University of Pikeville

The University of Pikeville Policies and Procedures on Research with Human Subjects

Office of the Vice President for Health Affairs
Office of Vice President for Academic Affairs
Institutional Review Board

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I. Introduction to the Manual

The University of Pikeville is committed to the pursuit of excellence in teaching, research and community service. In keeping with this mission, the University encourages research in all disciplines including research that addresses human social issues and human needs. In doing so, the University of Pikeville requires that researchers respect and protect the rights, privacy, and welfare of individuals recruited for and participating in research. All members of the University of Pikeville community share in the collective responsibility for the protection of human research participants and, more broadly, for the ethical conduct of research. This collaboration must operate in a culture of trust, mutual assurance, and integrity by upholding the highest ethical principles in the conduct of research and the pursuit of knowledge. The University will not approve or accept any activities that violate human rights, demean human dignity, or operate according to principles that directly opposed those for which the University must stand.

The University of Pikeville's policies and procedures regarding research with human subjects are designed to protect individuals from harm, provide equitable selection of subjects, maximize benefits and minimize the risks of research participation. *The University of Pikeville Policies and Procedures on Research with Human Subjects* serves as the official policy manual and reference guide for the University of Pikeville Institutional Review Board (IRB) and researchers. The manual details the policies, procedures, regulations, and protocol submission requirements governing human subjects research at the University of Pikeville.

II. Ethical and Regulatory Foundations

A. Ethical Foundation for Human Subject Protections

The University of Pikeville is committed to ensuring that all research involving human subjects or human material in which it is engaged is conducted in accordance with the ethical principles stated in the Belmont Report.
http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html
The Belmont Report, published in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, provides the ethical foundation for the federal regulations for the protection of human research subjects. Three fundamental principles are articulated:

1. Respect for Persons

Individuals should be treated as autonomous agents with the right to make decisions for themselves. Those with diminished autonomy (e.g. minors, prisoners, persons who are mentally disabled) are entitled to additional protections. Application of this principle requires that human subjects are enrolled into research studies only under the conditions of effective informed consent. This involves a process in which participation in the research is acknowledged by the research subject (or by a legally authorized representative) as a voluntary act free from coercion or undue influence from the investigator or members of the research team. Exceptions to this informed consent requirement must be outlined in the federal regulations and subsequently approved by the University of Pikeville IRB.

2. Beneficence

The research study must be designed and implemented so as to maximize possible benefits and minimize possible harms. Application of this principle involves a

risk/benefit analysis in which the risks to subjects must be reasonable compared to the potential for benefit either to subjects directly or to society. Risk evaluation must include the consideration of both the probability and magnitude of harm, including psychological, physical, legal, social, and economic harm.

3. Justice

The possibility for benefits and the potential burdens of the research should be equitably distributed among the potential research subjects. Application of this principle requires the close scrutiny of the enrollment process to ensure that particular classes (welfare patients, racial and ethnic minorities, or persons confined to institutions) are not selected for their compromised position or convenience to the research investigator, or are systematically excluded.

B. Regulatory Mandates

The IRB adheres to the following regulations and policies for human subject research activities that fall under its authority:

1. The Federal Policy regulations for the protection of human research subjects (45 CFR Part 46; "Common Rule") (http://www.hhs.gov/ohrp/humansubjects/commonrule/index.html).
2. When research involves articles subject to regulation by the FDA, the FDA regulations for the protection of human subjects (21 CFR Parts 50) (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50)and Institutional Review Boards (21 CFR Parts 56) (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56).
3. Where applicable, other federal, state and local regulations regarding research involving human subjects.
4. When making determinations concerning the rights and welfare of human subjects participating in research studies, the IRB will also refer to current versions of the Office of Human Research Protections (OHRP) *Protecting Human Research Subjects, Institutional Review Board Guidebook;* the *FDA's Information Sheets for IRBs and Clinical Investigators;* and to other interpretative directives, information documents and guidance materials disseminated by OHRP, DHHS, the National Institutes of Health (NIH) the FDA and other federal agencies (e.g., Office of Civil Rights).

III. Purpose of the IRB

The primary purpose of the IRB is to protect the rights and welfare of human subjects involved in research activities being conducted by faculty, students and staff of the University of Pikeville or anyone under its authority. In so doing, the IRB shall ensure adherence to the criteria for IRB approval as listed in 45 CFR 46.111 and 21CFR 56.111 i.e., that:

A. The risks to human research subjects are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose the research participants to risk, and whenever appropriate, by using procedures already being performed on subjects for diagnosis or treatment purposes.

B. The risks to human research subjects are reasonable in relation to the anticipated benefits (if any) to the individual, and the importance of the knowledge that may be expected to result.

1. For the purpose of IRB consideration, "benefit" is defined as a valued or desired outcome; an advantage.

2. For the purpose of IRB consideration, "risk" is defined as the probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. In evaluating risk, the IRB is to consider the conditions that make the situation dangerous, per se (i.e., as opposed to those chances that specific individuals are willing to undertake for some desired goals).
3. In evaluating risks and benefits, the IRB considers only those risks and benefits that may result from the research (i.e., as distinguished from risks and benefits of treatments or procedures that the patient would undergo if not participating in the research).
4. In evaluating risks and benefits, the IRB does not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of research on public policy).

C. The selection of human subjects for research participation is equitable.

D. Human research subjects are adequately informed of the risks and benefits of research participation and the procedures that will be involved in the research, and that informed consent is obtained from each prospective human research subject, or his/her legally authorized representative, in accordance with, and to the extent required by federal regulations and IRB policies.

E. Informed consent of human research subjects is obtained in advance of research participation and appropriately documented in accordance with, and to the extent required by federal regulations and IRB policies.

F. The research plan, when appropriate, makes adequate provisions for monitoring the data collected to ensure the safety of human research subjects.

G. There are adequate provisions to protect the privacy of human research subjects and to maintain the confidentiality of research data.

H. Appropriate additional safeguards have been included in the study to protect the rights and welfare of human research subjects who are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, decisionally impaired persons, or economically or educationally disadvantaged persons).

I. As a secondary purpose, the IRB must seek to ensure that the University, affiliate institutions, and the investigators that it serves are compliant with the ethical standards and regulations governing human subject research. The IRB serves to assist investigators in the design of ethical and regulatory compliant human subject research studies.

IV. Institutional Authority under which the IRB is Established and Empowered

A. The University of Pikeville

The President of University of Pikeville and the Board of Trustees of the University of Pikeville, has delegated authority (through the Vice President for Health Affairs and the Vice President for Academic Affairs), to the University of Pikeville Institutional Review Board (IRB) to:

1. Review any and all activities to determine if they constitute human research.
2. Require and review applications necessary to engage in human research.
3. Conduct initial and periodical reviews to approve, require modifications (to secure approval) or disapprove all research activities involving human subjects, whether at the University of Pikeville facilities, or not, as long as University of Pikeville faculty, staff, or students are involved in carrying out the research. The approval of

research by the IRB of another institution does not guarantee approval by the IRB of the University of Pikeville.

V. The Authority of the IRB

A. The IRB shall review and have the authority to approve, require modifications (to secure approval), or disapprove all research activities involving human subjects that fall under its authority, including research that qualifies for "exempt" status under the provisions of 45 CFR 46. Furthermore, the IRB shall have the ability to review any activity involving human subjects and the faculty, staff or students of the University to determine if that activity constitutes research. If the IRB determines the activity constitutes research, then the IRB has full authority over such research.

B. The IRB shall have the authority to determine that a project submitted by an investigator does not meet the regulatory definition of human subject research under 45 CFR 46.102(f) and 21 CFR 56.102(f).

C. The IRB shall have the authority to require progress reports from investigators and to conduct continuing reviews of approved human subject research studies at intervals appropriate to the degree of risk. Research studies qualifying for "exempt" status in accordance with 45 CFR 46.101(b) will not be subject to continuing review.

D. The IRB shall have the authority to approve prospectively all modifications to previously approved research protocols and/or informed consent documents, the only exception being a protocol deviation that may be necessary to eliminate an apparent immediate hazard to a given research subject. All such emergency deviations shall be documented in detail and presented to the IRB within 3 business days.

E. The IRB shall have the authority to observe or have a third party observe the conduct of approved human subject research studies, including the informed consent process.

F. The IRB shall have the authority to suspend and/or terminate the approval of, human subject research activities that are not being conducted in accordance with the IRB's requirements or have been associated with unexpected serious harm to subjects.

G. Stating that which is implicit in the above authorities, the IRB shall have the authority to place restrictions on human subject research activities in order to protect the rights and welfare of the subjects.

VI. Management of the IRB

A. Institutional Official

The President and the Board of Trustees of the University of Pikeville have delegated authority and responsibility for the University's IRB to the Vice President for Health Affairs and the Vice President for Academic Affairs, who shall install and empower the IRB for the University of Pikeville. The IRB shall be managed as determined by the Vice President for Health Affairs and the Vice President for Academic Affairs. Management on a day-to-day basis shall be carried out under the direction of the IRB Chair and administrative staff operating under broad delegated authority from the Vice President for Health Affairs and the Vice President for Academic Affairs. The Vice President for Health Affairs and the Vice President for Academic Affairs shall ensure that adequate facilities, equipment, and resources are available to support the IRB-related activities and staff. The Vice President for Health Affairs and the Vice President for Academic Affairs shall also be responsible for

approving organizational relationships with other institutions or sites (e.g., hospitals) wherein the human subject research activities of University faculty, students or staff may or will be conducted. The IRB reports to the Vice President for Health Affairs and the Vice President for Academic Affairs through the IRB Chair.

VII. IRB Membership

A. Appointment of IRB Members

Appointments of voting IRB members are made by the Vice President for Health Affairs and the Vice President for Academic Affairs.

1. The Vice President for Health Affairs and the Vice President for Academic Affairs or a designee may request recommendations for faculty volunteers from the academic department chairs as needed, based on considerations including, but not limited to, required committee composition, expertise and experience; knowledge of the individual's interest; recommendations of institutional leadership; and/or investigators involved in research studies currently or previously approved by the IRB.
2. The Vice President for Health Affairs and the Vice President for Academic Affairs shall also appoint non-scientific and/or non-affiliated members to the IRB based on considerations including, but not limited to, required committee composition, expertise and experience; knowledge of the individual's interest; recommendations of current or past non-scientific and/or nonaffiliated members. Non-affiliate members shall not be immediate Family members of University of Pikeville affiliated personnel.
3. The Vice President for Health Affairs and the Vice President for Academic Affairs or a designee will review each new member's educational background, work history, as well as his/her current vocation to determine the member's status on the IRB (i.e., scientific versus non-scientific, affiliated vs. non-affiliated) on the IRB rosters.
4. The term of service on the IRB shall be 3 years. However, roughly half of the first appointed IRB members shall be given a 5 year term of service. Each appointed member shall only be able to serve two consecutive terms before sitting out for at least one year.

B. Composition of IRB

1. Each IRB Committee will be comprised of at least five members, and contain at least one faculty member from each academic division of the university -including a member from the basic sciences division and clinical sciences division of the KYCOM, and one community leader.
2. The membership of the IRB will be sufficiently qualified through the experience and expertise of its members to promote respect for its advice and counsel in safeguarding the rights and welfare of human research subjects.
3. The IRB should include a person able to ascertain the acceptability of the proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.
4. The IRB should include a fair mix of gender, race, profession, and area of expertise such as is available to serve.

5. The IRB will include at least one member whose background is primarily related to the biomedical sciences, at least one member whose background is primarily related to the psychosocial sciences, and at least one member whose concerns are of a nonscientific nature (i.e., "non-scientific member"), and one member from the community as a liaison to the wishes and thoughts of the community. The community representative shall be a leader in the community, which shall be determined by the Vice President for Health Affairs and the Vice President for Academic Affairs and shall be broadly construed. The community representative shall have expenses of attending meetings covered, but otherwise shall be a volunteer to ensure an unbiased opinion. Expenses shall include travel and lodging if necessary; further, it shall include investigatory activities if the community representative requests prior approval of the IRB to investigate public feeling on a matter.

C. Election of the IRB Chair

The members of the IRB shall elect a Chair and Vice-Chair from a pool of volunteers. The terms of appointment of the IRB Chair, and IRB Vice-Chair shall be three years.

D. Responsibilities of the IRB Chair

The IRB Chair shall hold leadership responsibility for IRB review and approval of human subject research in accordance with current guidelines, institutional policies, and federal and state regulations governing human subject protections. (Please refer to the research check list provided by the IRB to help determine if activity of faculty, staff, or students is "human subject research" falling under IRB purview.) All research investigators involved in the conduct of human subject research that falls under the authority of the IRB shall take direction in this regard from the IRB Chair. In addition, the IRB Chair shall:

1. Oversee the development and implementation of appropriate policies, procedures and guidelines directed at human subject protections and the functions and activities of the IRB. The IRB Chair is responsible for reviewing the IRB's policies and procedures for currency, accuracy and consistency on an ongoing basis but not less than every three years. Ad hoc committees will be formed to review guidance issued by regulatory agencies to determine whether updated to the policies and procedures are required.
2. Communicate IRB decisions, directives, and sanctions relating to known or suspected problems in the conduct of human subject research to involved investigators.
3. Have authority to request audits of human subject research activities.
4. Have the authority to suspend some or all research activities if human subject safety issues are identified. Note: this authority is only exercised if an action is required prior to a convened meeting and it is not feasible to assemble an emergency meeting. When this authority is exercised, it shall be reported at the next convened University IRB meeting.
5. Represent the IRB in interactions related to issues surrounding the ethical and regulation-compliant conduct of human subject research, such as interactions involving:
    a. Other University or hospital committees and offices involved in the oversight of human research studies.
    b. Applicable federal and state regulatory agencies.
6. Approve written correspondence to state and federal regulatory agencies having jurisdiction over human subject research prior to final approval and signature of the appropriate institutional official.

7. Represent the IRB at national and local meetings related to institutional review board activities and human subject protections.

E. Responsibilities of the IRB Vice-Chair

The primary responsibility of the IRB Vice-Chair is to conduct the business of the IRB Chair when the Chair is not available. Therefore the Vice-Chair shall receive the same training as the Chair and shall have the same authority as the Chair in the Chair's absence.

F. Evaluation of IRB Leadership

1. Chair

The IRB Chair shall be evaluated on an annual basis by the Vice President for Health Affairs and the Vice President for Academic Affairs. The basis for this evaluation shall include, but not be limited to, the Chair's knowledge and consistent application of the ethical principles of the Belmont Report and the federal regulations and IRB policies governing human subject protections; the Chair's responsiveness to the concerns of IRB committee members; the Chair's ability to interact constructively with and to manage the activities of the IRB Vice-Chair; the Chair's ability to manage the efficient and effective conduct of IRB committee meetings; and the Chair's ability to interact with and achieve the respect of human subject investigators.

2. Vice-Chair

The IRB Vice-Chair shall be evaluated on an annual basis by the IRB Chair. The basis for this evaluation shall include, but not be limited to, the Vice-Chair's knowledge and consistent application of the ethical principles of the Belmont Report and the federal regulations and IRB policies governing human subject protections; the Vice-Chair's responsiveness to the concerns of IRB Committee members; the Vice-Chair's ability to manage the efficient and effective conduct of IRB Committee meetings and post meeting activities; and the Vice-Chair's ability to interact with and achieve the respect of human subject investigators.

3. IRB Support Staff

The IRB support staff will be evaluated per polices of the University of Pikeville Department of Human Resources.

G. Compensation of the IRB Leadership

The IRB Chair and IRB Vice-Chair shall be compensated for their IRB duties and responsibilities. The rate of compensation shall be at the discretion of the University of Pikeville Department of Human Resources and shall take into account the professional background of the individual and the expected time commitment of the appointed position to IRB activities.

H. Indemnification

The University of Pikeville Policy sets forth the conditions under which indemnification and legal defense shall be available to faculty and staff. Indemnification shall be afforded to the IRB Chair, IRB Vice-Chair, and IRB staff as set forth in that policy.

I. Termination of IRB Chair and Vice-Chair

1. Once elected by the IRB at large, only the Vice President for Health Affairs and the Vice President for Academic Affairs have the authority to terminate the term of the IRB Chair and IRB Vice-Chair.
2. Termination (i.e., by the Vice President for Health Affairs and the Vice President for Academic Affairs) or resignation of appointment by the IRB Chair and IRB Vice-Chairs

shall be subject to a minimum of 3 months advanced notice unless extenuating circumstances exist.

VIII. IRB Committee

The IRB shall function under the Robert's Rules of Order unless otherwise described in this document. If Robert's Rules of Order differ from this document then procedures outlined in this document shall be followed.

A. Subcommittees and Task Forces

The IRB, IRB Chair, or an IRB Committee may form subcommittees/task forces on an ad hoc basis to address various specific issues related to the use of human subjects in research and human subject protections, including, but not limited to: psychosocial impact, community perception, regulation interpretation, etc.

B. Consultants

1. At any time during the review of a proposed research study, the IRB may determine that the current membership of the IRB does not include appropriate expertise to conduct an adequate study evaluation and may enlist consultants. The IRB Chair, Vice President for Health Affairs and the Vice President for Academic Affairs shall determine compensation and contract with consultants.
2. Consultants shall be provided with whatever documentation is necessary to render expert aid to the Committee, including a copy of the IRB protocol and consent documents, as well as any attachments (investigator brochures, multicenter protocols, etc.) if necessary, prior to the IRB meeting.
3. Consultants are held to the same standards as members of the IRB Committee.
4. Consultants may attend the meeting to participate in the review and discussion of the research study; however, s/he may not vote or count towards quorum.
5. If the consultant is unable to attend the meeting, his/her written comments will be taken into consideration by the Committee during its review of the respective research protocol and will be documented in the IRB meeting minutes.

C. Term of Service:

1. Committee members are initially appointed to a term of three years.
2. Committee members may be requested to accept reappointment to the IRB for an additional term of three years.
3. At the end of a six-year term, members will be asked to rotate off the IRB for a minimum of 1 year.

