In this chapter:

6.1 Authority of the Institution and Authority of the IRB

AAHRPP Std./ Element	Description
I.1.A	The University of Louisville (UofL) has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program.
I.1.C	The University of Louisville (UofL) has and follows written policies and procedures that allow the Institutional Review Board to function independently of other organizational entities in protecting research participants.

Authority of the Institution

The President of University of Louisville University has delegated the authority and responsibility to establish, maintain and oversee the HRPP to the Executive Vice President for Research and Innovation (EVPRI) as specified in the President's Delegation of Authority letter.

The Executive Vice President for Research and Innovation delegates independence and authority to the IRBs. UofL has demonstrated a commitment to human subject protections by establishing a human subjects protection program lead by a University of Louisville official, the Executive Vice President for Research and Innovation (EVPRI), with sufficient standing, authority and independence to ensure implementation and maintenance of the program. The University utilizes a centralized program to review all human subjects' research. The University of Louisville, at present, operates two Institutional Review Boards (IRBs), Biomedical IRB and Social Behavioral Educational (SBE) IRB, that review projects in a wide range of medical, biomedical, social, education and behavioral fields. As a part of the University of Louisville's continued commitment to human subjects' protections, the resources allocated to the IRB are constantly monitored to ensure the existence of adequate support of IRB functions (See Chapter 2, Resources Supporting the Human Subjects Protection Program).

All human subject research conducted by or under the auspices of the University of Louisville will be performed in accordance with Title 45 Code of Federal Regulations, Parts 46, 160 and 164 and Title 21 Code of Federal Regulations Parts 50, 56, 312, and 812. In addition, the actions of the Institutional Review Boards (IRBs) at the University of Louisville will also conform to all applicable Federal (Food and Drug Administration, National Institutes of Health, Department of Education, Department of Energy, Office for Human Research Protections, etc.), regulations, guidance, state and local laws.

Activities that constitute human subject research are determined by the University of Louisville IRBs and the IRBs delegate this decision to the IRB chair or experienced member designee. The decision by the chair or designee is based on whether the activity:

1. Represents "research," involves "humans" as participants, and "engages" the University of Louisville (as defined in 45 CFR 46.102(d), 45 CFR 46.102(f), and the OHRP guidance document "Engagement of Institutions in Research" respectively).

2. Represents a clinical investigation of a test article involving one or more humans as participants (as defined in 21 CFR 50.3(c), 21 CFR 50.5(j), and 21 CFR 50.5(f) respectively) or individuals (humans) on whose specimens an investigational device is used (21 CFR 812.3(p)).

Research is defined in federal regulations[1] as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

[1] 45 CFR 46

Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, or is not subject to 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 submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

Human subjects are defined in the "Common Rule" as "living individuals about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information." The FDA regulations define human subjects as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control or individuals on whose specimens an investigational device is used. A subject may be either a healthy human or a patient. The appropriate definition depending on the type of human research will generally apply to all human research conducted by investigators at the University of Louisville.

All human subjects research carried out at the University or under its auspices must be reviewed and approved by an IRB prior to the start of the research. The IRBs are guided by the principles of *The Belmont Report* and the regulations and policies set forth by the DHHS and its subordinate agencies and offices in reviewing all human subjects' protocols.

University of Louisville IRBs review human subject's research projects when:

1. the research is sponsored by the institution or one of its affiliated institutions,
2. the research is conducted by or under the direction of any employee or agent of the institution in connection with his or her institutional responsibilities,
3. the research is conducted by or under the direction of any employee or agent of the institution using any property or facility of the institution,
4. the research involves the use of the institution's non-public information to identify or contact human subjects, or
5. any research determined by the Institutional Official (IO).

The EVPRI has the authority to review decisions of the IRB. In the case of an approval decision, should the EVPRI conclude that a project does not fully comply with policies or obligations of the University of Louisville, the project may be disapproved, suspended, or terminated on behalf of the institution. In the case of a decision by the IRB to disapprove, suspend, or terminate a project, the EVPRI or any other officer or agency of the University of Louisville, state government, or federal government may not reverse the decision. Affiliated Institutional officials retain the same authority as the University's Institutional Official for their respective organizations. Affiliated institutions will utilize their own internal policies and procedures to manage conflicts of interest unique to their institution.

The University of Louisville Privacy Officer may review the IRB Privacy Board decisions but has no authority over the actions of the IRB. Should the Privacy Officer and the Privacy Board disagree; the Privacy Officer and the Privacy Board will meet and review the research proposal and authorizations. The Privacy Officer and the Privacy Board, in consensus, will determine the appropriate authorization language.

If a project does not fully comply with policies or obligations of the University of Louisville, the project may be disapproved, suspended, or terminated on behalf of the institution.

Research covered by this policy that has been approved by a University IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, as per 45 CFR 46.112 and 21 CFR 56.112, those officials may not approve the research if a University of Louisville IRB has disapproved it.

