holds are not suspensions or terminations.

REFERENCE DOCUMENTS

Guidance for Industry: E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1), March 2018, Section 4.12

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATIONS

21 CFR § 56.108(b)(3) and 21 CFR § 56.113
45 CFR § 46.108(a)(4)(ii) and 45 CFR § 46.113
AAHRPP Standards II.2.H and III.2.D

Penn Medicine
Lancaster General Hospital

POLICY TITLE: **Reporting and Review of Allegations of Non-Compliance with the Human Research Protection Program** **Policy No. 702**	
Policy Author: Jonathan B. Derr, MS, MBA	**Last Review/Revision Date: 01/01/15, 02/04/16, 11/16/17, 10/15/2018, 10/06/22**
Policy Owner: Edmond K. Kabagambe, DVM, MS, PhD, MBA	

POLICY PURPOSE: This Policy establishes a mechanism for individuals engaged in human subject research conducted at Lancaster General Health (LG Health) or overseen by the Lancaster General Hospital (LGH) Institutional Review Board (IRB) to report circumstances that may constitute non-compliance with the LG Health Human Research Protection Program (HRPP). This Policy further describes how allegations of non-compliance with the HRPP will be reviewed.

APPLICABILITY/SCOPE/EXCLUSIONS: This Policy applies to all individuals engaged in human subject research at LG Health.

POLICY STATEMENTS: Any individual engaged in human subject research conducted at LG Health or overseen by the LGH IRB shall immediately report any circumstance or occurrence that may constitute non-compliance with the LG Health HRPP. The IRB and HRPP shall review all alleged occurrences of non-compliance.

PROCEDURES

1. **Reporting Non-Compliance with the HRPP.** When any individual becomes aware of an occurrence that may constitute non-compliance with the HRPP, that individual must immediately contact the IRB Chair and the IRB Office. The IRB Chair will promptly review the occurrence, or delegate the review to a member of the HRPP Leadership or to the Research Quality Assurance Office (RQAO). The IRB will determine if non-compliance has occurred when reviewing complaints, protocol deviations, unanticipated problems and audit outcomes.

2. **Reporting Apparent IRB Non-Compliance**
When there has been apparent serious or continuing noncompliance on the part of the IRB (e.g., repeated failure to make a required determination), the HRPP Director will gather the relevant facts and report the matter, with any recommendations, to the Institutional Official (IO). The IO may take actions as needed to further investigate the matter (e.g., a directed audit) prior to determining whether the apparent noncompliance is serious or continuing. The IO may also require corrective and preventive actions as warranted to remedy the matter and prevent recurrence. Serious or continuing noncompliance on the part of the IRB will be reported as necessary following the procedures outlined in Section 4.

3. **Review of Occurrences of Non-Compliance with the HRPP**

   a. The IRB Chair or delegate will review the occurrence to determine if the allegation of non-compliance has a basis in fact. The IRB Chair or delegate may seek additional information from any individual to assist in determining whether the allegation of non-compliance has a basis in fact. If the IRB Chair or delegate determines that the allegation has no basis in fact, no further action is necessary. If the IRB Chair or delegate determines that the allegation has a basis in fact, or cannot determine if there is a basis in fact, the IRB Chair or delegate will report this finding to the HRPP Leadership, and the HRPP Leadership will conduct, or appoint an ad-hoc committee to conduct, an investigation. If the IRB Chair

or delegate determines that the allegation requires inquiry for research misconduct, the inquiry will be referred to the Compliance Officer and will proceed according to the Research Misconduct Policy.

b. An investigation of an allegation of non-compliance by the HRPP Leadership or appointed committee shall be completed as soon as possible and within a maximum of thirty (30) days. In conducting its investigation, the HRPP or appointed committee shall have access to and review any and all documentation necessary to fully evaluate the allegation. The HRPP or appointed committee may also conduct interviews of involved parties.

c. After completing an investigation, the HRPP or appointed committee will determine if the incident of non-compliance was serious or continuing and recommend to the IRB restrictions, conditions, education, or other remedial actions to resolve the non-compliance. If the non-compliance was found to be serious or continuing, the incident will be presented to the convened IRB for concurrence with the determination and for approval of any actions to be taken. If the non-compliance was not found to be serious or continuing, an expedited reviewer may review the findings and approve actions to be required. The IRB will notify all affected parties, including an investigator, of the findings and of its decisions regarding what actions are required to remedy the non-compliance. Possible actions the full board may take to resolve an incident of serious non-compliance include, but are not limited to:

i. Suspension of IRB approval;
ii. Termination of IRB approval;
iii. Notification of current research subject when such information might relate to a subject's willingness to continue to take part in the research;
iv. Modification of a protocol;
v. Modification of the information disclosed during the informed consent process;
vi. Providing additional information to past research subjects;
vii. Require current research subjects to re-consent;
viii. Modification of the continuing review schedule;
ix. Monitoring the research;
x. Monitoring the informed consent process; or
xi. Referral to other LG Health entities or committees.