D. Compensation of IRB Members

1. Affiliated IRB members do not receive any direct monetary compensation for participation on the Board.
2. Unaffiliated IRB Committee members will be reimbursed for actual expenses of attending meetings. Proper documentation required.

E. Indemnification

The University of Pikeville shall provide IRB members and hired consultants indemnification from lawsuit arising from the decisions of the IRB in so far as there is no gross negligence or malice on the part of the IRB or members thereof, pursuant to University of Pikeville policies.

H. Responsibilities of IRB Members

General Responsibilities of all IRB Members include:

1. Reviewing any research conducted by University of Pikeville faculty, staff , or students to determine if it constitutes human subject research under 45 CFR 46.111, 21 CFR 56.111 (if applicable), and any other relevant regulation. This review is independent and takes precedent over determinations by deans, department heads, and researchers.
2. Reviewing research study proposals and evaluating them from the perspective of the regulatory criteria for approval addressed under 45 CFR 46.111, 21 CFR 56.111 (if applicable), and any other relevant ethical, scientific, or compliance considerations.
3. Reviewing informed consent documents and evaluating them from the perspective of addressing the required and additional elements of informed consent addressed under 45 CFR 46.116, 21 CFR 50.20 (if applicable), and any other relevant ethical or compliance considerations.
4. Attending IRB meetings in person, unless exigent circumstances prevent such attendance on an occasional basis; reporting promptly at the designated time that the meeting convenes; and remaining in attendance at the meeting until the full agenda has been addressed.
5. Participating in IRB deliberations concerning issues inherent to proposed research studies and related informed consent documents; and making recommendations for reducing risk and improving the informed consent process, and anything else that might improving human subject protections.
6. Voting for full approval, approval subject to modification(s), reconsideration, or disapproval of the human subject research as outlined in Section XII.L.8.
7. Evaluating the risk level (i.e., minimal or greater than minimal) of the proposed research. In performing this evaluation, IRB members shall use the following absolute definition for "minimal risk" at 45 CFR 46.102(i).

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life (i.e., of the general population) or during the performance of routine physical or psychological examinations or tests.

8. Deciding, for research studies of greater than minimal risk if:
    a. Complexity, conflict-of-interest concerns, vulnerable populations, or if the informed consent process and/or other aspects of the research study should be audited by internal or external entities for content and compliance.
    b. Review is warranted on a more frequent basis than the requisite annual review.
9. Deciding, for research studies involving an experimental device or treatment not yet approved by an appropriate regulatory agency, if the device or treatment and its proposed use constitute a non-significant or significant risk to research subjects.
10. Deciding, for research studies subject to IRB continuation approval, if verification is required from sources other than the investigator that no material changes have occurred since previous IRB review.
11. Recommending improvements to IRB policies and procedures so as to enhance the IRB review process and/or human subject protections.
12. Informing the IRB Chair or an IRB Vice-Chair of human subject research noncompliance problems or ethical issues of which they become aware.
13. Conforming, at all times, their behavior to be within legal and ethical principles accepted by the IRB; including, but not limited to, maintaining

confidentiality/nondisclosure of human subject research submitted for IRB review and approval, and good faith participation in IRB deliberations without discrimination, conflict-of-interest, or the appearance thereof.

14. Recusal from voting when an actual or perceived conflict of interest exists.

I. Responsibilities of Designated Reviewers

In addition to the responsibilities outlined above, responsibilities of those assigned as reviewers include:

1. Providing written evaluations of the research protocol and informed consent document(s) to the IRB in advance of the IRB meeting.
2. Completing the IRB Reviewer Checklist and providing it to the IRB.
3. Basing their review and approval decisions on all available information and not just the IRB research application.

J. IRB Roster

1. The IRB membership roster will include the following information:

a. Names of members.
b. Earned degrees.
c. Representative capacities.
d. Scientific/nonscientific status.
e. Affiliation status (whether the IRB member or an immediate family member of the IRB member is affiliated with the organization).
f. Indications of experience sufficient to describe each IRB member's chief anticipated contributions.
g. Employment or other relationship between each IRB member and the organization.

2. Maintenance of the IRB Roster

a. The Chair is responsible for submitting an updated membership roster before each meeting.
b. The IRB Membership Rosters should be publicly posted (For example, on the University of Pikeville website).

K. Evaluation of Committee Members

The IRB Chair and Vice-Chair shall evaluate the performance of the IRB membership. Specifically, the Chair will evaluate the performance of board members with respect to their awareness and understanding of relevant ethical issues, regulations, and institutional policies. If concerns are identified, the IRB Chair and/or Vice-Chair will address these with the individual committee member and then provide necessary guidance materials or educational sessions. Attendance of the IRB members at meetings will be monitored. Any issues that arise related to nonattendance will be brought to the attention of the IRB Chair to determine whether action is necessary.

L. Resignation and Termination of IRB Members

1. Resignation of IRB membership status, based on the wishes of the IRB member, shall be submitted, in writing, to the Vice President for Health Affairs, the Vice President for Academic Affairs, the IRB Chair, and the member's department chair.
2. IRB membership status may be terminated by the Vice President for Health Affairs and the Vice President for Academic Affairs independently or upon recommendation of the IRB Chair. Termination must be justified in writing.

Sufficient justifications include, but are not limited to, failure to attend and/or otherwise actively participate in IRB functions.

IX. General Procedures for All IRB Submissions

Investigators involved in the conduct of human subject research that falls under the authority of the IRB shall be provided with instructions and guidelines for the submission of research studies and informed consent documents for IRB review and approval. The following are general procedures for the IRB in processing all IRB submissions.

A. Assignment of IRB Number

1. New Protocols

All new protocols are required to be submitted electronically as MS word or PDF files. IRB numbers are assigned by the system with the prefix "PROTOCOL." The number assigned reflects the year and month of submission with consecutive numbers thereafter (e.g., PROTOCOL-12/09-0003 would mean the protocol was submitted in December of 2009 and was the 3rd protocol submitted in the year).

2. Renewals

Renewals will retain the number originally assigned with the addition of REN followed by a four digit suffix to indicate the most recent date (Month/Year) of IRB continuation approval (eg. PROTOCOL 12/09-003 REN 12/11).

3. Modifications

Modifications will be assigned the same IRB number as the original study but with the prefix "MOD" (eg. MOD 12/09-0003). If modified more than once, a suffix will be assigned to the modifications to indicate the sequential number of the modification (MOD 12/00-0003-01).

B. Initial Screening

1. All research involving human subject or human materials requires an initial screening by the IRB Chair to determine the level of review necessary (Exempt, Expedited, or Full) and therefore, the proper procedure and forms to be filled out by the Principal Investigator (PI).
2. Once the PI has completed the proper procedure and forms, the PI will submit it to the IRB where it will be reviewed for completeness, before being considered on its merits. Incomplete submissions will be returned to the PI for correction.
3. Once all required elements are present, the study will be considered on its merits by the IRB.

C. Conflict of Interest

For research studies submitted for initial and continuing IRB review and approval, the IRB will verify signed Conflict of Interest (COI) statements for accuracy and completeness. In the event of a discrepancy, the IRB Chair/Vice-Chair shall be notified. All proposed human subject research in which a listed investigator has a significant financial conflict of interest shall be submitted for review by the IRB, the Vice President for Health Affairs, and the Vice President for Academic Affairs.

D. Verification of Training Requirements

1. Basic Training Modules

In order to submit human research protocols to the IRB, a PI and research coordinator(s) must have completed the IRB recommended educational training. PIs and other members of the research team will be told what educational modules they need to complete during the initial screening process.

On-line training modules will be made available. Persons without University of Pikeville Information Technologies (IT) access must contact the IRB to obtain these educational materials.

E. Calculation of Initial Approval Date

The IRB shall calculate the date of initial IRB approval in the following manner:

1. When a research study is approved at a convened meeting, the date of the convened meeting shall be the date of IRB approval.
2. When the research study is approved subject to modifications at a convened meeting, the date of IRB approval shall be the date that the requested changes are verified by the Chair, Vice-Chair, or his/her designee.
3. When a research study is reviewed and approved through an expedited review process, the date that approval is extended by the Chair, Vice-Chair, or his/her designee shall be the date of IRB approval.

F. Calculation of Expiration Date

The IRB shall calculate the date of expiration in the following manner:

1. When a research study is fully approved, the date of expiration shall be the date of the approval minus one day. For example, if the committee meeting date is 10/17/06, then the date of IRB expiration is 10/16/07 for an annual approval.

G. Investigator Communications

The PI shall be notified, in writing, of the IRB's decision to approve, reconsider, or disapprove the proposed research, or of the modifications required to secure IRB approval of the research study. Comments will be issued to investigators once either the minutes from the full board meeting have been accepted, or the comments have been finalized for expedited or exempt submissions. All correspondence to a PI will contain, at a minimum: the name of the PI the title of the project, the IRB number assigned to the submission.

1. **If the communication is a decision of the IRB on a protocol, decisions are limited to**:
   - **a. "Full" Approval**

     If a convened IRB determines that the study can be approved as submitted, the investigator will be issued a "Full" approval letter.
   - **b. "Approved Subject to Minor Modifications" (comments must be directive)**

     If the IRB decides to approve a research study subject to modifications, it shall include in its written notification the specific revisions stipulated by the IRB in order to obtain "Final" approval to conduct the research. The written notification shall instruct the investigators to revise the research and informed consent document(s) in accordance with the specific revisions stipulated by the IRB and to resubmit for final IRB approval.
   - **c. "Reconsideration"**

     If a convened IRB decides to reconsider a research activity, the written notification to the investigator shall include:

     i. A statement of the primary reason(s) for the IRB's decision to reconsider the research;

     ii. A listing of additional problems and/or deficiencies identified by the IRB;

iii. Instructions relating to resubmission of the research for full-board IRB review, including statements that the PI should address in writing the comments and concerns of the first IRB review and that s/he may appear in person to address additional questions or concerns related to full-board IRB review of the resubmitted protocol.

d. "Disapproval"

If a convened IRB decides to disapprove a research activity, the written notification to the investigator shall include a statement of the primary reason(s) for the IRB's decision to disapprove the research.

2. Investigator Responses

Responses of the PI shall be returned to the IRB reviewer who conducted the initial review (i.e., or to another IRB reviewer if the initial reviewer will be unavailable for an extended period) for final approval. In the event of a failure to resolve problems or concerns related to the investigator's response(s), the IRB submission (to include prior correspondence between the IRB reviewer and investigator) shall be reviewed at a convened meeting of an IRB committee (i.e., full-board IRB review).

3. Response Deadline

If a response by the PI is necessary, communication to the PI shall specify that s/he must respond to the comments or concerns of the IRB reviewer within 6 weeks of the date of the communication, and that failure to respond within this 6-week period will result in withdrawal of the project by the IRB.

4. Content of IRB Concurrence/Approval

If a protocol is approved, the PI shall be notified of IRB concurrence/approval through written correspondence prepared and discharged by the IRB Chair or designee. All correspondence shall contain:

a. The name of the PI.
b. The title of the project.
c. The IRB number assigned to the submission.
d. The name of the non-conflicted IRB Chair or Vice-Chair granting final concurrence/approval.
e. The date of IRB approval/concurrence.
f. The date of IRB expiration (for expedited and full board studies only).
g. The date of IRB modifications (for modification requests only).
h. A statement that modifications to the IRB approved research study will require either notification to the IRB (for "no human subjects research" or "exempt" determinations) or approval by the IRB (for "expedited" or "full-board" studies).
i. For studies that are designated as "**no human subject research**" the correspondence shall indicate a concurrence that the project does not meet either the definition of "research" at 45 CFR 46.102(d) or "clinical investigation" at 21 CFR 56.102(c); or the definition of "human subject" at 45 CFR 46.102(f) or 21 CFR 56.102(e).
j. For activities determined by the IRB Reviewer to meet either the DHHS or FDA definition of "human subject research," the PI shall be advised to submit the project for exempt, expedited or full-board IRB review as appropriate.
k. For studies that are designated as "**exempt**" the correspondence shall include the basis for granting exempt status [i.e., 45 CFR 46.101(b)(1-6) and/or 21 CFR

56.104(d)]. For research activities that involve human subjects but are determined to not qualify for exempt status, the PI shall be advised to submit the research for expedited or full-board IRB review as appropriate.

l. For studies that are approved as "**expedited**" the correspondence shall include the basis for granting expedited approval of the research (i.e., the minimal risk status of the research and the applicable category or categories of research activities listed in the OHRP and FDA document, "Categories of Research That May Be Reviewed by the Institutional Review Board [IRB] through an Expedited Review Procedure") shall be documented, with justification, within the IRB Research Protocol and/or review materials.

m. For studies submitted and approved as a "**full-board IRB review"** the correspondence shall include a statement that the study was approved after full-board IRB review and that the details of the meeting are available in the IRB file.

5. Lapses in IRB Approval

If a previously approved study is not renewed, reviewed, and reapproved by the IRB prior to the expiration date of the previous IRB approval, the PI will be required to cease all research activities described in the IRB protocol (including data analysis) until notification of final IRB approval for continuation of the research has been issued. In this circumstance, the PI shall be advised that, if it is felt that there is an overriding safety concern or ethical issue, s/he may petition the IRB Chair for permission to continue certain research activities that impact the rights and welfare of current research subjects. However, under no circumstances can new subjects be enrolled into a research study after expiration of IRB approval. If such a lapse occurs, the protocol will be fully reviewed by the entire IRB prior to a renewal decision.

X. Formal Determination that a Project is Either Not Research, or Does Not Involve Human Subjects or Material

Because investigators sometimes require a formal determination from the IRB that their project is either not research, or does not involve human subjects (e.g., dissertation committee requirements), investigators may ask the IRB to make the determination that a project does not involve human subjects. Such a determination is made by a formal communication from the IRB to the PI as above with the exception that the proposal is not issued an IRB number.

A. Criteria for Determination of "No Human Subject Research"

The IRB Reviewer can make the following determinations:

1. The activity does not meet either the definition of research as specified under 45 CFR 46.102 (d) or the definition of clinical investigation as specified in 21 CFR 56.102 (c).
2. The activity is research but does not involve human subjects 45 CFR 102 (f) or 21 CFR 56.102 (e).
3. In making this determination, the following are used as references:
    a. The IRB reviewer refers to the OHRP's decision Chart #1 "Is An Activity Research Involving Human Subjects?" (See chart at http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html).
    b. **FDA Regulations**
    The IRB reviewer refers to 21 CFR 50.1 (a) for a definition of the scope of clinical investigations regulated by the U.S. Food and Drug Administration.

Activities that meet any of the following criteria do not qualify for the "No Human Subject Research Designation."

i. Any use of a drug or medical device not approved by the FDA, regardless of the presence of an Investigational New Drug (IND) or Investigational Device Exception (IDE) designation.
ii. Any use of a drug in any manner (even if approved and even if used in an activity which does not meet the DHHS definition of research) other than the use of an FDA approved drug in the course of medical practice.
iii. Any use of a medical device in any manner (even if approved and even if used in an activity which does not meet the DHHS definition of research) other than the use of an FDA approved medical device in the course of medical practice.
iv. Any use of an FDA regulated item in which the data will be submitted to or held for inspection by FDA.

B. Determination that activity IS Human Subject Research

The IRB Reviewer may determine that the proposed activity is human subject research because it meets the DHHS definition of research (45 CFR 46.102(d)); and involves individuals who meet the definition of human subject (45 CFR 46.102(f); or meets the FDA definition of clinical investigation as described above (IX.C.2).

For activities determined by the IRB Reviewer to meet either the DHHS or FDA definition of "human subject research," the PI shall be advised to submit the research for exempt, expedited or full-board IRB review, as appropriate.

XI. Exempt Determinations

A. Provision of Review Materials

The IRB reviewers are expected to conduct an in-depth review of all materials. Therefore they must have access to the complete IRB submission including the following (as applicable):

1. Protocol application.
2. Recruitment materials (e.g., advertisements, flyers, phone screening procedures, scripts, and/or screening questions, etc.).
3. Measures that will be utilized in the study (e.g. survey instruments, questionnaires, interview scripts, recruitment material, etc.).
4. Grant application (if applicable).
5. Verification of approval from site(s) outside of the University of Pikeville.
6. Other materials specific to the proposed study.

B. Criteria for Exemption

The IRB reviewer determines if the proposed research is exempt from federal policies governing human subject protections. This determination is made in accordance with:

1. The OHRP Decision Chart # 2- "Is the Research Involving Human Subjects Eligible for Exemption under 45 CFR 46.101 (b)?"The criteria for exemption as specified under 45 CFR 46.101 (b)(1), (b)(2) and (b)(4) and 21 CFR 56.104(c) and (d). If an investigator wishes to request an exemption under 45 CFR 46.101(b)(3), (b)(5) or (b)(6), s/he is instructed to submit the initial IRB checklist Titled "**EXEMPT REVIEW CATEGORIES**" and contact the IRB Chair for guidance.

2. If subjects are under the age of 18 years, the exemption criteria described in 45 CFR 46.101(b)(2), are not applicable with the exception of research limited to (a) the use of educational tests or (b) to observations of public behavior when the investigator does not participate in the activities being observed. **NOTE: The exemption criteria in 45 CFR 46.101 (b) do not apply to studies involving prisoners. The exemption criteria [with the exception of** 45 CFR 46.101(b)(6) / **21 CFR 56.104(d)] do not apply to FDA-regulated research studies.**

C. Review of Grant Application

For Federally-supported research, the IRB reviewer will ensure that the research application is essentially consistent with the grant application.

1. Determination that Activity Meets the Exempt Criteria

The PI of the research activity will be notified of IRB determination if the proposed research is exempt through a standard correspondence. This notification letter shall specify, at a minimum:

a. The IRB number assigned to the submission.
b. The regulatory basis for granting exempt status [i.e., 45 CFR 46.101 (b) (1-6) and/or 21 CFR 56.104(d)].
c. That the IRB should be notified in advance of any proposed substantive modifications of the exempt research activity.