Authority of the IRBs

The authority conveyed to the Biomedical and SBE IRBs includes the following:

1. review, approve, and ratify all non-exempt human subject research covered by the Federal-wide assurance in which it is determined that the risks to participants are reasonable in relation to potential benefits to participants and society;
2. approve pending receipt of specific required modifications. The IRB will draft correspondence to investigators requesting specific modifications to the protocol or the informed consent form. The requested modification must be specific enough to allow the IRB chair to determine whether the responsive materials provided by the investigator match the modifications required by the IRB. The IRB will be informed of these approvals at the next regularly scheduled meeting. When the convened IRB requests clarifications, requests for additional information, or modifications that cannot be described specifically, the protocol will be tabled, pending subsequent review by the convened IRB of responsive material;
3. review and determine the exempt status of new research projects;
4. defer pending further communication between the investigator and the IRB. Studies are deferred when the IRB has substantive concerns or significant requests for clarification. Responses to the IRB correspondence in this category must be returned to the full IRB for deliberation and review;
5. review and disapprove the initiation of new research projects in which it is determined that the risks to participants are not reasonable in relation to potential benefits to participants and society;
6. require from investigators revisions in research protocols and informed consent documents as a condition for initial or continuing approval;
7. monitor the activities in approved projects including regularly scheduled continuing review at least annually, and verification of compliance with approved research protocols and informed consent procedures;
8. develop mechanisms for prompt reporting to the IRB of any planned changes in approved projects prior to the implementation of those changes;
9. develop mechanisms for prompt reporting to the IRB of any adverse experiences occurring in approved projects, or reporting of unanticipated problems involving risks to subjects or others (UPIRTSO), in other projects related in context to the approved projects;
10. suspend or terminate previously approved research;
11. restrict aspects of research for the purposes of human subjects protection;
12. review and monitor the use of test articles (investigational drugs, biologicals and devices) for the purpose of treatment of serious or life-threatening illnesses (Biomedical IRB only);
13. serve as the privacy board of the University of Louisville's hybrid covered entity (HCE);[2]
14. recommend sanctions to the Office of the Executive Vice President for Research (OEVPR) for cases of non-compliance investigated and found actionable by the IRBs;
15. report human research guidelines violations to the appropriate state or federal agency.

Purpose of the IRB

The purpose of the Human Subjects Protection Program and the University of Louisville IRBs is to protect the rights, dignity, welfare, and privacy of human research subjects at the University by adhering to the principles of the *Belmont Report* and the regulations of the Department of Health and Human Services (DHHS). The Program is committed to advancing responsible conduct in research, ethical treatment of human research subjects, and ensuring that the right of every human being to voluntary, informed consent to research is respected.

The purpose of the UofL IRBs is to:

1. Approve, modify (to secure approval), or disapprove all human research conducted by the organization,

[2] HIPAA regulations – 45 CFR 160, 162, and 164

2. Suspend or terminate research not conducted in accordance with the regulations, statutes and principles or IRB's requirements mentioned above or when unanticipated problems occur,
3. Observe, or to have a third party observe, the consent process,
4. Observe, or have a third party observe, the conduct of the research, and
5. Serve as the Privacy Board for the University of Louisville.

The Human Subjects Protection Program serves its purpose by:

1. Administratively supporting the University's Institutional Review Boards,
2. Reviewing all research involving human research subjects before it is initiated,
3. Working to protect the rights and welfare of human research subjects by fostering and advancing the ethical and professional conduct of persons and organizations that engage in research with human participants,
4. Providing education to researchers, research staff and the public,
5. Conducting periodic reviews of research involving human subjects.

Prohibition against Others Using IRB Approval Authority or Using Undue Influence

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

To help forestall undue influence of IRB members, the IRB preserves the anonymity of members assigned as reviewers to specific protocols or protocol events.

Any IRB member or staff who believes that they have been subject to inappropriate influence should report this immediately to the IRB chair or the Director, Human Subjects Protection Program, who will report the attempt to influence to the Executive Vice President for Research and Innovation (EVPRI). The EVPRI will investigate, or have investigated, the attempt to influence and determine an appropriate response to the attempt based on penalties similar to those outlined in the University's Administrative Sanctions for Violations of University of Louisville Research Policies. This policy may be found on the EVPRI Home Page (http://louisville.edu/research) under Policies and Procedures.

The types of response to attempts to unduly influence the IRB are determined as appropriate to the situation, by either the Director, Human Subjects Protection Program or the Executive Vice President for Research and Innovation.

The IRB has the statutory and institutional authority to take any action necessary to protect the rights and welfare of human research participants involved in research. For example, the IRB assesses suspected or alleged protocol deviations, participant complaints, or violations of external regulations or University of Louisville policies. The IRB has the authority to suspend or terminate the enrollment or ongoing involvement of research participants in research as it determines necessary for the protection of those participants. The IRB also has the authority to observe or monitor any human research to whatever extent it considers necessary to protect research participants, (45 CFR 46.109, 46.112, and 46.113).

Decisions of the IRB

IRB approval is always necessary before a research project involving research participants may begin. An IRB decision to not approve a human research project, or require modifications as a condition for approval, cannot be overturned by any University of Louisville official or University of Louisville committee.