Similarly, an expedited reviewer of an incident determined not to be serious or continuing may take the above actions, but with the exclusion of suspension or termination of IRB approval, to resolve the incident.

4. **Reporting of Findings.** Following HRPP investigation, any finding of serious or continuing non-compliance in research overseen by the IRB must be reported to the LG Health Institutional Official. Any finding of serious or continuing non-compliance in research conducted at LG Health also must be reported to the President of LG Health.

An incident of non-compliance in research overseen by the IRB will be reported to applicable regulatory agencies, including the Office for Human Research Protections (OHRP) for federally sponsored studies and the Food and Drug Administration (FDA) for studies under its jurisdiction, as follows:

a. The Institutional Official or designee is responsible for preparing reports in accordance with the instructions of the Federal department or agency (e.g., OHRP, FDA).

b. The IRB Chair will review the report and recommend modifications as needed.

c. The Institutional Official is the signatory for all correspondence from LG Health.

d. The Institutional Official sends a copy of the report to:

1. The IRB by including the report in the next agenda packet as an information item.

2. The following federal agencies:

- OHRP, if the research is conducted or supported by the Department of Health and Human Services (DHHS), or if an engaged institution's FWA has been voluntarily extended to all non-exempt human subjects research
- FDA, if the study is subject to FDA regulations
- If the research is conducted or supported by a Common Rule department or agency other than DHHS, the report is sent to the party identified by the department or agency. A list of contacts is available on OHRP's Reporting Incidents webpage.
- If the study is conducted or supported by a federal department or agency that has not adopted the Common Rule, and reporting is required, the report is sent to the party identified by the department or agency.

Note: Reports are not submitted to federal departments or agencies, such as OHRP or FDA, unless the research is subject to federal regulations or another mandate that necessitates such reporting.

3. The investigator.

4. Sponsor, if the study is sponsored.

5. The Privacy Officer of LG Health, if the event involved unauthorized use, loss, or disclosure of individually-identifiable patient information from LG Health.

6. The Privacy Officer of LG Health if the event involved violations of information security requirements of LG Health.

7. LG Health Legal Services and Risk Management, if appropriate.

8. Others as deemed appropriate by the Institutional Official.

The Institutional Official ensures that all steps of this Policy are completed within thirty (30) working days of the determination. For more serious actions, the Institutional Official will expedite reporting. If additional time is needed to gather facts, or determine corrective actions, a preliminary report will be submitted within 30 days, to be followed by a final report as described above.

5. Reporting to AAHRPP

LG Health's HRPP is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). In addition to the information that LGH routinely provides to AAHRPP in annual reports and the re-accreditation application, AAHRPP requires that any of the following are reported to AAHRPP as soon as possible, generally within 48 hours after the organization or any researcher (if the researcher is notified rather than the organization) becomes aware:

- Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions Placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections;
- Any litigation, arbitration, or settlements initiated related to human research protections; and/or
- Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding LG Health's HRPP.

The Institutional Official or their designee is responsible for ensuring that such reports are made to AAHRPP and for informing appropriate organizational officials. Investigators, research staff, HRPP/IRB staff, IRB members, and other organizational officials or offices (e.g., Compliance, Legal, etc.) are responsible for informing the HRPP/IRB office as soon as they become aware of any of the above so that these reporting obligations may be fulfilled.

ROLES/REPONSIBILITIES

It is the responsibility of all persons engaged in human subjects' research overseen by the LGH IRB to report circumstances that may constitute non-compliance with the LG Health HRPP.

DEFINITIONS

Non-Compliance: Failure to comply with any law, regulation, ethical standard, accreditation standard, HRPP policy or procedure, IRB policy or procedure, or IRB determination. Non-compliance may be minor or sporadic or may be serious or continuing. Protocol deviations may be considered non-compliance if they represent a continuing lack of research rigor that compromises the scientific validity of a study and thereby alters its risk-benefit ratio.

Continuing Non-Compliance: A pattern of non-compliance which, in the opinion of the IRB, demonstrates a likelihood that non-compliance will continue to occur absent intervention.

Serious Non-Compliance: Non-compliance which, in the opinion of the IRB, increases risks to research subjects or compromises the integrity of the LG Health HRPP.

REFERENCE DOCUMENTS

REGULATORY/ACCREDITATION/INDUSTRY STANDARD CITATION(S)

AAHRPP Standards I.5.D and III.2.D