2. Determination that Activity Does NOT Meet the Exempt Criteria

For research activities that involve human subjects but are determined to not qualify for exempt status, the PI is advised to resubmit the research for expedited or full-board IRB review.

D. Special Considerations: Waiver of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Authorization and Exempt Review

The IRB may grant a waiver of HIPAA Authorization for an **exempt study** for the following: "recording of medical Information, without identifiers," by or under the oversight of a PI who would normally have access to this information by virtue of his/her patient care responsibilities.

E. Frequency of Review

Protocols designated for **"exempt"** are NOT required to be submitted for annual renewal, but may be reviewed to ensure they meet exempt status from time to time.

XII. Expedited Reviews

This section applies to initial IRB review, modifications, renewals, renewals with modifications, and approval of research that qualifies for expedited review.

A. Reviewer Designation

Research studies submitted for "**Expedited Review**" status are reviewed by an IRB member designated by the IRB Chair. No one may serve as a reviewer if they are from the same academic division or have a material conflict of interest.

B. Duty of IRB Reviewer

1. Reviewers are expected to conduct an in-depth review of all materials and are provided access to Reviewer Checklists as a guide to ensure inclusion of the regulatory criteria and informed consent requirements that must be met as per 45 CFR 46.111 and 21 CFR 56.111 (if applicable).

2. In addition, assigned reviewers are expected to evaluate informed consent documents from the perspective of addressing the required and additional elements of informed consent addressed under 45 CFR 46.116, 21 CFR 50.20 (if applicable) and any other relevant ethical or compliance considerations (if applicable).

C. Provision of Review Materials

The IRB Reviewer has access to the complete IRB submission including the following (as applicable):

1. Protocol application.
2. Renewal Report Form.
3. Modification Cover Sheet.
4. Investigator- or sponsor-provided protocol.
5. Informed consent documents.
6. Recruitment materials (e.g., advertisements, flyers, phone screening procedures, scripts, and/or screening questions, etc.).
7. Measures that will be utilized in the study (e.g., survey instruments, questionnaires, interview scripts, recruitment material, etc.).
8. Confirmation of scientific review or names of persons qualified to review the scientific merit of the protocol. The reviewer is not restricted to utilizing the persons listed for scientific review.
9. Grant application (if any).
10. Other materials specific to the proposed study (e.g., Investigator's Brochure or relevant investigator correspondence with regulatory agencies, etc.)

D. Determination of "Expedited Review" vs. "Full-Board Review"

1. The IRB Reviewer determines whether the proposed research qualifies for expedited review in accordance with the "Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure" as published by the OHRP, 45 CFR 46.110 and FDA 21 CFR 56.110
2. The IRB reviewer may utilize as guidance the OHRP Decision Chart # 8 – May the IRB review be done by Expedited Procedures 45 CFR 46.110?
3. **Initial "Expedited Review" is not acceptable for research studies where the subjects are prisoners (not free to leave) including all forms of forced detainment -including but NOT limited to: prisons, jails, mental health institutions, hospitals, juvenile detentions, boot camps, schools (K-12).**

E. Review of Grant Application

For Federally-supported research, the IRB Reviewer ensures that the research application is essentially consistent with the grant application.

F. Industry Sponsored Research

For industry sponsored research, the IRB Reviewer shall not be limited to information presented in the sponsor's clinical protocol to make a decision.

G. Investigator Communications

Comments or concerns of the IRB Reviewer are documented and provided to the investigator. Responses of the PI are reviewed by the IRB Reviewer who conducted the expedited review (or to another non-conflicted IRB Reviewer if the initial reviewer is unavailable for an extended time). In the event of a failure to resolve problems or concerns related to the investigator's response(s), the IRB submission (including prior

correspondence between the IRB Reviewer and investigator) will be reviewed at a convened meeting of an IRB committee (i.e., full-board IRB review).

H. Documentation of Determination:

Expedited reviewers cannot disapprove or approve an IRB submission or modification.

After reviewing the protocol submission, the IRB Reviewer documents his/her determination on the Expedited Review Form. The IRB Chair or Vice-Chair reviews the protocol submission along with the IRB reviewer's determination and then makes the final determination surrounding the protocol submission.

Final expedited approval of the research study and corresponding informed consent document(s) is granted by a non-conflicted IRB Chair or Vice-Chair.

If an IRB submission is determined to not meet the criteria for an expedited review, the PI will be advised by the IRB that their submission has been referred for full-board IRB review.

1. Basis for Approval

The minimal risk status of the research and the applicable category or categories of research activities listed "Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure" will be documented, with justification, within the IRB Research Protocol and/or review materials.

2. Expedited Approval Notification

The PI is notified of IRB approval via email indicating the name of the IRB Chair or Vice-Chair who granted the final expedited approval. This letter specifies, at a minimum:

a. The IRB number assigned to the submission.
b. The basis for granting expedited review and approval, including identification of the applicable category or categories.
c. The date of IRB approval and the date the IRB approval expires.

XIII. Procedures Specific to Protocols Reviewed by the Convened IRB.

These procedures are specific to those protocols undergoing review by the convened IRB. Please refer to Section IX for those procedures that are relevant for review of all protocol submissions.

A. Meeting Assignment

1. Human subject research requiring full-board IRB review and approval will be assigned to the next scheduled full-board IRB meeting (i.e., subject to the availability of IRB Committee members with appropriate expertise).
2. If more than one IRB subcommittee exists, protocols previously voted by the IRB for reconsideration or disapproval shall generally be assigned to the same IRB subcommittee that previously reviewed the respective research.
3. Audit reports (including modification submissions related to auditing findings), unanticipated problems involving risks to human subjects or others and issues related to serious or continuing non-compliance shall be assigned to a full IRB Committee meeting presided by the IRB chair. All other research submissions may be assigned to a general IRB subcommittee.

B. Reviewer Assignment

1. For full-board IRB review, at least three IRB members serve as full reviewers (i.e., a primary, secondary, and tertiary reviewer). They will be expected to have read and considered the entire proposal.
2. For research involving primarily biomedical intervention(s), the primary reviewer will be a physician or health care practitioner with adequate expertise in the area of the research; the secondary reviewer will be a scientific member of the committee; and the tertiary reviewer, if applicable, will be a member whose primary responsibility will be review of the consent document to ensure readability by a layperson.
3. For research involving primarily psychosocial interventions, the primary reviewer will be a scientific member with adequate expertise in the area of the research; the secondary reviewer will be a scientific member of the committee; and the tertiary reviewer, if applicable, will be a member whose primary responsibility will be review of the consent document to ensure readability by a layperson.

C. Distribution of Meeting Materials

1. The committee meeting agenda and review materials for submissions will be distributed to the IRB committee members at a minimum of five days prior to the scheduled IRB committee meeting. The five day minimum will not apply in the event of a meeting called due to serious unforeseen circumstances.
2. The agenda indicates:
    a. The meeting date, time and location.
    b. Previous meeting minutes for review and approval.
    c. Educational topics for discussion.
    d. Conflict of interest disclosure.
    e. Listing of interested parties for proposals under discussion.
    f. Listing of all experts or consultants (with credentials) scheduled to be present for the meeting.
    g. Any previously approved proposals that have come up for review.
    h. Adverse event information (involving any and all study participants) to be reviewed.
    i. New proposals, modifications, renewals, and other unanticipated problems.
    j. Any proposals that have been granted "exempt" status.
    k. Any determinations of "expedited" status and eventual dispositions.
    l. Any policy issues that may need discussion and/or modification.
3. All members will have electronic access to the complete submission for IRB review which includes the following, when applicable:
    a. The protocol application.
    b. Renewal Report Form.
    c. Modification Cover Sheet.
    d. Investigator written or sponsor-provided protocol.
    e. Informed consent documents.
    f. Recruitment materials to include advertisements, flyers, phone screening procedures, scripts, and/or screening questions.
    g. Measures that will be utilized in the study, e.g. survey instruments, questionnaires, interview scripts, recruitment material, etc.

h. Scientific evaluation.
i. Grant application.
j. Information relevant to humanitarian use devices.
k. Other materials specific to the proposed study (e.g. investigator's brochure or investigator correspondence with applicable regulatory agencies. etc.)

D. Review of Materials Prior to the Meeting

1. Assigned reviewers are expected to conduct an in-depth review of all materials in advance of the meeting. Reviewers are provided with access to the IRB Reviewer Checklists as a guide to ensure inclusion of the regulatory criteria and informed consent requirements that must be met as per 45 CFR 46.111 and 21 CFR 56.111 (if applicable). In addition, assigned reviewers are expected to evaluate informed consent documents from the perspective of addressing the required and additional elements of informed consent addressed under 45 CFR 46.116, 21 CFR 50.20 (if applicable) and any other relevant ethical or compliance considerations.
2. Committee members who are not assigned as reviewers are expected to review the provided materials in advance of the meeting in enough depth to be familiar with the materials and prepared to discuss them at the meeting.

E. Verification and Maintenance of Quorum

1. Except when an expedited review procedure is authorized and used, the IRB will review proposed research at full board convened meetings at which a majority (i.e., > 50%) of the IRB members (counting the Chair) are present. A quorum will also require at least one non-scientific member.
2. A consultant may attend the meeting to participate in the review and discussion of the research study; however, s/he may not vote or count towards quorum. His/her comments shall be recorded either in memo format or on a reviewer report form.
3. Quorum includes those participating in the meeting via teleconference. Members present via teleconference are noted as such in the meeting minutes. Such members must receive all pertinent information prior to the meeting and be able to actively and equally participate in all discussions.
4. The presiding IRB Chair will be responsible for ensuring that quorum is maintained and will certify that a quorum was present in the minutes of each meeting.

F. Conflict of Interest

Potential conflicts of interest are assessed both prior to and at every meeting. If recusal due to conflict of interest reduces the attendance below a quorum, the topic under discussion must be tabled until an alternate committee member can participate in the meeting.

G. Notification of Protocols Reviewed Via Expedited Process

All IRB Committee members are provided with a list of protocols approved through an expedited review mechanism since the last meeting. This includes exempt and expedited submissions as well as full board studies that required a response to comments. Reviewers raising concerns about protocols approved in this manner should contact the IRB Chair. If concerns are not satisfied, then the committee member shall submit the concerns in writing to the Vice President for Health Affairs and the Vice President for Academic Affairs for review and then forwarding on to the IRB for inclusion in the file.

H. Review of Meeting Minutes from Prior Meeting

Before each meeting, the Chair or Vice-Chair will poll the members to determine if the meeting minutes from the prior meeting are approvable as submitted or if any modifications to the prior meeting minutes are warranted. A vote will be taken for this action and documented in the minutes.

I. Presentation of IRB Materials

Each research study requiring review and approval by the full-board IRB shall be addressed separately at the convened meeting of the IRB Committee.

1. The primary reviewer leads the discussion of the study at the IRB meeting and will provide a brief summary of the proposed research followed by:
    a. A presentation of significant concerns related to the research and informed consent document(s).
    b. Recommendations regarding the risk level (i.e., minimal, greater than minimal) of the research.
    c. Recommendations for full approval, approval subject to modifications, reconsideration, or disapproval of the conduct of the proposed research.
2. The secondary reviewer and non-scientific reviewers will subsequently provide any additional comments or concerns as well as recommendations regarding points (b) and (c) above surrounding the research submission.
3. Following the reviewer presentations, the research protocol and informed consent document(s) will be discussed by all IRB Committee members.
4. Pertinent comments and concerns of the IRB Committee members will be recorded by the Secretary assigned to the meeting for inclusion in the minutes of the committee meeting.

J. Absence of primary reviewers

If the primary reviewer is absent, the IRB Chair or Vice-Chair will be responsible for ensuring that at least one IRB member or consultant with adequate expertise in the areas of the research is in attendance at the convened meeting and has conducted an in-depth review of all submitted materials. The IRB Committee will consider the written comments of an absent primary reviewer in its review of the research.

However, if there is not at least one IRB member or consultant with adequate expertise in the areas of the research in attendance at the convened meeting who has conducted an in-depth review of all submitted materials, the IRB will table consideration of the research until the next available meeting.

K. IRB Determinations

At the conclusion of the primary reviewer presentations, the IRB shall deliberate on the following items in sub-sections 1-6. Then the IRB will determine if any of the actions in sub-section 7 are necessary in order to make a motion and take a vote. If action is necessary, these actions will be motioned and voted on. If further information is made necessary from discussion it must be received prior to continuation of deliberation (essentially tabling the protocol until further information is received). If no further receipt of information is necessary then a member of the IRB will make one of the motions outlined in sub-section 8 and the IRB will vote as outlined in sub-section 9.

1. Applicable Checklists

For research involving any of the following subject matters, the IRB Chair or Vice-Chair shall review with the IRB members a checklist of conditions that require further

documentation and scrutiny for approval of the research and, if applicable, additional consent form requirements.

a. Vulnerable Subjects.
    i. Children.
    ii. Fetal Tissue.
    iii. Neonates.
    iv. Pregnant women.
    v. Prisoners.
    vi. Persons requiring a Proxy/legal guardian.
    vii. Terminally ill persons (less than 6 months to live
b. Waiver Forms
    i. Waiver of Consent & HIPAA for a Retrospective Study.
    ii. Waiver of Consent to Identify Subjects.
    iii. Waiver of Informed Consent.
    iv. Waiver to Obtain a Signed Consent.
    v. Waiver of HIPAA Authorization.
    vi. Waiver of HIPAA for Recruitment.
    vii. Waiver of HIPAA Exempt.
    viii. Waiver for Emergency Research Documentation Form.
c. Non-local and foreign research.
d. Non-significant risk devices.
e. The Chair of the meeting should ensure that all points are discussed during Committee deliberations. The Secretary is responsible for documenting the applicable points during preparation of the meeting minutes for final concurrence by the IRB Chair.

2. Level of Risk

When considering risks, the IRB considers physical, psychological, social, economic, and legal risks. IRB members will be polled to determine the risk level (minimal, greater than minimal) of the proposed research. The basis for this determination will be documented, with justification, in the IRB Research Protocol and/or the meeting minutes. The proposal will be categorized accordingly.

3. Frequency of IRB Continuing Review

For research studies involving greater than minimal risk or other significant human subject protection concerns, the IRB shall determine if IRB continuing review is warranted on a more frequent basis than the requisite annual review and, if so, shall establish the parameters for an appropriate continuing review interval. In making this determination, the following may be taken into consideration by an IRB Committee:

a. Phase I and II clinical trials involving use of an unapproved investigational drug or device.
b. Involvement of recombinant DNA or other types of gene transfer protocols.
c. Research activities that pose a significant likelihood of a life threatening or serious adverse event to involved subjects.
d. Research where multiple adverse events have been observed during the conduct of the study.
e. Previously raised concerns about an investigator during an audit.
f. Recommendations from other institutional committees.

g. Any other concern raised by an IRB member.

4. Monitoring of Informed Consent

For research determined to be of greater than minimal risk or if potential conflict of interest or coercion concerns exist, the IRB members may request that random monitoring of the informed consent process be undertaken. The IRB Chair will notify the PI of this request and a review/observation of the actual informed consent process may take place at any time and be conducted by any member of the IRB. The date and time of the investigation and/or observation will be discussed at the next available meeting of the IRB and entered into the minutes as well as added to the appropriate IRB research protocol.

5. New Information

Throughout the lifespan of a research protocol, the IRB may determine that currently enrolled subjects need to be notified of new information or significant new findings that alter the risk benefit ratio and may affect their willingness to continue study participation. New information may be presented to research participants via an addendum consent form or a modified consent form.

6. Verification from Other Sources

Protecting the rights and welfare of participants sometimes requires that the IRB verify independently, utilizing sources other than the investigator, that no significant changes occur during the IRB designated approval period. Additional sources may include: audit by IRB members, regulatory agencies, investigational pharmacy records, incident reports, radiation safety or source documents, as well as information from staff, research participants, families, sponsors or others. Criteria for determining if verification is required shall include, but not be limited to:

a. Complex protocols involving unusual levels or types of risks to subjects.
b. Protocols conducted by PIs who previously have failed to comply with Federal regulations or the requirements or determinations of the IRB.
c. Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources.

7. Possible IRB Committee Actions for Research Studies

The following are actions that may be taken by the IRB during the review of protocol submissions. In addition, there are also actions that are utilized by the IRB Committee when reviewing unanticipated problems involving risk to human subject, as well as serious, or continuing noncompliance.

a. Require that a study be submitted for continuing review at an interval less than annually.
b. Request an audit of the informed consent process.
c. Request a complete audit of the study.
d. Request that the investigator appear before the Committee to provide information related to the submission.
e. Request review of a federally funded research study by the Secretary, DHHS if designated for approval under 45 CFR 46.407 (subpart D – Additional Protections for Research Involving Children). If the study is not federally funded, review by an independent expert panel will be sought.
f. Request review of a federally funded research study by the Secretary, DHHS if designated for approval under 45 CFR 46.207 (Subpart B – Additional Protections

for Pregnant Women, Human Fetuses and Neonates involved in research). If a study is not federally funded, review by an independent expert panel will be sought.

g. Terminate or suspend any or all research activities or IRB approval of the research study. When terminating or suspending some or all research activities, the IRB will consider what additional actions the principal investigator or institution should take in order to protect the rights and welfare of current human subjects. These additional actions may include but are not limited to:

i. Making arrangements for clinical care outside the research.
ii. Allowing continuation of some research activities under the supervision of an independent monitor.
iii. Requiring or permitting follow-up of the human subjects for safety reasons.
iv. Requiring adverse events or outcomes to be reported to the IRB and the sponsor.
v. Notifying current human subjects of the IRB's decision to terminate or suspend the research study.
vi. Notifying former human subjects of the IRB's decision to terminate or suspend the research study.
vii. Recommend suspending the PI's privileges to serve as a PI or requiring a replacement of the PI for the research study in question.