The IRB must provide the investigator with a written statement of the reasons for not approving proposed research and must give the investigator an opportunity to respond in person or in writing. The IRB must carefully and fairly evaluate the investigator's response in reaching a final determination.

If an investigator has concerns with respect to procedures or decisions of the IRB, the investigator may discuss his/her concerns with the Associate Vice President for Research and Innovation with the understanding that no University official or committee may approve a protocol that has not been approved by the decision of one of the IRBs, nor apply undue pressure on the IRB(s) to reverse a decision. Investigators must first put their concern(s) in writing to the Associate Vice President for Research and Innovation, who may use his or her sole discretion to determine the process for responding to an investigator's concern, including:

- Notifying the IRB of the concern and requesting a response and relevant information from its records
- Submitting the concern to mediation if the investigator agrees to participate
- Appointing a fact-finder to review the matter and report back
- Seeking assistance from consultants or internal administrative units such as the Office of Audit Services or Office of University Counsel.

Responsibilities to Regulatory Agencies

The IRB must comply with the requirements of all relevant federal regulatory and compliance enforcement agencies or offices, including OHRP and FDA, as well as relevant agencies of the Commonwealth of Kentucky.

6.2 Review of IRB Composition, Members and IRB Chairs

AAHRPP Std./ Element	Description
II.1.B	The IRB has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB are periodically reviewed and adjusted as appropriate.

Each IRB has a qualified Chair, members and staff whose membership and composition is reviewed and adjusted annually by the HSPPO Director in consultation with the EVPRI and the IRB Chair(s). This review ensures that individual IRB Chairs and members have the knowledge, skills and abilities appropriate to their respective roles and perform their responsibilities in an acceptable manner.

University of Louisville policy requires that the IRB be constructed according to DHHS regulations and FDA regulations (45 CFR 46.107 and 21 CFR 56.107). Additionally, the IRB shall include a nonscientific IRB member, educated and with experience in unambiguously nonscientific areas. These individuals may not have meaningful scientific or medical training or experience. Health professionals, regardless of discipline, may not be considered nonscientists. At least one nonscientist IRB member must always be present to have a quorum.

Appointment of Members and Length of Service

IRB members are nominated from a variety of sources, including previous IRB members, division chiefs, department chairs, compliance administrators, faculty, hospital pharmacy and nursing staff, research laboratories, senior administrative IRB staff, and various public groups. Consideration is given to balancing race, gender, expertise, and cultural backgrounds. People with active licensure from various clinical disciplines are sought.

A background knowledge of and current familiarity with affiliated institutional concerns helps ensure that the local research context is brought to IRB deliberations. Sensitivity to issues such as community attitudes and international dimensions is valued. Newly identified nominees are contacted by the HSPPO Assistant Director (or delegate) about

their willingness to voluntarily serve on the IRB and their availability for the coming year. When a nominee agrees to serve on the IRB, his or her CV and any relevant correspondence are reviewed by the HSPPO Director and the appropriate IRB Chairs/Vice Chairs.

AAHRPP Std./ Element	Description
II.1.C	The University of Louisville has and follows written policies and procedures to separate competing business interests from ethics review functions.

To avoid any possible conflicting interests or influence on IRB determinations due to competing business interests, individuals who are responsible for development activities (including raising funds), or are in a position to influence programmatic and budgetary decisions may not serve as IRB Members. See Chapter 6.7.

University of Louisville IRB members or alternates (hereafter referred to collectively as members) will be appointed by the EVPRI in accordance with 45 CFR 46 and 21 CFR. Committee members, chairs, and vice-chairs serve at the discretion of the EVPRI.

IRB members are appointed utilizing the following criteria:

1. Each IRB will consist of at least five and not more than twenty-one voting members, with varying backgrounds to promote complete and adequate review of human research activities commonly conducted by the institution.

2. Each IRB will be sufficiently qualified through the experience, expertise, and diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

3. No IRB will consist entirely of men or entirely of women. Qualified persons of both sexes will be considered so long as no selection is made to the IRB only on the basis of gender.

4. Each IRB will consist of members of various professions including at least one scientist, one nonscientist, and one member who is not otherwise affiliated with the institution, and who is not part of the immediate family of a person who is affiliated with the institution (community member).

5. No IRB will consist entirely of members of one profession. Each IRB will consist of members of various professions including at least one scientist, one nonscientist, and one member who is not otherwise affiliated with the institution, and who is not part of the immediate family of a person who is affiliated with the institution (community member).[3]

After an extensive review of a potential member's education, experience and other characteristics that might add diversity to the IRB, a new IRB member is formally appointed by the EVPRI. Members serve five-year renewable terms (from date of appointment). At the conclusion of the calendar year, members' contributions are evaluated by the IRB Chair with the HSPPO Director and HSPPO Assistant Director. If their service is satisfactory, and continued membership is mutually desired, they are eligible for reappointment. All members may be re-appointed at the end of their terms without lapse in service.