8. Motions

Based on its review of initial or ongoing review of research, the IRB shall decide to approve, reconsider, disapprove, or shall stipulate specific modifications of the proposed research and/or consent document(s) as required to secure IRB approval of the research. Following is a brief description of each of the possible motions.

a. **Full Approval:** No changes to the research or informed consent document(s) required. The PI may initiate the research immediately upon receipt of the written notification of full approval to conduct the research.

b. **Approval Subject to Modifications:** Conduct of the research can be granted full approval by the IRB Chair or IRB Vice-Chair pending PI concurrence with specific revisions stipulated by the IRB with directive comments. The PI may not initiate the research until such time that s/he has modified the research protocol and/or informed consent document(s) to comply with the specific revisions stipulated by the IRB; such revisions have been reviewed and approved by the IRB Chair or IRB Vice-Chair; and the PI has received written notification of full approval to conduct the research.

c. **Reconsideration:** Approval to conduct the research requires substantive clarifications or modifications of the research design or procedures or substantive revisions of the informed consent document(s). The PI must respond to the identified concerns, clarifications, modifications, or revisions, and resubmit the revised research and/or informed consent document(s) for full-board IRB review.

d. **Disapproval:** The proposed research has fundamental design problems and/or presents significant ethical or safety concerns to involved human subjects. The PI must undertake a major revision of the research before it can be resubmitted for full-board IRB review.

e. **Tabled:** Insufficient information is available to review the proposed research in an adequate manner. The PI must provide this information before it can be resubmitted for full-board IRB review. The proposed research may also be tabled due to loss of quorum or lack of appropriate expertise present at the meeting.

9. Call for Vote

Following open discussion of the above applicable referenced items, the IRB Chair or Vice-Chair will call for a vote of the Committee to grant full approval, approval subject to modifications, reconsideration, or disapproval of the proposed research.

a. The absence of members due to a conflict (i.e., a listed investigator, financial, or other conflict) during the discussion of the research protocol, and the vote, will be documented in the minutes of the full-board IRB meeting to include the reason for their absence (e.g., listed investigator on research study under consideration, financial interest in sponsor of the research, or the technology being evaluated).

b. The vote of the majority of the IRB members present at the meeting will determine the final approval status (i.e., full approval, approval subject to modifications, reconsideration, disapproval) of the conduct of the proposed research.

c. The IRB member must attend (in person, virtual, or teleconference) the meeting when the vote is taken in order for their vote to count.

L. Meeting Minutes Shall Include

1. Attendance

The minutes of the IRB meetings will specify the members of the committee who were present at the meeting, members who were absent, but provided written comments, and members who were absent. IRB staff (i.e., not serving as members of the committee), consultants to the committee, and guests will be listed separately.

2. Interested parties

A determination of interested parties for the meeting shall be made and listed in the minutes. Interested parties are the individuals or organizations who are impacted by the decision of the IRB on that day.

3. Protocol Specific Information

Each research submission reviewed by the IRB will be listed separately by IRB number, PI's name, and protocol title. For each research submission, the minutes shall address:

a. The action (i.e., full approval, approval subject to modifications, reconsideration, disapproval, tabled) taken by the Committee and the corresponding numerical vote.
    i. Documentation of the numerical vote will address the number of IRB members voting for, or against, the action taken by the committee and the number of IRB members abstaining from the vote. The vote will be reflected as the number for the action, the number against the action, and abstentions (e.g., 13 members for the action; 0 members against the action; 1 abstention).
b. The risk level of the research as determined by the Committee.
c. The IRB review interval designated by the Committee.
d. Pertinent comments and concerns of the primary IRB reviewers, including comments and concerns expressed during open discussion of the research

submission (e.g. significant new findings to be communicated to research subjects, a summary of controverted issues and their resolutions).

i. Comments shall be listed anonymously (e.g., committee member 1 voiced concern over privacy.)

ii. In order to ensure that human subject protection issues are fully addressed at the IRB meeting, many times housekeeping problems (i.e., grammatical and typographical errors) are not presented for Committee discussion. However, in preparing the meeting minutes, which are used directly to generate IRB response letters to the involved investigators, these housekeeping problems are included, especially as they relate to the consent form and ensuring its understanding by potential research subjects.

4. Additional Documentation Requirements

a. Reconsideration or Disapproval of Protocols.

For research submissions voted for reconsideration or disapproval, the following information should be recorded in the minutes:

i. A summary of the primary reason(s) for such determination by the full-board IRB.

ii. Where applicable (i.e., wherein there was a vote for reconsideration or disapproval in the face of majority vote for approval), a summary of the unresolved controverted issues.

b. Regulatory Forms

If applicable, the IRB chair will ensure that all criteria of the respective regulatory forms are included in the meeting minutes. The forms shall be made available for review by the IRB Chair or Vice-Chair by email attachment for 3 days prior to submission.

5. Approval and Utilization of Minutes

a. Minutes of the IRB committee meeting will be reviewed and accepted by the IRB Chair or Vice-Chair overseeing the respective meeting.

b. Following their acceptance by an IRB Vice-Chair or IRB Chair, pertinent aspects of the minutes of the IRB committee meeting will be directly used to generate written notifications of IRB decisions regarding the approval status of the research submission for dissemination to the respective PIs.

c. The minutes of the IRB committee meeting shall be included with the materials prepared for review at the next convened meeting of the respective IRB committee, and shall be voted for approval at the convened meeting.

XIV. Informed Consent and Documentation

A. General Overview of Informed Consent

Informed consent is one of the primary ethical requirements underpinning research involving humans; it reflects the basic principle of respect for persons. It should always be remembered that informed consent is an ongoing process, not a single event.

1. During its review of the informed consent process, the IRB requires per 45 CFR 46.116 and if applicable 21 CFR 50.20 that:

a. Adequate opportunity is provided to the subject or the subject's legally authorized representative to read the consent document before it is signed.
b. The consent process minimizes the possibility of coercion or undue influence.
c. The consent discussion is in language understandable to the subject or the subject's legally authorized representative.
d. The information being communicated to the subject or the subject's legally authorized representative during the consent process does not include any exculpatory language through which the subject or the subject's legally authorized representative is made to waive or appear to waive any legal rights; or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

2. In addition, the IRB requires that the consent document include all of the basic elements except those for which a regulatory basis is stated for the waiver or alteration. The IRB may also require that additional elements or information be given to the prospective subjects when, in the IRB's judgment, the information would meaningfully add to the protection of the rights and welfare of the research subject.

B. Basic Elements of Informed Consent - 45 CFR 46.116 (a) or 21 CFR 50.25(a)

1. A statement that the study involves **research.**
2. A description of any reasonably foreseeable **risks** or discomforts to the subject.
3. A description of **benefits** to the subject or others that may be reasonably expected from the research.
4. The disclosure of appropriate **alternative procedures** or course of treatment, if any, that might be advantageous to the subject.
5. A statement describing the extent to which **confidentiality** of records identifying the subject will be maintained.
6. For research involving more than minimal risk, an explanation as to whether or not any **compensation** or any medical treatments are available if injury occurs during study participation.
7. An explanation of **whom to contact** for answers to questions related to the research and rights of the research subjects or research related injury.
8. A statement that participation is **voluntary**, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which he/she is otherwise entitled.

C. Additional Elements of Informed Consent - 45 CFR 46.116 (b) or 21 CFR 50.25(b)

1. 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 <u>currently unforeseeable</u>.
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

3. Any additional costs to the subject that may result from participation in the research.
4. The consequences of a subject's decision to withdraw from the research and easy procedures for orderly termination of participation by the subject.
5. 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.
6. The approximate number (or target number if the study is just getting started) of subjects involved in the study.

D. Consent Form Addendum

A consent form addendum may be used to inform enrolled subjects of significant new findings that may have a bearing on their willingness to continue participation in the study. When subjects need to be informed of specific changes, an addendum consent, which focuses on the new information, may be more appropriate than a modified consent document.

E. Waiver to Document Informed Consent

1. Regulatory Requirements

Following expedited or full-board review and the receipt of a "Waiver of Signed Consent" form , the IRB under **RARE** circumstances may waive the requirement to obtain a signed consent form for some or all subjects if it finds that either:

a. 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 [i.e., see 45 CFR 46.117 (c) (2); 21 CFR 56.109 (c) (1)].
b. Or the only record linking the subject and the research would be the informed consent document and the principal risk would be potential harm resulting from a breach of confidentiality [i.e., see 45 CFR 46.117 (c) (1)] except for cases concerning **FDA regulations (21 CFR Parts 50, 56).**
    i. Subject to granting a waiver of the requirement to obtain a signed informed consent based on this criterion, the IRB shall require the principal investigator to ask each subject whether s/he wants documentation linking him/her to the research, and the subject's wishes will govern.

2. Upon granting a waiver of the requirement for obtaining a signed informed consent, the IRB reviews and approves the information that will be provided to potential subjects to obtain their verbal consent for study participation, and the procedure(s) that will be used by the investigators to document obtaining verbal consent.

F. Waiver or Alteration of Consent

The IRB requires that informed consent be sought from each prospective subject or the subject's legally authorized representative prior to participation in research activities, with the following exceptions:

1. The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent.

2. The IRB may waive the requirement to obtain informed consent if it finds and documents that the research activity meets the criteria for a waiver of consent as addressed under 45 CFR 46.116(d) as follows:
    a. The research involves no more than minimal risk to the subjects.
    b. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
    c. The research could not practicably be carried out without the waiver or alteration.
    d. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
3. The IRB may waive the requirement to obtain informed consent if it finds and documents that the research activity meets the criteria for a waiver of consent as addressed under 45 CFR 46.116 (c) This IRB does not typically receive requests of this type. If investigators wish to request this waiver, they should contact the IRB for further guidance.
4. **The IRB does not waive the requirement to obtain informed consent if the research study is subject to the FDA regulations (21 CFR Parts 50, 56) governing human subject protections except for planned emergency research 21 CFR 50.24.**
5. A waiver of the requirement to obtain informed consent [45 CFR 46.116 (c) or (d)] is generally not granted under an expedited review procedure and is deferred to the full board. Exceptions to this policy may be granted by the IRB Chair or his/her designee.
6. Waiver of Consent for Planned Emergency Research
   The IRB (subsequent to full-board review) may approve a research study without requiring that informed consent of all research subjects be obtained if it finds and documents that the research activity meets the criteria for an exception to the requirement to obtain informed consent for emergency research as addressed under planned emergency research 21 CFR 50.24. See Section XVI.D.
7. Waiver of Parental Consent for Abused or Neglected Children
8. The IRB may waive the requirement for parental consent if it determines that the research study is designated for conditions or for a subject population (e.g., neglected or abused children) for which parental or guardian permission is not a reasonable requirement to protect the subjects (see Section XIV.A.4(a) and also refer to 45 CFR 46.408).

G. Proxy

For research involving subjects who are or may be decisionally impaired, the IRB may approve the research only by full-board review and only if it finds that proxy consent is appropriate.

H. HIPAA Authorization

The IRB requires that written HIPAA authorization be sought from each subject or the subject's authorized representative prior to participation in any research activity that involves the use of the subject's protected health information (i.e., identifiable medical record information) maintained by a covered entity (i.e., health care provider, health care plan, health care clearinghouse). HIPAA authorization must also be obtained for the placement of research data into the subject's medical record information maintained by the

covered entity. When protected health information (PHI) will be accessed, used and/or disclosed for research purposes, the research consent may include all the necessary elements under HIPAA thereby alleviating the need for a separate HIPAA Authorization.

1. Regulatory Requirements

The necessary HIPAA elements include the following:

a. A specific description of PHI that will be collected for research and the purpose of collecting this information.
b. A specific description of any research-derived information that will be placed in the individual's medical record.
c. The person or class of persons who may use or disclose the PHI collected for research.
d. The person or class of persons to whom PHI collected for research may be re-disclosed and the purpose of such re-disclosure.
e. The expiration date of the authorization.
f. Consequences to the individual of a refusal to sign the authorization.
g. Individual's right to revoke authorization and consequences of such revocation.

2. Waiver of HIPAA Authorization

The IRB may approve a HIPAA authorization process which does not include, or which alters some or all of the elements of a valid written authorization [specified under 45 CFR 164.508(c)], or waive the requirement for written HIPAA authorization if it finds and documents that the use of the subjects' protected health information meets the criteria for a waiver as addressed under 45 CFR 164.512 (i)(2)(ii). In granting an alteration or waiver of HIPAA authorization, the IRB must determine that the alteration or waiver, in whole or in part satisfies each of the following criteria:

a. The use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
    i. An adequate plan to protect the identifiers from improper use and disclosure.
    ii. An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.
    iii. An adequate written assurance that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted (i.e., under the HIPAA regulations).
b. The research could not practicably be conducted without the waiver or alteration.
c. The research could not practicably be conducted without access to the use of the protected health information.

3. Documentation of Approval Concurrence

Documentation of the IRB's approval of an alteration or waiver of HIPAA authorization must include all of the items listed below:

a. A statement that the alteration or waiver of authorization has been reviewed under either full-board or expedited review procedures.
b. A statement that the IRB has determined that the alteration or waiver, in whole or in part, of the authorization satisfies each of the waiver criteria under 45 CFR 164.512(i)(2)(ii).
c. A statement identifying the date on which the alteration or waiver of authorization was approved.
d. A brief description of the protected health information for which use or access has been determined to be necessary by the IRB.
e. The documentation of the alternation or waiver of authorization must be signed by the IRB Chair or other IRB member, as designated by the IRB Chair.
f. The PI must fill out a "Authorization of Alteration or Waiver of HIPAA" form and approval of this form must be voted on and included in the minutes (if full board) or in a note to Vice-Chair (if expedited) that the applicable criteria have been met.

4. Preparatory to Research

There may be instances where an individual will need limited access to health records in order to prepare a research protocol for submission to the IRB. All preliminary access to protected health information (PHI) will be governed by the repository of that information and will be disclosed on the IRB protocol submission.

I. Research on Deceased Individuals

Research involving deceased individuals is not considered research on human subjects according to 45CFR 46.102(f) and does not require IRB oversight unless the research involves both living and deceased individuals. However, the PI should still submit an exemption form with the IRB and follow all other privacy regulations and protocols.

J. Consent for HIV Testing

For studies involving HIV testing a separate consent can be used by investigators. This consent notifies subjects that their information will be handled in compliance with applicable law on HIV-related confidential information, that they will be notified of the testing results and that counseling will be available to them prior to and after HIV testing.

XV. Considerations for Special Subject Populations

A. Research Involving Children

The University of Pikeville adheres to the regulatory requirements for research with children as outlined in 45 CFR 46 Subpart D and 21 CFR 50 Subpart D. When reviewing research with children, the IRB membership includes at least one member who is knowledgeable about or experienced in working with children.

1. Definitions

a. Children - Federal law defines "children" as persons who have not attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. Under Kentucky law, persons under the age of eighteen (18) generally meet

this definition of "children" with the exception noted below. As a result, permission of the child's parent(s) or guardian(s) must generally be obtained prior to the participation of that child in research.

i. The provisions that permit a minor to be considered emancipated vary depending upon the circumstance. Unless a minor has been emancipated by court order, which should be confirmed by requesting a copy of the order, a minor should NOT be considered emancipated for research purposes.

b. Guardian - Under federal law guardian means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

i. A child's "guardian" may provide legally effective informed consent for participation in research. If a guardian provides consent, the court order or legal authorization to consent to general medical care should be copied and included in the research records with the consent document.

ii. Without a court order, foster parents or Children and Youth Services cannot consent for the participation of a foster child in a research study.

2. Applicable Categories of Research

The IRB reviews all research involving children as participants and approves only research that satisfies all of the conditions of applicable subpart sections. The IRB assesses the potential risks and benefits for each research proposal, and the provisions for permission and assent, to determine if the activity satisfies the conditions for a category of research permitted in children, as specified in DHHS 45 CFR 46.404, 46.405, 46.406, 46.407 and 46.409 and FDA 21 CFR 50.51, 50.52, 50.53, 50.54 and 50.56. The research categories are described as follows:

a. 45 CFRF 46.404 and 21 CFR 50.51

Research that does not involve greater than minimal risk may be approved if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

b. 45 CFR 46.405 and 21 CFR 50.52

Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual participant, or a monitoring procedure that is likely to contribute to the participant's well-being may be approved if the IRB finds that:

i. The risk is justified by the anticipated benefit to the participant.

ii. The relationship of anticipated benefit to risk is at least as favorable as that presented by available alternative approaches.

iii. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

c. 45 CFR 46.406 and 21 CFR 50.53

Research involving greater than minimal risk with no prospect of direct benefit to individual participants, but likely to yield generalizable knowledge about the participant's disorder or condition, may be approved if the IRB finds that:

i. The risk represents a minor increase over minimal risk.

ii. The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations.

iii. The intervention or procedure is likely to yield generalizable knowledge about the participant's disorder or condition which is of vital importance for the understanding or amelioration of the participant's disorder or condition.

iv. Adequate provisions are made for soliciting assent of the children or permission of their parents or guardians.

d. (45 CFR 46.407 and 21 CFR 50.54)

Research that is not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health of welfare of children may be approved if the IRB and the Secretary of Health and Human Services (DHHS), after consultation with a panel of experts in pertinent disciplines and following an opportunity for public review and comment, find that the research in fact satisfies one of the above three conditions; or the following:

i. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of children.

ii. The research will be conducted in accordance with sound ethical principles.

iii. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

e. If the research study is not Federally-supported or subject to FDA regulation, the IRB will request review by a panel of pediatric experts to determine the applicability of approval under Section 45 CFR 46.407.