Members are expected to attend IRB meetings on a regular basis, serve as primary reviewers for research within their areas of expertise, and serve as general reviewers on all research. Members may also be asked to participate in

[3] 45 CFR 46.107, 21 CFR 56.107

subcommittees, ad hoc committees, audits, and education, as long as there is no conflict of interest with their IRB responsibilities or their other personal or professional roles.

Once appointed, the IRB member will complete the following forms on an annual basis:

1. An Attestation and Disclosure Form (ADF); and
2. A Non-disclosure agreement (NDA).

The IRB members will be reminded to complete the ADF by electronic reminder messages sent through the IRB electronic submission system. Annual NDAs will be emailed to the members and IRB staff will ensure that the NDAs are signed and returned.

Appointment of IRB Chair and Length of Service

IRB Chairs are nominated from a variety of sources, including previous and current IRB members, division chiefs, deans, department chairs, and compliance administrators. In addition to the characteristics sought in an IRB member, these individuals possess demonstrated skills in leadership and group process. Typically, they have served on an IRB previously.

IRB Chairs are formally appointed by the EVPRI. Chairs serve five-year renewable terms. At the conclusion of the IRB calendar year (and on an interim basis if needed) the IRB Chairs' contributions are evaluated by the HSPPO Director. If their service is satisfactory, and their continued service is mutually desired, they are eligible for reappointment.

These individuals are respected, active members of the University community who are well informed in regulations relevant to the use of human subjects in research. The term of service is at the discretion of the EVPR. Whenever the chair or vice chair is not available to conduct IRB business, the chair or vice chair may designate a board member to assume his/her responsibilities during the period of his/her absence.

IRB chairs and vice chairs should have experience in conducting human subjects research, have thorough knowledge of federal regulations and state statutes concerning human subjects research, and understanding of University of Louisville research policies, conflict of interest policies and knowledge of ethical guidelines governing research.

Responsibilities of the chair, or their designee, include: determining the type of review (exempt, expedited, full board), assigning primary reviewers, running full board meetings, reviewing minutes prepared by staff, reviewing specific revisions to protocols/consent documents that are required as conditions of approval, and reviewing local serious adverse event reports and any reports of unanticipated problems involving risks to subjects or others. In addition, they serve as a resource for investigators and IRB members regarding issues related to University, state and federal policies on human subjects' research.

The IRB Chair works with IRB members, institutional officials, and investigators to ensure that the rights and welfare of research participants are adequately protected.

Compensation of IRB Members

IRB Chairs' departments receive a percentage of their salaries to offset the time dedicated to IRB duties. IRB members who are affiliated faculty or staff members generally do not receive monetary compensation for their service on the IRB. However, it is recognized that service on the IRB requires a significant investment of time for all members.

IRB members who are not otherwise affiliated with the University of Louisville or its collaborating institutions who are not compensated by their sponsor or employer will be paid for their service on the IRBs at the rate of $25.00 per hour, unless waived by the committee member. As stated in OHRP guidance, compensating unaffiliated members in this way does not create an affiliation or cause a conflict of interest.

Alternate IRB Members

Alternates replace regular IRB members who are unable to attend convened meetings of the IRB. They are required to have the same qualifications and characteristics of expertise and diversity as the regular IRB members for whom they substitute. When an alternate substitutes for a regular member, the alternate member receives the same materials that the regular member would have access to through the Electronic Submission System (ESS).

IRB membership rosters specify which regular member each alternate member is qualified to replace. The expertise or qualifications of alternate members are similar to those of the regular member they replace, and in some case, alternate members are able to represent similar interests or a specific vulnerable population. Terms of appointment, length of service, and duties are exactly as for regular IRB members. Alternate members must adhere to the same conflict of interest standards and documentation requirements as regular IRB members.

If an alternate member attends a convened meeting at which his or her regular member is in attendance, one of them does not vote. Ad hoc substitutions for regular or alternate IRB members are not permitted.

The HSPPO Director and HSPPO Assistant Director serve as alternate members of both the Biomedical IRB and the SBE IRB.

Administrative Designees

The HSPPO IRB Analysts perform pre-review of all items submitted to the IRB for review and approval. They are considered Administrative Designees. Administrative Designees may also request administrative modifications to submitted materials prior to assignment of submissions to IRB Chairs, Vice Chairs and IRB reviewers.

The Analysts may perform administrative approvals for the following items:

1. Study Personnel Changes (excluding PI changes)
2. Study closure to enrollment (exception- if due to major safety issue)
3. Study closure (exception-if due to acts of non-compliance)
4. Study closures when PI withdraws submission pre-IRB approval
5. Changes to HIPAA documents requested by HIPAA reviewer when the Primary Reviewer has “approved as submitted”
6. Grammar/formatting changes in documents that do not change the content or meaning of the document
7. Additions/Deletions of study sites
8. IRB Authorization Agreements (IAA)**.** These are processed in coordination with HSPPO Director and/or Assistant Director, including amendments for IAA continuing review letters where another institution is the IRB of record.
9. Enrollment changes (increases/decreases)
10. DSMC letters that indicate no changes
11. Submissions that the reviewer “approves with changes” and the only requested change is adding specific section(s) of the IRB template language (such as the 1099 language, Clinicaltrials.gov language, or other verbatim section of the current IRB template).

Ex Officio IRB Members

An ex officio member is designated as an IRB member by virtue of that individual’s office. Some ex officio members serve on other University of Louisville compliance committees and may provide expertise to IRB members. Ex officio members may participate in the IRB deliberations to provide information and expertise as requested by the IRB. Ex officio members are expected to adhere to the same conflict of interest standards and documentation requirements as regular IRB members and alternates. Ex officio members may not vote on any IRB action or determination, and for this reason are sometimes referred to as “non-voting” members.

The Biomedical IRB accepts permanent ex officio representatives from the following areas:

Office of University Counsel
Institutional Biosafety Committee
Radiation Safety Committee
Institutional Animal Care and Use Committee (IACUC)
Research Officials from Affiliated Hospital Organizations

The SBE IRB accepts permanent ex officio representatives from the following areas:

- Office of University Counsel
- Research Officials from Affiliated Hospital Organizations where behavioral research sites are located
- Jefferson County Public Schools

The IRB may accept additional permanent ex officio members with the agreement of the IRB Chair and the HSPPO Director.

Removal of IRB Members
Members of the IRB may be removed before the end of their term if their participation in IRB activities is deemed to be inadequate, inappropriate, or damaging to the reputation of the University and its research activities. Removal may be initiated by the EVPR, at the recommendation of the chair of the IRB on which the member participates, or the chair of the member's department or dean of the college or school the member represents.

Liability Coverage for IRB members
University of Louisville provides liability coverage under its insurance programs for IRB members acting in good faith in the performance of their IRB duties. The University of Louisville Office of Risk Management provides liability coverage of volunteer individuals, including community IRB members. All University of Louisville, University-related faculty, staff, and students are likewise covered in their capacity as employees and students.

6.3 IRB Member Duties and Responsibilities

Duties of members include reviewing human subject application materials in advance of meetings and being prepared to discuss issues related to human subjects protections, serving as primary reviewer when requested by the chair, and having an understanding of the specific requirements of human subjects regulations. Member duties include:

1. Protecting the rights and welfare of research subjects.

2. Determining that risks to subjects are minimized.

3. Ensuring that the investigators:

    a. use procedures that are consistent with sound research design and that do not expose subjects to risk,

    b. whenever appropriate, use procedures already being performed on the subjects for diagnostic or treatment purposes, and

c. ensuring that the investigator follows a procedure for properly documenting informed consent (IRB members are encouraged to review chapter 4, Informed Consent in the University of Louisville Investigator's Guide for a comprehensive review of the informed consent process).

4. Determining that risks to the subjects are reasonable in relation to the anticipated benefits to subjects, if any, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB member should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB member should not consider possible long-range effects of applying knowledge gained in the research.

5. Determining that selection of subjects is equitable. In making this assessment, the following should be taken into account:

   a. The purpose(s) of the research and the setting in which it is conducted.

   b. The IRB members should be particularly cognizant of special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, cognitively or mentally impaired persons, or economically or educationally disadvantaged persons.

   c. Women and members of minority groups and their subpopulations must be included in all clinical research, unless a clear and compelling rationale and justification establishes to the satisfaction of the IRB that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances may be made based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research.

   d. The inclusion (recruitment process) of women and members of minority groups and their subpopulations must be addressed in developing a research design or contract proposal appropriate to the scientific objectives of the study/contract. The research plan/proposal should describe the composition of the proposed study population in terms of sex/gender and racial/ethnic group, and provide a rationale for selection of such subjects. Such a plan/proposal should contain a description of the proposed outreach programs for recruiting women and minorities as participants.

6. Determining if the informed consent is adequate and contains all other federally or locally mandated elements, and if not, request clarifications and changes in the consent form in order to adequately explain the purpose of the research, the risks and benefits entailed therein.

7. Determining that the research plan makes adequate provision for ensuring the safety of the subjects.

8. Determining that there are adequate provisions to protect the privacy of subjects and to maintain the privacy of the subjects and confidentiality of the data, in accordance with the DHHS and FDA regulations.[4] Investigators who conduct research under the direction of the University of Louisville must develop a plan for each protocol submitted to protect the privacy and confidentiality of subjects. The conditions for maintaining confidentiality of the subjects and the research records are required for the life of the data. The assigned protocol reviewer is responsible for assessing the efficacy of the plan.

[4] 45 CFR 46, 160, 164 and 21 CFR 50

9. Ensuring additional safeguards are in place to protect the rights and welfare of subjects that are likely to be vulnerable to coercion or undue influence, such as children, students, prisoners, pregnant women, cognitively or mentally impaired persons, or economically or educationally disadvantaged persons.[5,6]

10. Before the IRB meeting, the IRB member should:

    a. Review all required documentation in the application submission package before the assigned project(s) is/are presented.
    b. Discuss any questions about the assigned projects with the investigator, other IRB members, or consultants prior to the IRB meeting.
    c. Decide whether the investigator should attend the meeting to discuss any problems or concerns noted with the project.
    d. Determine if specific changes are needed in the application, protocol or consent form, and come to the meeting with recommended wording to be transmitted to the investigator.