3. 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 and 45 CFR 46.407 or 21 CFR 50.53 and 21 CFR 50.54 only if such research is:

a. Related to their status as wards.

b. Conducted in schools, camps, hospitals, institutions or similar settings in which the majority of children involved as participants are not wards (45 CFR 46.409 or 21 CFR 50.56).

c. Where the proposed research involves Wards of the Commonwealth of Kentucky or any other agency, institution, or entity, an advocate will be appointed 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* (i.e., see 45 CFR 46.409 (b) and, if applicable, 21 CFR 50.56).

i. One individual may serve as an advocate for more than one child-Ward.

ii. 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 of

advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

4. Consent Requirements

If a research study is designated as meeting the criteria for (45 CFR 46.404 or 21 CFR 50.51); or (45 CFR 46.405 or 21 CFR 50.52), the IRB shall determine whether adequate provisions have been made to solicit the permission of each child's parents or guardians, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless one parent has sole legal responsibility for the care and custody of the child. Where parent permission must be obtained, the IRB may determine that the permission of one parent is sufficient. If a research study is designated as meeting the criteria for (45 CFR 406 or 21 CFR 50.53); or (45 CFR 46.407 or 21 CFR 50.54), the IRB requires the permission of both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless one parent has sole legal responsibility for the care and custody of the child. **Special Consideration:** No child, regardless of age, shall be forced, or coerced to engage in research regardless of parental consent. (See "Assent" below)

a. Waiver of Parental Consent for Abused or Neglected Children

Unless the research study is subject to FDA regulations (21 CFR Parts 50 and 56), the IRB may waive the requirement for parental consent if it determines that the research study is designated for conditions or for a subject population (e.g., neglected or abused children) for which parental or guardian permission is not a reasonable requirement to protect the subjects (see 45 CFR 46.408). If the IRB grants this type of waiver based on this criterion, it must substitute an appropriate mechanism for protecting the children-subjects. The choice of such mechanism will depend on the nature and purposes of the proposed research activities; the risk and anticipate benefit to the children-subjects; and the age, maturity, status, and condition of the proposed subject population.

b. Emancipated Minors

Children under 18 that do not have a certified court order of emancipation shall not be considered emancipated for decisions related to participation in research.

c. Consent for Children Participating in Non-Local Research

If the research includes enrollment of participants in other states or countries, the PI is responsible for providing the IRB with sufficient information to verify the age at which participants in other jurisdictions have the ability to consent to participation in research, including any medical treatments or procedures if applicable. The IRB may, if it appears advisable, require the submission of an opinion rendered by an attorney from any applicable jurisdiction on age at which an individual can consent to participation in research.

5. Assent Requirements

No child shall be forced or coerced to participate in research. Therefore, adequate provisions must be made for soliciting the assent of the children-subjects when in the judgment of the IRB the children-subjects are capable of providing assent. In determining whether children-subjects are capable of providing assent, the IRB shall take into account the ages, maturity, and psychological state of the involved children. This judgment may be made for all children to be involved in given research study, or for each child, as the IRB deems appropriate. If a child is incapable of providing assent,

it does not automatically prohibit that child from participating. Research may continue without formal assent if, and only if, the child does not resist participation AND the IRB determines:

a. That the capability of some or all of the children-subjects is so limited that they cannot reasonably be consulted.
b. The IRB finds and documents that:
    i. The research involves no more than minimal risk to the children subjects.
    ii. The research could not practicably be carried out without the waiver.
    iii. Whenever appropriate, the children-subjects will be provided with additional pertinent information after participation.
    iv. The benefit to the child is potentially so great as to drastically out measure any risk or incapability/lack of assent.

B. Research Involving Prisoners

True informed consent and assent are obstacles when concerning incarcerated individuals. The IRB shall only allow research involving "no risk" or under RARE circumstances "minimal risk" for individuals that meet the following criteria:

1. Definitions

a. Prisoner - A prisoner is defined as "an individual involuntarily confined or detained in a penal institution" and encompasses individuals sentenced to such an institution under 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.
b. Prisoner Representative - An individual who is currently or formerly a prisoner or, alternatively, an individual who has a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner.

2. If a subject becomes a prisoner after enrollment in a research study the investigator should notify the IRB immediately.

Either the prisoner-subject must be withdrawn from study participation; or the IRB must, at the earliest opportunity, re-review the research protocol and consent form in accordance with the listed requirements. The IRB can either:

a. Approve the involvement of the prisoner-subject in the research.
b. Determine that this subject must be withdrawn from the research. **Note that if the subject-prisoner is withdrawn from study participation, s/he must be fully informed of the reason for such action.**

C. Research Involving Pregnant Women

1. Definitions

a. Dead fetus - A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.
b. Delivery - Complete separation of the fetus from the woman by expulsion or extraction or any other means.
c. Fetus - The product of conception from implantation until delivery.
d. Neonate -Newborn.

e. Nonviable neonate - A neonate after delivery that, although living, is not viable.

f. Pregnancy -The period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

i. If a study would normally qualify as "EXEMPT," pregnancy status shall not impact participation and, therefore, testing is not necessary.

g. Viable (as it pertains to the neonate) -Being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

2. Regulatory Requirements

The University of Pikeville IRB will only consider research involving pregnant women, fetuses, or neonates if it finds that the research meets the regulatory criteria for approval addressed under the federal regulations at 45 CFR 46 Subpart B (45 CFR 46.204, "Research involving pregnant women or fetuses prior to delivery"; 45 CFR 46.205, "Research involving neonates"; 45 CFR 46.206, "Research involving, after delivery, the placenta, the dead fetus, or fetal material"). Even then, the research will be highly scrutinized for risk, merit, and necessity prior to approval, and special restrictions are likely to apply. Any such research must present an opportunity to understand, prevent, or alleviate a **serious** problem affecting the health or welfare of pregnant women or fetus and be of minimal risk to the woman or fetus.

3. Consent

a. Pregnant Women/Fetus Prior to Delivery

For research involving pregnant women or the fetus prior to delivery, the documented, written informed consent of the pregnant women or her authorized representative will be obtained in accordance with the provisions of 45 CFR 46.204; There will be NO waiver of informed consent in accordance with 45 CFR 46.116(d) or a waiver of the requirement to document informed consent in accordance with 45 CFR 46.117(c).

b. Neonates of Uncertain Viability

For research involving neonates of uncertain viability, the documented, written informed consent of either parent or the authorized representative of either parent will be obtained in accordance with the provisions of 45 CFR 46.205.

c. Nonviable Neonates

For research involving nonviable neonates (i.e., neonates determined to be unable, after delivery, to survive to the point of independently maintaining heartbeat and respiration), the documented, written informed consent of both parents will be obtained in accordance with the provisions of 45 CFR 46.205.

i. If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the IRB may approve the research based on the consent of one parent.

ii. Note: the IRB will **not** grant approval for authorized representative (i.e., proxy) consent or a waiver of the requirement to obtain consent [i.e., 45 CFR 46.116 (c) or 45 CFR 46.116 (d)] for research involving nonviable neonates.

d. Fetal Material Derived from Abortion

For research involving the dead fetus or fetal material derived from an induced abortion, the documented written informed consent of the mother must be obtained in accordance with the following criteria:

i. The research protocol must specify that informed consent for use of the fetal tissue for research will be obtained separately from, and after, the consent is obtained for the abortion.
ii. No remuneration, compensation or other consideration of any kind may be offered to a woman to consent to the use of fetal tissues for research.
iii. The donor may not designate the recipient of fetal tissue.
iv. All persons who participate in the procurement, use or transplantation of fetal tissue must be informed as to the source of the tissue (e.g., abortion, miscarriage, still birth, ectopic pregnancy). Any protocol that involves an intervention derived from fetal tissue must include the information as part of the informed consent document and/or process.

D. Research Involving Decisionally Impaired Individuals

1. Definitions

a. Decisionally impaired - Any Person who has a diminished capacity to understand the risks and benefits for participation in research and to autonomously provide informed consent is decisionally impaired. This decisional impairment may result from a psychiatric, organic, developmental, or other disorder that affects cognitive or emotional functions, or may result from the effect of drugs or alcohol. The impairment may be temporary, permanent or may fluctuate.
b. 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.

2. Internal Review Requirements

Although not specifically addressed in the regulations as a vulnerable population, The University of Pikeville IRB requires additional safeguards for research involving persons with decisional impairment. The IRB shall approve the research only if it finds that:

a. The research bears a direct relationship to the decisionally impaired subject’s condition or circumstance.
b. The research meets one of the following criteria:
    i. Presenting no greater than minimal risk to the involved subjects.
    ii. Presents an increase over minimal risk to involved subjects, but which offers the potential for direct individual benefit to the subject.
    iii. Presents a minor increase over minimal risk to involved subjects and which does not have the potential for direct individual benefit; provided that the knowledge sought has direct relevance for understanding or eventually alleviating the subjects' disorder or condition.
c. In evaluating a protocol involving the enrollment of persons with decisional impairment, the IRB understands that there are many levels of impairment.

However, it will require the use of proxy consent as well as assent of the individual to approve research protocols involving persons of impaired decisional capacity.

3. Consent

In general, all adults, regardless of diagnosis or condition, should be presumed competent to consent to participation in research unless there is evidence of serious disability that would impair reasoning or judgment. However, once a person or persons are deemed impaired, the PI must use consent by proxy.

4. Assent

No decisionally impaired person will be coerced into participating in research at the University of Pikeville. The assent of decisionally impaired subjects will be obtained prior to participation in research. If a person who cannot provide assent is included in a research project, the IRB will not approve that research protocol.

E. Research Involving Subjects in Long Term Facilities (Nursing homes, mental health institutions)

1. In regards to nursing homes, if the PI can document that the participants are not decisionally impaired, the IRB will treat these protocols as they would any other protocol.
2. In regards to mental health institutions, even if an individual is self-admitted, the IRB will require the use of consent by proxy and the benefit from the research must be direct and incontrovertible. Again, Assent is required.

F. Research Involving Student Records

For research involving student (public school or private school) records, where the identity of the students may be ascertained, informed consent shall be sought in accordance with the Guidelines for the Collection, Maintenance and Dissemination of Student Records outlined in **Family Educational Rights and Privacy Act (FERPA)**. In addition, approval from the school district IRB, if required, must be provided prior to final approval.

F. Research Involving Employees

The University of Pikeville employees may enroll in research protocols approved by the IRB. However, to avoid the appearance of coercion, studies shall not include employees of the investigator or employees over whom the investigator has any input or authority.

G. Research Involving Emergency Medical Services

For research involving Emergency Medical Service (EMS) operations the IRB shall require that investigators obtain prior approval of the Department of Health.

XVI. Review of Advertising

The IRB requires that direct advertising for research subjects (i.e., advertising that is intended to be seen or heard by prospective subjects to solicit their participation in a study) be approved by the IRB **prior to dissemination**.

A. Items Included in Direct Advertising

Direct advertising includes, but is not limited to, newspaper, radio, TV, bulletin boards, posters, and flyers that are intended for prospective subjects.

B. Items not Included in Direct Advertising

Direct advertising does not include:

1. Communications intended to be seen or heard by health professions, such as “Dear Doctor” letters and doctor-to-doctor letters (even when soliciting for study subjects).
2. News stories.

3. Publicity intended for other audiences, such as financial page advertisements directed toward prospective investors.
4. Listings of clinical trials on the Internet when the system format limits the information provided to basic trial information, such as the title, purpose of the study, protocol summary, basic eligibility criteria, study site locations, and how to contact the study site for additional information.

C. Advertisements Directed at Potential Research Subjects

Advertisements directed at potential research subjects should be reviewed at the time of initial IRB review of the protocol. Due to the nature of advertising and production, the final form of the advertisement that the public will see may not be available at the time of review. Therefore when the final version becomes available it will be reviewed in an expedited manner by the IRB Chair, or his/her designee.

1. The IRB shall review a final version of printed advertisements to evaluate the relative size of type used and other visual effects.
2. When advertisements are to be taped for broadcast, the IRB shall, at a minimum, review and approve the wording of the advertisement for approval of the research, and subsequently review the final audio or videotape prior to dissemination.

D. Approval Criteria

During IRB review of advertisements, the following criteria must be met:

1. Advertisements cannot state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the protocol and consent document.
2. Advertisements cannot claim, either explicitly or implicitly, that the drug, biologic, device, or other type of intervention is safe or effective for the purposes under investigation.
3. Advertisements cannot claim, either explicitly or implicitly, that the test article or other research intervention is known to be superior or equivalent to any other drug, biologic, device or intervention.
4. Advertisements for recruitment into a research study involving an investigational drug, biologic, or device should not use terms such as “new treatment,” “new medication,” or “new drug,” without explaining that the test article is investigational.
5. Advertisements cannot promise “free medical treatment” when the intent is only to state that subjects will not be charged for taking part in the investigation.
6. Advertisements may state that subjects will be “reimbursed” for time and travel expenses, but should not emphasize the payment or the amount to be paid by such means as larger or bold type. Advertisements aimed at recruitment of children cannot contain the dollar amount of the compensation.
7. Advertisements cannot include exculpatory language through which the participant or their legally authorized representative waive legal rights or releases the investigator, the sponsor or institution from liability for negligence.
8. The advertisement should generally be limited to the information that potential subjects need to determine their eligibility and interest in the research. When appropriately worded, the following items may be included in advertisements, but are not required:
    a. The name and address of the clinical investigator and/or research facility.
    b. The condition under study and/or the purpose of the research.

c. In summary form, the criteria that will be used to determine eligibility for study participation.
d. A brief list of participation benefits, if any. If a benefit is included, then risks must also be included.
e. The time or other commitment required of the subjects.
f. The location of the research and the person or office to contact for further information.

E. Investigator Notifications

Investigators shall be notified in writing of IRB approval of advertisements directed at potential research subjects.

1. For advertisements reviewed at the time of initial IRB review of the research study, the written notification of IRB approval of the research shall include a statement that the advertisement was preliminarily approved by the IRB.
2. For final advertisements reviewed by an expedited process, the written notification of IRB approval will specify the IRB number of the research study corresponding to the advertisement. In addition, the correspondence will specify that any modification of the advertisement requires re-approval by the IRB prior to dissemination.

XVII. Considerations for FDA Regulated Research

A. IRB Review of Studies Utilizing Drugs, Biologics and Devices

The US Food and Drug Administration (FDA) regulates clinical studies conducted on drugs, biologics, devices, diagnostics, and in some cases dietary supplements and food additives.

All such research studies must be conducted in accordance with FDA requirements for the protection of human subjects and IRBs, regardless of source of funding (21 CFR Parts 50 and 56). More than one set of regulations may apply. For example, clinical trials involving FDA regulated test articles that are supported by the Department of Health and Human Services (DHHS) fall under the jurisdiction of both the FDA and the DHHS Office for Human Research Protections (OHRP). Such trials must comply with the FDA and the DHHS human participant regulations. Where regulations differ, the IRB will always apply the stricter regulation. In addition to the other applicable requirements outlined in this document, for studies involving drugs, biologics or devices the IRB shall follow the procedures outlined below. As specified in Section XII.C, reviewers are provided with the sponsor protocol as well as other materials specific to the study, e.g. the investigator brochure and correspondence with the applicable regulatory agencies.

1. Research Involving Drugs and Biological Products

For studies that involve FDA regulated drugs and biological products the IRB will comply with and enforce the requirements of 21 CFR Parts 312 and 600.

a. Research Involving Unapproved / Investigational Drugs and Biological Products

In general, the submission of an Investigational New Drug (IND) application is required for any clinical research study that proposes the use (e.g., as a research tool to explore a biological phenomenon or disease process) or evaluation (i.e. for safety and/or effectiveness) of an unapproved drug or biological product. For studies that involve investigational drugs or biological products, the IRB shall require evidence that the FDA has issued

an Investigational New Drug (IND) number. This confirmation will be made by determining if the IND number provided on the IRB coversheet matches that recorded on the sponsor protocol, communication from the sponsor, or communication from the FDA, and or direct query to the FDA.

b. Research Involving Approved Drugs or Biological Products

For research using an approved drug or biologic, where the investigator has not provided a valid IND number, the IRB shall evaluate the protocol to determine if an IND is required. In general, the submission of an IND is required for any off label use of any previously approved drug. An IND is also necessary if the study involves a route of administration or dosage level, or use in a subject population or other factor that significantly increases the risks (or decreases the acceptability of risks) associated with the use of the product.

c. Dietary Supplements

Dietary supplements are exempt from FDA regulation as "drugs" provided that they are being evaluated and/or are labeled for intended use in affecting the structure or function of the body (i.e., a structure/function claim) (Dietary Supplement Health and Education Act). However, the evaluation of a dietary supplement for the diagnosis, prevention, mitigation, treatment or cure of a specific disease or condition (i.e., a disease claim) requires the prior submission of an IND application.

2. Research Involving the Use of Medical Devices

a. Definitions

i. A medical device -Any health care product that does not achieve its primary intended purpose by chemical action or by being metabolized. Examples of medical devices include, but are not limited to, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts or stents, intraocular lenses, orthopedic pins, and radiographic imaging equipment. Medical devices also include diagnostic aids such as reagents and test kits for in vitro diagnosis of disease or other medical conditions such as pregnancy.

1. For research involving medical devices, the UOP IRB will comply with the requirements set forth in 21 CFR Part 812. These regulations describe two types of investigational device studies, "significant risk" and "non-significant risk." The determination that a device study presents a "significant risk" or a "non-significant risk" is initially made by the sponsor/investigator. If the sponsor/investigator considers the device study to be of "non-significant risk," the sponsor/investigator must provide the IRB with an explanation of this determination and copies of the respective research protocol and informed consent document. The sponsor should inform the IRB of the FDA's assessment of the risk status of the proposed device study, if such an assessment has been made. The IRB may question whether other IRBs have reviewed the

proposed device study and what determination they made or the IRB may consult with the FDA for its opinion.

a. "significant risk device study" is defined by FDA regulations as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and/or a) is intended as an implant; b) is used in supporting or sustaining human life; c) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health; or d) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. An "implant" is defined by the FDA as "a device that is placed into a surgically or naturally formed cavity of the human body and is intended to remain there for a period of 30 days or more." The FDA may determine that devices placed into human subjects for shorter periods of time are also implants.
b. "non-significant risk device study" is a study of a device that does not meet the FDA's definition for a "significant risk device study."

b. **Risk Determination by IRB**

In making the risk determination, the IRB considers both the device as well as the nature of harm that may result from the use of the device. The IRB may agree or disagree with the determination of the sponsor/investigator.

i. If the IRB determines that the device study presents "non-significant risk," and approves the research study and informed consent document(s), the study may proceed without further notification of the FDA.
ii. If the IRB determines that the device study presents a "significant risk," the sponsor must notify the FDA that the device study has been determined to be of "significant risk" and if electing to proceed with the study, must submit and IDE application.
iii. The device study may not commence until the FDA approves the IDE and the IRB approves the device and informed consent document(s).
iv. The IRB determination of "significant" vs. "non-significant" risk will be recorded in the IRB meeting minutes.