As soon as deemed appropriate by the IRB chair, the committee member may prepare and present initial submission reviews at full-committee meetings, review and present continuation and review materials at full-committee meetings, present local serious adverse event reports or reports of unanticipated problems at full-committee meetings, and recommend any changes, additions, deletions or actions in any of the above.

6.4 Scientific and Scholarly Expertise of IRB Members

Wide-ranging scientific or scholarly expertise among IRB members allows the IRB to review the broad variety of research in which University of Louisville investigators are engaged. These policies and procedures require IRB members to be knowledgeable about all relevant regulatory requirements, and to strive to remain impartial and objective during protocol review, deliberation and voting. The IRB includes several members who are particularly knowledgeable about research ethics and the vulnerable research participants included in University of Louisville research.

The IRB uses a “primary reviewer” system. The HSPPO Assistant Director (IRB Administrator) or Senior IRB Analysts, in consultation with the IRB Chair where appropriate, assign protocols to primary reviewers, based on each individual’s scientific, scholarly, professional, or clinical expertise. Primary reviewers must have the relevant expertise to conduct an in-depth review of the protocols to which they are assigned. If the IRB administrator cannot identify a primary reviewer with the appropriate scientific or scholarly expertise, the IRB administrator arranges for expert consultation and will not place the protocol on an agenda until appropriate expertise is made available. Primary reviewers are expected to conduct an in-depth review, and it is the responsibility of primary reviewers to notify the IRB Chair or IRB staff should they feel unqualified or unable to do so. In such cases, the IRB Chair will assign primary review responsibilities to another member who is appropriately qualified or obtain consultation from one or more experts outside the IRB.

When the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, the review process includes one or more individuals who are knowledgeable about or experienced in working with these participants (children, pregnant women, adults unable to consent, students, etc.). The IRB staff reviews each application to determine whether it involves participants vulnerable to coercion or undue influence, and considers the participant population when assigning reviewers.

The IRB is constituted to possess and make use of collective knowledge of applicable regulatory and legal requirements; knowledge of professional standards and practices; knowledge of the local research context and research sites, and their capabilities and limitations; knowledge of community standards and attitudes; scientific, scholarly, clinical, and professional expertise; racial, ethnic, and cultural diversity; and representation of participants’ perspectives.

[5] 45 CFR 46.111(a)
[6] 21 CFR 56.111(a)

6.5 Obtaining Additional Expertise – Consultants and Ad Hoc Reviewers

The IRB Chair or IRB staff reviews the proposed convened meeting agenda and determines whether the IRB has the required expertise to review upcoming research. If not:

- The HSPPO Assistant Director (IRB Administrator), in consultation with the IRB Chair, will invite individuals with competence in the specific areas needed to assist in evaluating issues that require expertise beyond or in addition to that available on the IRB.

- On an as-needed basis, an IRB primary reviewer may invite individuals with competence in special areas to assist in evaluating specific issues.

Reasons for seeking additional or special competence from outside experts may include (but are not limited to) the need for additional scientific, clinical, or scholarly expertise; the need for particular knowledge and understanding about potentially vulnerable populations of subjects; the desire to ensure appropriate consideration of race, gender, language, cultural background, and sensitivity to such issues as community attitudes.

The HSPPO Assistant Director (IRB Administrator), or the IRB Chair makes initial contact with a proposed consultant and notifies the consultant of the IRB member conflict of interest policy. When a consultant is used, that fact, and the pertinent information gained from the consultant's assessment, is documented at the time of the protocol discussion, and recorded in the IRB minutes. In some cases, a consultant may provide the IRB with a written report of his or her assessment which is kept with the protocol file. The IRB staff can assist in making the consultation arrangements and in obtaining the required conflict of interest documentation.

All consultants, internal or external to University of Louisville University, must comply with the IRB conflict of interest policy. They are not considered ad hoc IRB members, and cannot vote with the IRB.

6.6 IRB Member, IRB Staff, and Consultant Conflicting Interest

AAHRPP Std./ Element	Description
II.1.D	The IRB has and follows written policies and procedures so that members and consultants do not participate in the review of research protocols or plans in which they have a conflict of interest, except to provide information requested by the IRB.

See 45 CFR 46.107(e); 21 CFR 56.107(e).

IRB Member's Disclosure of a Conflicting Interest

Conflicting Interests may be declared when:

- Protocols and reports are first received by members assigned to review;
- During discussion and voting in convened meetings; and
- When consultants are asked to advise the IRB

This policy applies to all projects reviewed by the IRB, regardless of whether the project is exempt or considered during full Board review, expedited, or continuing review. This policy also applies to reviews of non-compliance reports and unanticipated problems involving risks to participants or others.

IRB Intake procedures take into account conflicts of interest when assigning new protocols to an IRB, such as when any IRB member is named in the research protocol or has a spousal relationship with any research personnel.

IRB members who realize they have a conflicting interest when they are first assigned a protocol or report for review must notify the IRB staff or IRB Chair immediately so that the protocol can be reassigned.

IRB members review the Agenda before a convened meeting with the issue of conflicts in mind. Any conflicting interest for protocols to be voted on must be reported to the IRB Chair or HSPPO Director before the meeting whenever possible.

The IRB Chair begins each meeting with a reminder that proceedings are confidential. This is followed by a reminder of the requirement that each member must disclose any conflicting interest and recuse him or herself from the discussion of and vote on the project by leaving the room, except if the member is providing information at the IRB's request.

Consultant's Disclosure of a Conflicting Interest

The definition of conflicting interest as defined in the Guidelines for IRB Members on Conflicting Interest extends to any consultant who may be asked to review a protocol. The IRB Administrator who contacts a consultant to enquire about review of a project is responsible for asking if the consultant has a conflicting interest in the project. If such an interest exists, then the protocol will not be assigned to the consultant.

If the consultant is internal to the University of Louisville, the consultant will complete an Attestation and Disclosure Form (individual conflict of interest) within the IRB ESS. If the consultant is external to the University of Louisville, an ADF will be sent to the consultant via email. The consultant will answer the same questions and provide the same information that a regular IRB member would be required to make in their ADF. The consultant's ADF must be completed and returned to the HSPPO prior to the contracted consultant's review. A statement will be added to the minutes indicating that a completed ADF has been received for the consultant and it is on file with the HSPPO.

If a consultant with a conflicting interest is the only appropriate resource for the IRB, (e.g., is the only scientist with sufficient technical understanding of the project) and if that consultant has been asked to provide information to the IRB, then the conflict of interest must be disclosed to the IRB members reviewing the protocol or present in the convened meeting where the information is presented. Such a consultant is excluded from discussion except to provide information requested by the IRB, and must leave the meeting room during discussion and voting.

IRB Staff and Conflicting Interest

IRB Staff must not participate in the review of research protocols, and must not make exempt determinations for research protocols in which they have a conflict of interest. IRB staff who realize they have a conflicting interest when they are first assigned a protocol or report for review must notify their supervisor immediately so that the protocol can be reassigned.

The University of Louisville Attestation and Disclosure Form is completed annually by IRB Staff who are involved in protocol review.

6.7 Separating Competing Business Interests from Ethics Review Functions

AAHRPP Std./ Element	Description
II.1.C	The University of Louisville has and follows written policies and procedures to separate competing business interests from ethics review functions.

The University of Louisville recognizes that officials who administer research programs, and individuals who are responsible for development activities (including raising funds), may represent competing business interests, or be in a position to influence programmatic and budgetary decisions and exert undue influence on IRBs or individual IRB members. To avoid such influence on IRB determinations, the Executive Vice President for Research and Innovation,

School Deans, Institute or Center Directors and other University of Louisville officers will not serve as voting members of the IRBs, unless there are compelling reasons to do so. Such reasons must be justified in writing and include specific measures to manage any conflict of interest or the possibility of undue influence.

Due to their supervisory and institutional decision-making functions, these individuals frequently encounter conflict of interest situations beyond those faced by most covered individuals. They often do not directly conduct sponsored activities, teach or conduct outreach in their administrative capacities but may be in a position to influence how these activities are conducted and reported. Their external interests and activities must be disclosed to prevent any real or perceived institutional conflicts of interest.

Thus, the institutional leaders, as described above, do not serve as members on the IRB or carry out day-to-day operations of the research review process.

6.8 Assessment and Evaluation of the IRB

AAHRPP Std./ Element	Description
II.1.B	The IRB has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB are periodically reviewed and adjusted as appropriate.

The composition and membership of each IRB is evaluated annually by the HSPPO Director and the IRB Chairs and is adjusted as needed to ensure appropriate knowledge of applicable regulatory and legal requirements; knowledge of professional standards and practices; knowledge of the local research context and research sites and their capabilities; knowledge of community standards and attitudes; scientific, scholarly, clinical, and professional expertise; racial, ethnic, and cultural diversity; and representation of participants' perspectives. Due to the increased complexity of human research protocols submitted, this often results in adding members. The composition of each IRB may change as often as needed. Education, training and periodic evaluation of IRB members, IRB Chairs, and IRB staff is discussed in Chapter 4.

6.9 Relationships with Other Affiliated Institutions

The University of Louisville IRBs coordinate IRB reviews with the affiliated institutions listed below. None of these affiliated institutions are a formal part of the UofL IRB structure, but there is communication between the institutions regarding status of review and/or conditions of approval. These institutions all have their own Federal-wide Assurances and they name the University of Louisville IRBs as IRBs who may review research for their facilities.

Jefferson County Public Schools (JCPS). When possible, a representative of the Jefferson County Public Schools serves on the SBE IRB. The SBE IRB may provide informal expertise and consultation to the JCPS IRB.

KentuckyOne Health (dba Jewish Hospital St. Mary's Healthcare and University of Louisville Hospital). The University of Louisville's two IRBs provide IRB review and oversight for human subjects research conducted at Jewish Hospital sites by University affiliated investigators.