B. IRB Review and Approval of Humanitarian Use Devices (HUDs)

For proposals involving HUDs, the IRB will comply with the requirements set forth in 21 CFR Part 814.Subpart H. A Humanitarian Use Device (HUD) is a device that the FDA has determined is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or are manifested in fewer than 4,000 individuals in the United States per year. The use of an HUD within its approved labeling does not constitute research. However, the FDA requires IRB review and approval before an HUD is used.

The processing and review of HUDs shall be handled in accordance with the other applicable sections of this policy. Following are some requirements and procedures unique to studies involving HUDs.

1. Initial IRB Approval

The IRB shall require that the clinical use of an HUD within any institution that falls under the jurisdiction of the IRB must be prior approved by a convened (i.e., full board) IRB. The following are requirements for such research.

a. There shall be written documentation of FDA approval of a Humanitarian Use Device Exemption (HDE) for the HUD and its proposed use.

b. The proposed clinical use of the HUD shall be limited to the clinical indication(s) appearing in the manufacturer's product labeling.

c. There shall be an appropriate clinical consent form addressing the HUD and its proposed clinical use.

2. Continuation of IRB Approval

The clinical use of an HUD must be reviewed at least annually. Criterion for continuation of IRB approval includes the following requirements. For continuing review, expedited review procedures (21 CFR 56.110) may be utilized unless the IRB determines that full board review should be performed. FDA believes that the expedited review procedures are appropriate for continuing review since the initial review would have been performed by the full board and use of an HUD within its approved labeling does not constitute research.

a. The clinical use of the HUD is limited to the clinical indications appearing in the manufacturer's product labeling.

b. Adverse events associated with the clinical use of the HUD are commensurate with the expected risks as addressed in the product labeling.

c. There is evidence of effectiveness or potential effectiveness of the HUD which exceeds its known or expected risks.

d. A summary for each patient in/on whom the HUD had been used during the past year, the clinical indication for the use of the HUD, any adverse events felt to be related or possibility related to the HUD and the clinical outcome of the use of the HUD.

3. Distribution of Meeting Materials

In addition to the materials distributed to IRB members outlined in Section XII.C, for studies involving an HUD, all IRB members shall be provided with:

a. A copy of the current manufacturer's product labeling, clinical brochure, and/or other pertinent manufacturer information

b. At continuing review, a summary, for each patient at the local site in whom the HUD has been used during the past year, of the clinical indication for use of the HUD, any adverse events felt to be related or possibly related to the HUD, and the clinical outcome of the use of the HUD.

4. Investigator Communications

Correspondence to the investigator should also include the following statement: Clinical use of the HUD must be limited to the manufacturer's product labeling and the clinical protocol approved by the IRB.

C. Emergency Use of Unapproved Drugs, Biologics, or Devices

Note that the term device for the purpose of this section of the policy includes emergency use
of an unapproved device as well as the emergency use of a humanitarian use device for an off-label indication.

Under the emergency use provisions in the FDA regulations [21 CFR 56.104(c)], the emergency use of an unapproved drug, biologic or device is an exemption from prior review and approval by the IRB. However, successive request for an emergency use exemption cannot be used to conduct a prospective research study.

D. Request for an Exception to Informed Consent Requirements: Studies Using In Vitro Diagnostic Devices with Specimens that are Not Individually Identifiable

In Vitro Diagnostics (IVDs) are reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, to cure, mitigate, treat, or prevent disease. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. IVDs that are being tested for possible future marketing are devices, and may also be biological products that are test articles under Food and Drug Administration regulations and are subject to FDA regulations governing investigational devices (IDE regulations). When IVDs are used in research involving human subjects (or human samples), FDA's regulations for the protection of human subjects (informed consent and IRB review) generally also apply.

1. **IDE Exempt Studies**

   Studies may be exempt from FDA's IDE regulations when the research meets all of the following criteria:

   a. The sponsor has labeled the device properly.
   b. The testing is non-invasive.
   c. The testing does not require an invasive sampling procedure that presents significant risk.
   d. The testing does not by design or intention introduce energy into a participant.
   e. The testing is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically-established diagnostic product or procedure.

2. **IRB Review**

   Unlike DHHS regulations, FDA regulations do not provide for exemption from IRB review when research involves existing specimens and the investigator records information without identifiers or linking codes. Nor do FDA regulations define "human subjects" with reference to the identifiability of the subject or of the subject's private information (i.e., the donors of specimens/samples remain "human subjects" even when the specimens/samples are de-identified). Current FDA guidance indicates that IRB review is required for any IVD study involving human specimens/samples, even when the research involves no identifiers and the biological materials cannot be linked to any identifying information.

3. **Informed Consent**

   With a few narrow exceptions [emergency and some Department of Defense (DOD) research], FDA regulations do not permit waiver of consent, even when studies are minimal risk and would meet criteria for waiver of consent under

DHHS regulations. Under FDA regulations, informed consent is required for IVD studies involving samples that are identifiable (i.e., are labeled with identifiers or accompanied by the patient's identifiable clinical information), as well as for studies in which the samples are not identifiable but are coded or linked to identifiable information.

4. Current FDA guidance (4/25/06), however, indicates that under some circumstances, when samples taken from excess clinical or research specimens cannot be identified (e.g., all linking codes and identifiers have been removed, or the investigator has no access to the code keys or identifying information), the agency will exercise "enforcement discretion" and permit the IRB to approve the study without requiring informed consent of the sample sources.
5. To be eligible for approval without a requirement for informed consent, FDA indicates that IVD research must meet the following criteria:
    a. The research must be conducted under an IRB-approved protocol.
    b. The research must meet criteria for an IDE exemption (see above).
    c. The research must use specimens left over from clinical care, specimen repositories, or other research (i.e., the specimens may not be collected specifically for the proposed research, and no additional specimen may be collected for the purpose of research).
    d. Individuals caring for the patients are different from and do not share information about the patient with those conducting the investigation.
    e. The specimens are provided for research without identifiers (codes are permissible only if neither the investigator nor anyone associated with the study has access to the code key or can identify the person who was the source of the specimen).
    f. Any clinical information supplied with the specimen must not be individually identifiable.
    g. No test results from the research may be reported to any subject or that subject's health care provider.
    h. The supplier of the specimens must have established policies and procedures to prevent the release of identifying information.
6. FDA recommends that the IRB review the policies and procedures that are in place to determine (1) that identifiers will not be released to investigators, and (2) whether there is the potential for test results to be needed for clinical patient management (e.g., FDA suggests that if the research involves a public health threat such as anthrax, it may be necessary to report positive results; therefore informed consent might be required).

E. Procedures for FDA Inspections of Investigator Sites

This policy applies to all principal investigators who conduct clinical investigations that are regulated by the FDA and clinical investigations that support applications for research or marketing permits for products regulated by the FDA. The purpose of this policy is to outline the specific procedures that should be followed when PIs conduct human subject research that is subject to FDA regulations are notified of an FDA inspection.

1. Responsibilities of Principal Investigator

a. Principal investigators conducting human subject research that is subject to FDA regulations are responsible for promptly notifying the Institutional

Review Board (IRB) about inspections being conducted by the FDA for the purpose of either *surveillance* or *compliance*.

i. A *surveillance* audit is a routine FDA inspection, concentrating on basic FDA requirements (i.e., good clinical practice compliance).
ii. A *compliance* inspection is based on a specific objective.

b. Investigators must also notify the IRB immediately of any FDA correspondence requesting that a clinical hold be placed on any human subject research.
c. Notifications must be made in writing and sent to the IRB Chair.
d. The notice should include reference to the IRB protocol number, the date and location of the planned inspection, any information available as to whether the inspection is for surveillance or compliance.
e. Investigators should facilitate arrangements to ensure that a member of the IRB is present for the FDA exit interview.
f. Investigators must provide the IRB with copies of any written correspondence received from the FDA as a result of the inspection, in particular any Form 483.
g. Investigators must submit all written responses prepared as a result of the FDA inspection to the IRB Committee **PRIOR** to sending the final response to the FDA.

XVIII. Management and Reporting of Unanticipated Problems Involving Risks to Human Subjects and Others and Procedures for Handling Serious and Continuing Non-Compliance.

A. It is the policy of the Institutional Review Board to:

1. Require the reporting of internal and external adverse events and unanticipated problems.
2. Review reports of adverse events, unanticipated problems and audit findings, and determine which meet the OHRP criteria for "unanticipated problems involving risks to human subjects or others."
3. Review reports and allegations of non-compliance with federal regulations or IRB policies and determine which events constitute serious noncompliance and/or continuing non-compliance.
4. Fulfill reporting requirements to the appropriate entities (Institutional officials, federal departments or agencies).

B. Definitions

1. Adverse Event: Any unfavorable medical or psychological occurrence, which may include abnormal signs (e.g., aberrant physical exam, laboratory finding, or behavior), symptoms, or disease, temporally associated with (occurs during participation), but not necessarily considered related to, the subject's participation in the research study.
2. Audit Finding: Any observation noted during a compliance review of research records. Research records are any documentation that is possibly related to the research. Research records include but are not limited to:
    a. Files (paper or electronic) documenting human subject study participation.
    b. Data collection forms.

c. Source documentation.
d. IRB correspondence.
e. Sponsor correspondence.
f. Progress reports.
g. Safety reports.
h. Drug/device accountability records.
i. Training records and other associated study documentation.

3. Intervention: In the opinion of the PI, there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.
4. Related to the Research Intervention: In the opinion of the PI, the incident, experience, or outcome was probably caused by the procedures involved in the research.
5. Continuing Non-Compliance: Repeated failure to understand and consistently comply with federal regulations and University IRB policies governing human subject protections and that, in the judgment of the University IRB, seriously compromises the protection of human research subjects or adversely affects the integrity of the university's human research protection program.
6. External Adverse Event**:** An adverse event that occurs at a site external to the authority of the University of Pikeville IRB and is reported to the university or investigator.
7. IRB File: A chronological record of all IRB correspondence (this includes but is not limited to protocol submissions, consent form documents, IRB approval letters, emails, unanticipated problems, adverse events, etc.) beginning with the initial submission to the most currently approved version related to the research study.
8. Internal Adverse Event**:** An adverse event that occurs at the University of Pikeville or other site that falls directly under the authority of the University of Pikeville IRB.
9. Research Intervention: A procedure or intervention performed specifically for the purpose of the research study.
10. Serious Adverse Event: An adverse event (causation is irrelevant) that meets one or more of the following criteria:
    a. Is fatal or life-threatening.
    b. Requires or prolongs hospitalization.
    c. A persistent or significant disability/incapacity.
    d. A congenital anomaly/birth defect.
    e. Based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.
11. Serious Non-Compliance: Failure to comply with any of the federal or state regulations or institutional policies governing human subject research that, in the judgment of the IRB, significantly compromises human research subject protection or the integrity of the University of Pikeville. Examples of serious noncompliance include, but are not limited to:
    a. Performing non-exempt human subject research without obtaining IRB approval.
    b. Implementing substantial modifications to a research study without obtaining formal IRB approval.

c. Failing to systematically obtain research subjects' informed consent as required by the IRB approved protocol.
d. Failing to comply with federal regulations governing human subject protections (this includes activities of the IRB and/or IRB staff).

12. Suspension of Approval: A temporary withdrawal of IRB approval for some or all activities of a currently approved research study.
13. Termination of Approval: A permanent withdrawal of IRB approval for some or all activities of a currently approved research study.
14. Unanticipated: Unforeseeable at the time of its occurrence.
15. Unanticipated Problem Involving Risks to Human Subjects or Others: Any accident, experience, or outcome that meets all of the following criteria:
    a. Unexpected in terms of nature, severity, or frequency.
    b. Related, or possibly related, to a subject's participation in the research.
    c. Places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
16. Unexpected: Not identified by nature, severity or frequency in the current University IRB approved research protocol or informed consent document.

C. Initial Processing of Adverse Events, Unanticipated Problems, Audit Findings and Reports and Allegations of Noncompliance

1. Internal and External Adverse Events

Internal Adverse Events (IAE) and External Adverse Events (EAE) reported to the IRB shall be received and processed promptly by the IRB Chair, or in his/her absence, by the designated IRB member to act on such matters in the absence of the IRB chair (usually the Vice-Chair)**.** Adverse events that meet the IRB's definition of an "unanticipated problem involving risk to human subjects or others" will require a full IRB meeting to be called where the matter can be discussed and a course of action set. All other adverse events may be discussed at the next scheduled meeting of the IRB. The IRB must also:

a. Enter the event into the IRB's Adverse Event Database.
b. Perform a retrospective review of adverse events reported for the research protocol.
c. Make an initial determination as to whether protocol and/or consent form modifications are required to address the reported adverse event. In making this determination, the IRB Chair will take into consideration the severity of the event, the number of reports describing the same or similar event, and the current consent form and research protocol risk statements.
d. Place a copy of the adverse event and associated documentation in the corresponding IRB file.

2. Unanticipated Problems Not Characterized as Adverse Events

a. Unanticipated problems received or identified by the IRB staff shall be brought to the attention of the IRB Chair, or in his absence, the Vice-Chair.
b. The IRB Chair (or Vice-Chair) shall determine if the report of an unanticipated problem contains complete information that will allow an adequate review for human subject protections. If, in the opinion of IRB Chair (or Vice-Chair), the information is incomplete, s/he may request

appropriate additional information from the individual submitting the report.

c. The IRB Chair (or Vice-Chair) shall determine if the reported unanticipated problem may involve a risk to human subjects or others or non-compliance with the federal regulations or the requirements or determinations of the University IRB.
d. Unanticipated problems that may represent an "unanticipated problem involving risks to human subjects or others," "serious noncompliance" or "continuing noncompliance" as defined above, will be referred to a convened IRB Committee.
e. For those unanticipated problems that **clearly do not** represent an unanticipated problem involving risks to human subjects or others, serious noncompliance, or continuing non-compliance, the IRB Chair or designee shall determine if any additional actions are warranted and, if applicable, shall communicate that in writing to the individual who initiated the report.
f. The unanticipated problem report, the determination of the IRB Chair (or Vice-Chair), and a record of the requested actions, if applicable, shall be documented in the IRB file.
g. Failure to comply with actions requested by the IRB Chair (or Vice Chair), in the absence of a suitable justification, shall constitute non-compliance and be brought to the attention of a convened IRB Committee.

3. Audit Findings

Audit findings will be submitted within 4 days of the date of the audit to the IRB in the following manner:

a. In addition to the audit check-list, the Audit will have a cover page indicating the date of audit, protocol number, PI, and if significant problems were observed or not.
b. If significant problems or issues are observed, the audit shall be presented to the IRB for immediate review of the IRB Chair or Vice Chair in the Chair's absence. IF necessary the IRB Chair or Vice Chair will call an immediate meeting to deal with the issues outlined in the audit.
c. If no significant issues are observed, the audit will be discussed at the next regularly scheduled meeting of the IRB.

4. Reports of Allegations of Noncompliance with Federal Regulations or IRB Policies

a. Reports or allegations of non-compliance with IRB approved protocols may be directed to any current member of the Institutional Review Board, or any Dean or Associate Dean of the University of Pikeville
b. The identity of the reporting individual will not be made public. However, persons who, in good faith, report suspected non-compliance shall not be retaliated against by any University of Pikeville personnel. Any person who believes that s/he has suffered retaliation for making a report under this policy should immediately report such alleged retaliation to any of the individuals listed above.
c. Upon receipt of an allegation of research non-compliance, it is the responsibility of the individual receiving the report to record detailed

information regarding the allegation. This report shall then be confidentially forwarded to the IRB Chair, who will make an initial assessment of the allegations that shall include:

i. A determination regarding whether or not research subjects or others are currently at risk of harm. If so, a plan must be immediately implemented to mitigate the risk. This may include immediate suspension of the research protocol as determined by the IRB Chair.
ii. A determination regarding the possibility that the allegation involves a violation of University of Pikeville policy other than IRB policies, in which case the matter shall be referred to the appropriate office for handling and the complainant shall be informed of the referral.
iii. An assessment regarding whether or not the report includes sufficient details to initiate an investigation.
iv. An assessment as to whether the individual about whom the allegations have been raised, i.e., the respondent, should be notified.
v. A determination as to whether the full IRB Committee should be notified immediately of the allegation or it can wait until the next convened meeting of the IRB.

D. Distribution of Information and Reviewer Assignment When Adverse Events, Reports of Unanticipated Problems, Audit Findings, and Reports and Allegations of Noncompliance are Presented to a Convened IRB Committee

1. Internal Adverse Events

a. All members of the convened Committee will have access to the following:
   i. The adverse event report.
   ii. The IRB-approved research protocol and consent documents.
b. Each internal adverse event will be assigned to two primary reviewers with relevant scientific expertise.

2. External Adverse Events

a. All members of the convened Committee will have access to the following:
   i. A summary of the reported external adverse events.
   ii. The IRB-approved research protocol and consent documents.
b. No primary reviewer system will be utilized for reviewing external adverse events.

3. Unanticipated Problems

a. All members of the convened Committee will have access to the following:
   i. All available documentation regarding the reported unanticipated problem.
   ii. The IRB-approved research protocol and consent documents, if necessary.
b. No primary reviewer system will be utilized for reviewing unanticipated problems.

4. Audit Findings

a. All members of the convened Committee will have access to the following:

i. The audit report and the investigator's response to the audit.
ii. The IRB-approved research protocol and consent documents, if necessary.

b. No primary reviewer system will be utilized for reviewing the audit findings.

5. Reports and Allegations of Noncompliance

a. All members of the convened Committee will have access to the following:
i. The assessment report into the alleged noncompliance.
ii. Investigator's response to allegations.
iii. The IRB-approved research protocol and consent documents, if necessary.

b. No primary review system will be utilized for reviewing reports and allegations of noncompliance.

E. Adverse events information necessary for full discussion at meeting

1. Review of Adverse Events

The IRB Chair will summarize the adverse event/unanticipated problems and his/her decision regarding the initial review. After the presentation from the primary reviewers, all members of the convened Committee will be given the opportunity to comment on the recommendations.

2. Review of Audit Findings

The audit findings and investigator response to the audit will be summarized by the assigned IRB member. All members of the convened Committee will be provided an opportunity to comment.

3. Review of Reports and Allegations of Noncompliance

The allegations of noncompliance and the investigators response (if applicable) will be summarized by the IRB member assigned as the lead investigator. All members of the convened meeting will be provided an opportunity to comment.

F. Possible IRB Committee Actions

The reviewing Committee shall take whatever actions deemed necessary to address adverse events, unanticipated problems, audit findings, and reports and allegations of research noncompliance. Examples of actions that might be taken include, but are not limited to:

1. Investigate the Event by:

a. Requesting additional records or information about the event and its outcome.
b. Interviewing the involved investigators, research staff, and/or research subjects.
c. Interviewing other individuals who may have knowledge of the event.
d. Requesting an independent audit of the event/protocol or of other related protocols.

2. Implement Administrative Actions, such as:

a. Requesting the IRB Chair (or Vice-Chair) to meet with the involved investigator and/or research staff, and the appropriate department chair and/or dean to discuss the event/problem.

b. Requesting a corrective plan of action and/or written standard operating procedures from the involved investigator and/or his/her department chair or dean.
c. Requiring members of the research team to participate in pertinent training and education programs.
d. Notifying other organizational entities involved as warranted (e.g., legal counsel, institutional risk management, as well as governmental regulatory entities).
e. Suspending the PI's privilege to serve as a PI or requiring a replacement of the PI for the protocol(s) in question.

3. Require Modifications of the Associated Protocol, such as:

a. Instructing the investigator to develop an addendum consent form to provide information concerning the event to subjects currently enrolled in the study.
b. Requiring the investigator to perform additional follow-up or monitoring of the enrolled subjects
c. Revising the timeframe for continuing IRB review.
d. For **multi-center studies** - if the IRB or the local investigator proposes changes to the protocol or informed consent document/process, in addition to those proposed by the study sponsor or the coordinating center, the IRB should request in writing that the local investigator discuss the proposed modifications with the study sponsor or coordinating center and submit a response or necessary modifications for review by the IRB.

4. Terminate or Suspend IRB Approval of the Research Study

When terminating or suspending some or all research activities, the IRB will consider what additional actions the PI or institution should take in order to protect the rights and welfare of current human subjects. These additional actions may include but are not limited to:

a. Transferring the human subjects to another research study (i.e., based on equivalent inclusion/exclusion criteria).
b. Making arrangements for clinical care outside the research.
c. Allowing continuation of some research activities under the supervision of an independent monitor.
d. Requiring or permitting follow-up of the human subjects for safety reasons.
e. Requiring additional adverse events or outcomes to be reported to the IRB and the sponsor.
f. Notifying current human subjects of the IRB's decision to terminate or suspend the research study.
g. Notifying former human subjects of the University IRB's decision to terminate or suspend the research study.

5. Require other action as determined to be appropriate by the IRB committee

6. Require no further action.

G. IRB Vote and Documentation in the Meeting Minutes

The IRB will determine the recommended actions, call for a vote and document the outcome in the Committee minutes. The IRB shall vote as to whether the event/problem/audit finding represents an unanticipated problem involving risks to human

subjects or others, serious non-compliance, and/or continuing non-compliance. This vote shall be recorded in the meeting minutes. If the IRB votes to suspend or terminate the research study, the reasons for the suspension or termination will be documented.

H. Time Frame for Communicating IRB Decisions

Reports shall be issued within 10 working days of the IRB Committee decision.

I. Contents of the Report of IRB Findings

At a minimum, the following information should be included in the report of IRB findings:

1. Name of the institution conducting the research.
2. Title of the associated research project and/or grant proposal.
3. Name of the principal investigator on the corresponding research protocol.
4. Number assigned by the IRB to the research project and the number of any applicable federal award(s) (grant, contract, or cooperative agreement).
5. A detailed description of the reason for the report.
6. Actions taken by the institution to address the reported issue.

XIX. Conflict of Interest

A. Disclosure

The IRB leadership, staff and affiliated IRB members are required to disclose ANY and ALL interests in proposed research activities. This includes direct involvement (such as direct investment, intellectual property rights), as well as indirect involvement (such as stock ownership, stock options, etc.), but does not include mutual funds wherein the owner does not have knowledge of the specific stocks bought or sold therein. An IRB member must also disclose if they have a direct family member or intimate associate (lover/best friend) who is directly or indirectly invested in the research.

B. Reviewer Assignment

IRB members shall not review or approve a research study in which s/he has a conflict of interest.

C. Consultants

Consultants to the IRB will be asked, at the time they are contacted to review a research study, if they (or a member of their immediate family) have a conflict with the study on which they are being asked to consult. No consultants will be assigned to review a research study in which s/he has a conflict of interest.

D. Investigators

1. Research investigators shall not be permitted to participate in decisions relating to the selection of IRB members responsible for performing the review of their research studies.
2. Investigators must disclose if they have a significant financial interest in a sponsor of the research or the technology being evaluated.
3. Investigators possessing a significant financial interest in the sponsor of the research or the technology being evaluated are generally prohibited from serving as PI.

E. Placement of Study on Agenda

No IRB reviewer or consultant shall be assigned to review a research study in which s/he has a conflict of interest. Research submissions will not be placed on the agenda of an IRB Committee meeting if the IRB Chair or Vice-Chair who will preside over the meeting is a listed investigator on the submission or holds a significant financial interest in the sponsor

of the research or the technology being evaluated. Under extenuating circumstances, exceptions to this policy can be made by the IRB Chair or his designee. In the event an exception is deemed necessary, the conflicted IRB Chair or Vice-Chair will be asked to step out of the room during the review, discussion, and vote of the research submission. Another IRB Committee member will act as Vice-Chair during the meeting and will review and approve that portion of the minutes.

F. Evaluations of Potential Conflicts at Meetings

IRB members and consultants are polled upon initiation of each IRB meeting to determine if they (or a member of their immediate family or intimate associates) are a listed investigator on any research study being reviewed at the meeting, or if they (or a member of their immediate family or intimate associates) hold a significant financial interest in the sponsor of any research study or any technology being evaluated in a research study being reviewed at the meeting.

G. Abstentions from Deliberations

1. IRB members and consultants will abstain from participation in any IRB deliberations or approval decisions relating to a research study in which they (or a member of their immediate family or intimate associates) have a potential financial conflict-of-interest.
2. IRB members and consultants will recuse themselves from the IRB meeting room during IRB deliberations and decisions relating to a research study in which the individual (or a member of his/her immediate family or intimate associates) is listed as an investigator or has a potential nonfinancial conflict (e.g., consultant on the project). An exception is to provide information specifically requested by the committee.

H. Documentation in Minutes

The absence of members or consultants due to a conflict (i.e., a listed investigator, financial, or other conflict) during the discussion of the research protocol and the vote shall be documented in the minutes of the full board IRB meeting to include the reason for their absence.

XX. IRB Record Keeping and Retention

The IRB staff shall be responsible for maintaining records related to the functions and activities of the IRB.

A. IRB Membership Records

The IRB staff shall maintain a database of IRB Committee members identified by name; earned degree(s); indications of experience such as board certifications, licenses, etc., sufficient to describe each member's primary anticipated contributions to IRB deliberations; representative capacity (e.g., scientific or non-scientific reviewer); and any employment or other relationship between the member and the University of Pikeville. Changes in IRB Committee membership shall be reported in a timely manner by the IRB Chair.

B. Research Submissions

The IRB shall maintain records (paper or electronic) of all research submitted for IRB review and approval.

1. Paper files will be maintained within the IRB by PI name and IRB number.

2. Electronic records will be maintained within the University of Pikeville Information Technology (IT) system with secure back-up on a monthly basis. The records must be password protected to protect potentially sensitive information. However, the records therein will be made available to any interested party who signs a notice of confidentiality contract.
3. Submissions will be retained regardless of whether the protocol was accepted or subjects were enrolled.
4. Research files shall be maintained by the IRB at a secure storage facility until 6 years following termination of IRB approval of the research (27 years for research involving children). Following the required maintenance interval, all IRB research files shall be deleted and/or shredded.

C. Not Human Subjects Research Designation/Exempt Submissions

For projects determined by the IRB to qualify for a no human subject research designation or exempt status, the IRB record shall contain the applicable application form, all investigator-IRB correspondence related to the submission, and the letter of exemption.

D. Expedited or Full Board Submissions

For research submitted for expedited or full board review, the IRB record shall contain:

1. The initial research application.
2. The approved informed consent document (if applicable).
3. The initial IRB approval letter.
4. All modification requests and the applicable IRB approval letter.
5. Continuing review requests and the applicable IRB approval letter.
6. For multicenter studies, the sponsor's protocol.
7. For studies involving an investigational drug or device, the investigational drug brochure.
8. For federally funded studies, the federal grant application for investigator-initiated studies involving a drug or device, all correspondence with the FDA including the IND or IDE application, 1571, 1572 and any other pertinent documentation.
9. Any reports of unanticipated problems involving risks to human subjects or others (including adverse events) encountered in the conduct of the research.
10. Advertisement used to recruit potential subjects as well as screening scripts.
11. All correspondence between the investigator/research team and the IRB.
12. All audits conducted by the IRB or any other body. Full audit reports, responses from investigators, as well as actions taken by the IRB.
13. Documentation of actions taken by the IRB in response to unanticipated problems involving risks to human subjects or others and/or identified non-compliance and the corresponding responses of investigators.

E. IRB Minutes

The agendas and minutes of full-board IRB shall be maintained indefinitely by the IRB.

F. Research Subject Complaints

The IRB shall maintain files of research subject complaints and the actions taken by the IRB staff, IRB Committee(s), or investigators to resolve such complaints. Such files are maintained until 6 years following termination of IRB approval of the respective research study (27 years for research involving children).

G. Adverse Events Reports

The IRB shall maintain a database of adverse events reported in compliance with the IRB's policies for the reporting of serious or unexpected adverse events

1. The written copies of such reports shall be maintained on file, by PI name, within the IRB.
2. Adverse event reports shall be maintained within the database and on file until 6 years following termination of IRB approval of the respective research study.

H. Emergency Use Reports

The IRB shall maintain files of emergency use requests and reports at a secure storage facility for an indefinite period of time. Files shall be maintained by physician name and the "EU" number.

I. Inspections by Authorized Representatives

IRB records are accessible for inspection and copying by duly appointed authorized representatives of interested parties.

XXI. Education and Training

A. IRB Board Members

1. Orientation

All prospective IRB Committee members are required to complete an initial orientation session prior to serving on the IRB. The orientation session is conducted by the IRB Chair. All new members are provided with a binder that contains the following information:

a. IRB Policy and Procedure Manual.
b. DHHS regulations (45 CFR 46) (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html)
c. Guidelines for the Conduct of Research Involving Human Subjects (https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/ethical_conduct/guidelines-conduct_research.pdf).
d. The Belmont Report (http://videocast.nih.gov/pdf/ohrp_appendix_belmont_report_vol_2.pdf).
e. The Nuremberg Code (http://ori.dhhs.gov/education/products/RCRintro/c03/b1c3.html).
f. World Medical Association Declaration of Helsinki (http://www.who.int/bulletin/archives/79(4)373.pdf).
g. FDA regulations (21 CFR 50 and 56) (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm ?CFRPart=50)(http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CF Rsearch.cfm?CFRPart=56).
h. HIPAA Q&A (http://www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/index .html).
i. *Institutional Review Board, Member Handbook*, most current edition.
j. Relevant IRB Forms.

2. Observation of IRB Meeting

All new IRB Committee members are required to observe at least one IRB committee meeting prior to functioning as a voting member.

3. Required Educational Modules

All IRB members are required to complete the "Protecting Human Research Participants" module (http://phrp.nihtraining.com/users/login.php).

4. Continuing Education

IRB members shall receive, on an ongoing basis, continuing education related to human subject protection issues and requirements.

a. Every month, the IRB Chair and Board Member Coordinator will identify a topic to be reviewed at each scheduled Committee meeting. The content will be recorded in the minutes for the meeting as well as the members present at the meeting.
b. In addition, an educational presentation for IRB board members will be held throughout the year on topics related to the protection of human subjects. The IRB will maintain documentation of the attendance of IRB board members at the sessions.
c. The IRB Chair, IRB Vice-Chairs, are to be routinely available to address any questions or concerns of the IRB members.
d. IRB members are provided access to reference materials and research protocol files maintained within the IRB as such access may relate to their functions as an IRB member.

B. Investigator and Research Personnel

1. Required Training Modules

In order to submit projects to the IRB, all investigators and staff of a research project involving human subjects are required to complete the following modules:

a. HIPAA training.
b. On-line Training Modules 1, 2, 3 and 4 (http://www.hhs.gov/ohrp/education/training/index.html).
c. Human Subject Research in Biomedical Science Training provided by the IRB.

2. IRB Guidebook.

The research community is provided with access to the Office for Human Research Protections (OHRP) IRB Guidebook. (http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm).

XXII. Undue Influence

If any IRB staff member, IRB member, Vice-Chair or member of the research community believes s/he has been subjected to undue influence, they should report this matter to the IRB Chair, who will investigate the matter and, in collaboration with the Vice President for Health Affairs and the Vice President for Academic Affairs will take appropriate action.

XXIII. Off-Site Research Activities

Special policies and procedures cover research activities conducted at performance settings that are considered to be "off-site" or "non-local." These are activities that are conducted at sites that do not fall under the authority of the University of Pikeville IRB, and (a) are not owned or

operated by the University of Pikeville, and (b) are geographically outside of the Pikeville, Kentucky, area. More than one IRB may be responsible for these off-site research activities. Special provisions for off-site research reflect the regulatory mandate that IRBs must have sufficient knowledge of the local research context to ensure that (a) selection of subjects is equitable, (b) subject privacy is protected and confidentiality of data is maintained, (c) informed consent is sought in a language that is understandable to the subject and under conditions that minimize the possibility of undue influence, and (d) appropriate safeguards exist to protect the rights and welfare of vulnerable subjects [45 CFR 46.111(a)(3), (a)(4), (a)(7), (b), and 46.116]. The following policies pertain not only to non-exempt research conducted at sites outside of the U.S., but also to off-site research conducted within the U.S. This is particularly important when the domestic research is being conducted in an environment comprised largely of subjects who differ markedly from those in the greater Pikeville, Kentucky, area because of differences in ethnicity or national origin (e.g., Hispanics; Russian immigrants), religion (e.g., Old Order Mennonites or Amish), and/or customs and values (e.g., Native Americans).

A. For any non-exempt research activity conducted at a non-local domestic or international institution or site, the following must be addressed in the IRB protocol:

1. The anticipated scope of the research activities to be conducted at the non-local institution or site.
2. The types of subject populations likely to be involved and the languages spoken by them.
3. The size and complexity of the institution or site where the research is being conducted.
4. Applicable law at that site.
5. Standards of professional conduct and practice.
6. The methods for ensuring equitable selection of subjects.
7. The methods for protecting subjects' privacy.
8. The methods for maintaining the confidentiality of the research data.
9. The methods for minimizing the possibility of coercion or undue influence in seeking consent.
10. The safeguards to protect the rights and welfare of vulnerable subjects.
11. Written confirmation is needed that facility personnel at the site the research is to be conducted have appropriate expertise to carry out the research procedures as reviewed and approved by the IRB. This includes the name and qualifications of the individuals designated as being responsible for conducting research for each foreign/non-local site that is specified.
12. If the research is supported by a division of DHHS, a Federal Wide Assurance (FWA) must be submitted (http://www.hhs.gov/ohrp/assurances/assurances/index.html).

B. Additional Requirements When Research is Conducted Outside of the United States

When human subject research is conducted outside of the United States, additional matters must be addressed. If the foreign site will be engaged in human subject research and if the research is federally funded in whole or in part, the foreign site must file an International FWA. The International FWA number should be provided in the protocol. Investigators may direct the foreign site to this OHRP site to obtain the necessary paperwork (http://www.hhs.gov/ohrp/international/index.html).

1. If investigational drugs or devices will be used at the foreign site, the foreign site must agree to abide by the FDA Guidance on Good Clinical Practice ("GCP Guidance"), which was developed as part of the work of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The Guidance is available at: (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf).
2. GCP Guidance provides a consistent set of definitions and requirements for recordkeeping, adverse event reporting and all other aspects of clinical trial conduct. The FDA clinical trials web site is helpful to ensure all regulations are followed (http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm).
3. Any agreement with the foreign site should expressly reference the GCP Guidance, and the University of Pikeville investigator must be comfortable that the foreign site is equipped to meet GCP Guidance standards.
4. If the investigational drugs or devices will be shipped from the university to the foreign site, the investigators must obtain written permission from the manufacturer and meet any necessary import requirements from the receiving country. Investigators should obtain written documentation from the foreign site stipulating that all necessary approvals for use of an investigational drug or device under the local laws have been obtained.

XXIV. Definitions

ADVERSE EVENT- ANY and ALL significant negative events or conditions that occur to a human research subject during or immediately following participation in a research study.

ANONYMITY- Anonymity exists when there are no identifiers on project materials which could link the data with individual subjects. Even the research investigator cannot know the identity of participants.

ASSENT - Agreement to participate in proposed research, given by an individual not competent to give legally valid informed consent (e.g., a child or mentally limited person). Mere failure to object may not be construed as assent.

ASSURANCE - A formal, written statement submitted to a federal agency attesting that an institution will comply with applicable rules governing research with human subjects.

BENEFIT - A valued or desired outcome. An advantage.

BIOLOGIC - Any virus, therapeutic serum, toxin, antitoxin or analogous product used for the prevention, treatment or cure of diseases or injuries of humans.

CHILDREN - Those who have not attained the legal age for consent (<18).

CLASS I, II, III DEVICES - Classification by the FDA of medical devices according to degree of potential risks or hazards.

CLINICAL TRIAL - A controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of an investigational drug or device. Clinical trials are typically conducted by investigators who have entered into an agreement with a sponsor to conduct the study. For clinical drug and device trials, investigators agree to conditions regarding the conduct of the study outlined by Food and Drug Administration (FDA). Clinical trial investigators agree to these conditions by signing a FDA form (FDA Form 1572) that certifies that the investigator has obtained IRB review and approval prior to conducting the study.

CODE OF FEDERAL REGULATIONS (CFR) - A compendium of rules issued by federal agencies on a multiplicity of topics.

COERCION - using authority or perceived authority to induce an action.

COGNITIVELY IMPAIRED - Having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders), an organic impairment (e.g., dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs, or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.

COMMUNITY BASED PARTICIPATORY RESEARCH - researcher actively participating in inducing social change.

COMPENSATION - Payment or medical care provided to subjects injured in research. Does not refer to payments (remuneration) for participation in research.

COMPETENCE - Technically, a legal term used to denote capacity to act on one's own behalf. The ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Competence may fluctuate as a function of the natural course of a mental illness, response to treatment, effects of medication, general physical health and other factors. Therefore, mental status should be reevaluated periodically. As a designation of legal status, competence or incompetence pertains to an adjudication in court proceedings that a person's abilities are so diminished that his or her decisions or actions (e.g., writing a will) should have no legal effect. Such adjudications are often determined by inability to manage business or monetary affairs and do not necessarily reflect a person's ability to function in other situations.

CONFIDENTIALITY - Right of privacy and of nonrelease of disclosed personal information. The investigator should protect subjects against invasion of privacy and loss of confidentiality. Lack of secure handling of completed personality tests, questionnaires, interview protocols or data and recorded materials augments risk and must be avoided.

CONTROL - Subjects who are not given a treatment under study or do not have a given disorder, background or risk that is the object of study, and who are comparable to subjects in the study.
CROSSOVER DESIGN - A type of clinical trial in which each subject is given, at different times, both an experimental and a control therapy.

DATA POINTS - Any text or numbers generated during a study.

DECEPTION - Intentionally telling a research subject an untruth/lie for research purposes, or to induce subject to participate in research

DOUBLE-BLIND DESIGN - A study comparing two or more treatments in which neither the investigators nor the subjects know to which treatment group individual subjects have been assigned.

EMANCIPATED MINOR - A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as self-support, marriage or procreation.

EXPERIMENTAL - A term often used to denote a therapy (drug, device or procedure) that is unproven or scientifically unvalidated with respect to safety and efficacy. A procedure may be considered "experimental" without necessarily being part of a formal study to evaluate its usefulness.

FETAL MATERIAL - The placenta, amniotic fluid, fetal membranes and the umbilical cord.

FETUS - The product of conception from the time of implantation until a determination is made, following expulsion or extraction, that it is viable. The term “fetus” generally refers to later phases of development. The term “embryo” is usually used for earlier phases of development.
2 Revised 8/1/05 .

GROUP C TREATMENT IND - "Group C" Treatment IND was established by agreement between the FDA and the National Cancer Institute (NCI). The Group C program is a means by which oncologists can use investigational drugs for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase III study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected.
GUARDIAN - A person who is authorized by law to consent on behalf of a child or handicapped individuals to general medical care.

HISTORICAL CONTROLS - Control subjects (followed at some time in the past or for whom data are available through records) who are used for comparison with subjects being treated concurrently. (Note: the condition of subjects may be compared with their own condition on a prior regimen, the effectiveness of which has already been established.)

HUMAN SUBJECT - Under DHHS regulations human subjects are living individuals about whom an investigator conducting research obtains 1) data through intervention or interaction with the individual or 2) identifiable private information. Intervention includes both the physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes. Interaction includes communication or interpersonal contact (e.g., questionnaires, interviews) between the investigator and the subject (45 CFR 46.102). Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.
Under FDA regulations a human subject is defined as “an individual who is or becomes a participant in research, either as a recipient of a test article or as a control [21 CFR 50.03, 21 CFR §56.103(e), 21 CFR §312.3(b)]. A subject may be either a healthy individual or a patient.” If the research involves a medical device, human subjects are individuals when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control [21 CFR §812.3(p)].

HUMAN SUBJECT RESEARCH - Under the Organization’s policies and procedures an activity is human subject research if it is either (1) human research subject to FDA regulation or (2)

human research subject to DHHS regulations. Activities are human research subject to FDA regulations when they meet the FDA definition of "research" and involve one or more "human subjects" as defined in FDA regulations. Activities are human research subject to DHHS regulations when they meet the DHHS definition of "research" and involve one more "human subjects" as defined in DHHS regulations [§46.102(f)]

HUMAN IN VITRO FERTILIZATION - Any fertilization involving human sperm and ova that occurs outside the human body. INCAPACITY - Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information and to make a choice. Often used as a synonym for incompetence.

INCOMPETENCE - Legally, the inability to manage one's affairs. Often used as a synonym for incapacity.

INFANT - An ex utero fetus judged viable (i.e., likely to survive to the point of sustaining life independently).

INFORMED CONSENT - Informed consent means "knowing consent," the exercise of a free power of choice without undue inducement, force, fraud, deceit, duress or other form of constraint or coercion. If the subjects are minors or are not capable of giving consent, parental, guardian or other legal representative consent is required. Use of a written consent form that includes all of the basic elements of informed consent must be documented by a signature of the subject or legally authorized representative.

INSTITUTION - A residential facility that provides food, shelter and professional services (including treatment, skilled nursing, intermediate or long-term care and custodial or residential care). Examples include general, mental or chronic disease hospitals, inpatient community mental health centers, halfway houses and nursing homes, alcohol and drug addiction treatment centers, homes for the aged or dependent, residential schools for the mentally or physically handicapped, and homes for dependent and neglected children

INTERACTION - Interaction includes communication or interpersonal contact between investigator and subject.

INTERVENTION - "Intervention" includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

INVESTIGATIONAL DEVICE - A medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.

INVESTIGATIONAL NEW DRUG (IND) - A drug permitted by the FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population, and thus, not yet licensed for marketing.

INVESTIGATIONAL DEVICE EXEMPTION (IDE) - An exemption from certain rules found in the Medical Device Amendments, allowing use of a not-yet-approved devices in clinical investigators.

INVESTIGATOR - Researcher involved in conducting the study.

LACTATION - The period of time during which a woman is providing her breast milk to an infant or child.

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.

LONGITUDINAL STUDY - A study designed to follow subjects forward through time.
MATURE MINOR - Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (e.g., consenting to medical care). Note that a mature minor is not necessarily an emancipated minor.

MEDICAL DEVICES - Diagnostic or therapeutic articles that do not interact chemically with the body. Such devices may include diagnostic test kits, crutches, electrodes, prescribed beds, pacemakers, arterial grafts, intraocular lenses and orthopedic pins.

MEMORANDUM OF UNDERSTANDING (MOU) - Document describing a bilateral or multilateral agreement between parties.

MINIMAL RISK - Risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

MONITOR - Designated individual selected by a sponsor or contract research organization to oversee the progress of a clinical investigation.

NONSIGNIFICANT RISK DEVICE - An investigational medical device that does not present significant risk as described above. The determination that a device presents a nonsignificant risk is first made by the sponsor. If the IRB agrees with the sponsor’s finding that a device presents nonsignificant risk, the device is considered a nonsignificant risk device.

NORMAL SUBJECT - Subjects used in study of normal physiology and behavior, or subjects who do not have the condition under study in a particular protocol used as comparisons with subjects who do have the condition. “Normal” does not necessarily connote normal in all respects. For example, patients with broken legs may serve as normal volunteers in studies of metabolism, cognitive development and the like. Similarly, patients with heart disease but without diabetes may be “normals” in a study of diabetes complicated by heart disease.
OPEN DESIGN - An experimental design in which both the investigator(s) and the subjects know the treatment group to which subjects are assigned.

PARALLEL TRACK IND - The FDA's Parallel Track policy permits wider access to new drugs for life-threatening diseases under a separate treatment protocol (Parallel Track IND) that "parallels" the controlled Phase II and III clinical trials performed to establish the safety and effectiveness of investigational new drugs. For example, under this prospective mechanism, persons with AIDS and HIV-related diseases who are not able to take standard therapy or for whom standard therapy is no longer effective, and who are not able to participate in ongoing controlled clinical trials, can have access to promising investigational new drugs. Applications to permit expanded availability of an investigational new drug under the Parallel Track mechanism must be submitted (typically by the manufacturer of the drug) to the FDA as an amendment to the existing IND.

PARENT - A child's biological or adoptive parent.

PERMISSION - The agreement of the parent(s) or guardian to the participation of the child, handicapped individual, or ward in the research.

PHASE I (CLINICAL) TRIAL - The first stage in testing an unapproved (by the FDA) drug in man. The drug is administered to a small number of normal subjects to generate preliminary information on its safe dosage, toxicity, tolerance, absorption and metabolism. However, in some instances, if the drug is intended to treat a specific disease, it may be appropriate to test the drug in patients with that disease.

PHASE II (CLINICAL) TRIAL - The second stage in testing a new drug in man, generally carried out on patients with the disease or condition of interest to obtain information on the treatment efficacy and to supplement information on safety obtained from Phase I trial.

PHASE III (CLINICAL) TRIAL - The third, and usually final stage in testing a drug in man. The study is designed to include a control treatment and random allocation to treatment on a large subject population in different clinical settings. The drug is used as would be when marketed and the study is primarily concerned with assessments of dosage effects and efficacy and safety. Once this phase is completed, the drug manufacturers may request permission to market the drug by submission of a New Drug Application to the FDA.

PHASE IV (CLINICAL) TRIAL - Generally carried out after FDA approval and licensure of the drug for that indication. The study is a randomized controlled trial designed to evaluate the long-term safety and efficacy of a drug for the given information.

PHLEBOTOMIST - An individual trained to draw blood.

PHYSICAL RISK - Any strenuous or unusual physical activity or procedure required of a subject, use of compounds which might alter the subject's biochemical milieu, exposure to strong stimulation or placement in a situation which could lead to violence. The investigator is responsible for anticipating circumstances which might endanger the subject's physical well-being and for bringing these circumstances to the attention of the IRB.

PHYSIOLOGICAL RISK - Any experimental condition that induces personality change or intense changes in a subject's feelings or motivations, or that may induce such changes which extend beyond the experimental or debriefing period. Subjection to deceit, to demeaning or dehumanizing procedures, to humiliation and embarrassment. The investigator has the responsibility to eliminate or minimize the effects of psychological risk to subjects and to bring these matters to the attention of the IRB.

PREGNANCY - The period from confirmation of implantation of a fertilized egg within the uterus until the fetus has entirely left the uterus (i.e., has been delivered). Although fertilization occurs a week or more before implantation, the current inability to detect the fertilization event or the presence of a newly fertilized egg makes a definition of pregnancy based on implantation necessary.

PRISONER - An individual involuntarily confined in a penal institution, including persons (a) sentenced under a criminal or civil statute, (b) detained pending arraignment, trial or sentencing, and © detained in other facilities (e.g., for drug detoxification or treatment of alcoholism) under statues or commitment procedures providing such alternatives to criminal prosecution or incarceration in penal institution [45 CFR 46.303(c)]. PRIVATE INFORMATION - "Private information" includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

PROSPECTIVE STUDIES - Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. These studies need not involve manipulation or intervention, but may be purely observational or involve only the collection of data.

PROTOCOL - A protocol is the researcher's plan of a scientific experiment or treatment. Full review or expedited protocol consists of a cover sheet, Unit/Department/Faculty Review form, Human Subjects Protocol Form, informed consent form(s), sample survey instrument(s) or questionnaire(s), and grant proposal, thesis or dissertation, or prospectus, so as to provide complete information regarding activities involving human subjects. Claim of Exemption from IRB forms are also available.

QUALITY ASSURANCE - A system of activities whose purpose is to provide assurance that the overall control of quality is being done effectively.

RADIOPHARMACEUTICALS - Drugs, compounds, or materials labeled or tagged with a radioisotope. These materials are largely physiological in action and, in many cases, function much like materials found in the body. The principal risk associated with these materials is the radiation exposure to the body or to specific organ systems when they are injected in the body.

RANDOMIZATION OR RANDOMIZED CLINICAL TRIALS - Assignment of subjects to different treatments, interventions or conditions according to chance rather than with reference to some aspect of their condition, history or prognosis.

RESEARCH - Under HHS Regulations (46.102) research is defined as a "systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." The general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects. For example, some "demonstration" and "service" programs may include research activities.
Under FDA Regulations (21 CFR 56.102) the term "clinical investigation" is synonymous with "research" and is defined as "any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Food, Drug and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. Clinical investigations regulated by the FDA under Sections 505(i) and 520(g) of the Act, include investigations of food, dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. The term "clinical investigation" does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part.
Research is subject to 21 CFR Parts 50 and 56 when it involves the use of any drug other than the use of an approved drug in the course of medical practice. Research is subject to 21 CFR Parts 50 and 56 when it involves the use of any medical device other than the use of an approved medical device in the course of medical practice.

RETROSPECTIVE STUDIES - Research conducted by reviewing records (i.e., birth and death certificates, medical records, school or employment records) or information about past events elicited through interviews with persons who have, and controls who do not have, a disease under investigation.

RISK - The probability of harm or injury (physical, psychological, social or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk." (See also "Minimal Risk.")

SIGNIFICANT RISK DEVICE - An investigational medical device that: (1) Is intended as an implant and presents a potential for serious risk to the health, safety or welfare of a subject; (2) Is purported or represented to be of use in supporting or sustaining human life and presents a potential for serious risk to the health, safety or welfare of a subject; (3) Is for a use of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health, and which presents a potential for serious risk to the health, safety or welfare of a subject; (4) Otherwise presents a potential for serious risk to the health, safety or welfare of a subject; or (5) Other than minimal risk.

SINGLE-BLIND DESIGN - Typically, a study designed in which the investigator, but not the subject, knows the treatment assignment. Occasionally the subject, rather than the investigator, knows the assignment.

SPONSOR - The company/person who initiates the study. The sponsor is typically the manufacturer or research institute that developed the drug or device. In this case, the sponsor does not actually conduct the clinical trial but rather distributes the investigational drug or device to clinical investigators who direct local conduct of the trial. A clinical investigator may, however, serve as both the sponsor and investigator (investigator-sponsor) of a clinical trial. The sponsor assumes general responsibility for the studies involving the investigational drug or device, including responsibility for compliance with applicable laws and regulations. The sponsor is responsible for obtaining FDA approval to conduct a trial and for reporting the results of the trial to the FDA.

STUDY COORDINATOR - Person appointed at the institute/center where the study is being conducted.

SUBJECT - A non-patient (normal) volunteer or a patient in clinical research.

TERMINALLY ILL - Terminally ill patients are those who are deteriorating from a life-threatening disease or condition for which no effective standard treatment exists and who have been given less than 6 months to live by their treating physician.

THERAPEUTIC RESEARCH - Research involving an intervention that has the likelihood of providing a therapeutic, diagnostic or preventive benefit to the subjects.

THERAPEUTIC INTENT - The research physician's intent to provide some benefit to improving a subject's condition (e.g., prolongation of life, shrinking of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily be effected). This term is sometimes associated with Phase I drug studies in which potentially toxic drugs are given to an individual with the hope of inducing some improvement in the patient's condition, as well as assessing the safety and pharmacology of a drug.

TREATMENT IND - Established by the FDA in 1987, a Treatment Investigational New Drug exemption (Treatment IND) is a treatment protocol that is added to an existing IND for a promising new investigational drug. The Treatment IND provides a prospective mechanism whereby physicians can treat multiple, eligible patients with the investigational new drug according to protocol. A Treatment IND may be granted by the FDA (i.e., typically to the drug manufacturer, but also to investigator-sponsors) after sufficient data have been collected to show that the drug may be effective and does not have unreasonable risks. Because data related to safety and side effects are collected, Treatment INDs also serve to expand the body of knowledge about the investigational new drug. There are four requirements that must be met before a Treatment IND can be issued by the FDA: a) the drug is intended to treat a serious or immediately life-threatening disease; b) there is no satisfactory alternative treatment available; c) the drug is

already under investigation, or trials have been completed; and d) the sponsor of the drug is actively pursuing its market approval.

TREATMENT AND PARALLEL TRACK INDs - Investigational new drugs may be made available outside of a clinical trial, through a treatment protocol, to multiple patients with life-threatening or other serious diseases for which no satisfactory alternative drug or other therapy exists. (For information related to the emergency use of an unapproved drug or device in a single patient, refer to section 2.4 of this IRB Reference Manual.)
UNANTICIPATED: Unforeseeable at the time of its occurrence.

UNANTICIPATED PROBLEM INVOLVING RISKS TO HUMAN SUBJECTS OR OTHERS: Any problem or event that, in the opinion of the principal investigator 1) was unanticipated; 2) involved risk to human subjects or others e.g., research staff, family members, University IRB staff, University or UPMC), and 3) was related to a research intervention.

UNEXPECTED - Not identified by nature, severity or frequency in the current University IRB-approved research protocol or informed consent document.

VULNERABLE POPULATION - Children, Fetal Tissue, Neonates, Pregnant women, Prisoners (captive audiences), Persons requiring a Proxy/legal guardian (decisionally impaired), Persons with a terminal illness (less than 6 months to live).