The KentuckyOne Health Office of Research Compliance (KHORC) reviews each study for completeness and issues a site approval letter for all research approved for their facilities. Investigators may not initiate research at the site until site approval is given.

Norton Healthcare, Inc. The University of Louisville's two IRBS provide IRB review and oversight for all human subjects research conducted at Norton Healthcare, Inc. sites by University affiliated investigators. Research studies by Norton Healthcare affiliated investigators (not otherwise UofL affiliated) are reviewed and overseen by an external IRB.

6.10 Review of Research by Other University Committees

The IRB is required at times to participate with other University committees that also have responsibility for the ethical oversight of research within the HSPP. In some cases, the approval of another University of Louisville body may be required prior to or in addition to IRB review.

Institutional Biosafety Committee: Protocols involving biosafety materials and requiring review by the Institutional Biosafety Committee (IBC) must be reviewed and receive an approval letter in addition to review by the IRB. The HSPP Director, Assistant Director and a senior member of the IRB staff are ex-officio members of the IBC. A senior member of the IRB staff attends the IBC meetings and receives communications directly from the IBC regarding submitted protocols. The Biological Safety Officer and Biosafety Specialist (from the Department of Environmental Health & Safety) are ex officio members of the biomedical IRB and attend biomedical IRB meetings.

The IBC is administratively located in the DEHS and ensures that research involving recombinant DNA complies with the National Institutes of Health (NIH) guidelines. All such research that is not exempt from NIH recombinant DNA guidelines must be registered with the University of Louisville DEHS. These registration documents are reviewed and approved by the IBC prior to initiation of research. The IBC notifies the IRB of its approval of projects using recombinant DNA, but deliberations of the IBC are not shared with the IRB unless there are specific subject protection issues raised by the IBC. IRB approval is contingent upon IBC approval when the research involves gene therapy.

Radiation Safety Committee: If a study involves any radioisotopes or radiation-producing machines, the Radiation Safety Committee must certify that it has reviewed a protocol using radioisotopes or radiation machines and recommends it for approval. Without this approval, a study which employs these modalities will either be tabled to a future convened meeting, or will be approved contingent on Radiation Safety Committee recommendation for approval.

If RSC review is completed after the IRB review, the IRB chair reviews any RSC comments. If the chair believes the suggested changes are appropriate and qualify as minor modifications, the IRB chair reviews these through an expedited process. If changes exceed minor modifications, the IRB chair refers the application back to the full board for review. If the chair determines that full-committee review is necessary, the HSPPO will notify the investigator and the RSC that the study has been placed on administrative hold until the concerns are addressed by the IRB.

6.11 Review by Other University Offices

Clinical Contracts Division (formerly Office of Industry Contracts): The Clinical Contracts Division (CCD) provides support services to faculty and staff conducting clinical trials and other research involving human subjects. The CCD supports research sponsored by industry, both nonprofit and for-profit organizations, as well as funded research that flows through third parties. This includes governmental flow-through if funding to the university is via industry sponsors and non- or for-profit organizations.

The CCD's support services include negotiation of contracts/agreements and the review and submission of proposals and applications. The IRB is notified once contracts are executed and IRB Compliance staff review the sponsored contracts to ensure research injury language presented in the executed contract matches the context of the language in the informed consent document(s).

Conflict of Interest Office: All investigator conflicting interest is managed via the Conflict of Interest Office (COI Office) and its associated Conflict Review Board (CRB). Information concerning Conflicts of Interest is shown within the integrated research administration system software utilized by the compliance units at the University of Louisville. The IRB will not approve a protocol until any disclosed COI has been reviewed and resolved by the CRB, and as appropriate, a plan or strategy to adequately eliminate, mitigate, or manage the conflict has been determined by the CRB.

Office of Sponsored Programs Administration (OSPA): Staff of the HSPPO and IRB may consult with the OSPA when questions arise concerning whether appropriate clearances have been received for the human subjects research involved in a grant application or award. Consultation is on an as-needed basis.

Office of Technology Transfer (OTT): Staff of the HSPPO and IRB may consult with the OTT concerning Material Transfer Agreements which may be associated with the shipment of blood, specimens, or data to another institution.

Privacy Office: Staff of the HSPPO and IRB members often consults with the University Privacy Officer on matters concerning the management of personal health information (PHI) as it relates to the enforcement of Health Insurance Portability and Accountability Act (HIPAA) of 1996 research regulations. Consultation is on an as-needed basis and may be initiated by the IRB, the HSPPO, or the Privacy Officer. Additionally, the HSPPO employs a HIPAA Analyst for review of submissions where HIPAA regulations apply. The HIPAA Analyst sends administrative modifications to the investigator for required modifications in authorizations or waivers.

Research Integrity Program: Staff of the HSPPO and the RIP share conflict of interest information as well as individual and institutional significant financial conflict of interest management plans. The HSPPO and RIP also work together and share information concerning possible research misconduct and violations of University of Louisville research oversight policies.

6.12 Relationships with Industry Sponsors and Other IND or IDE Holders

Unless specifically required by the FDA or requested by the sponsor, the IRB will not routinely provide written notification of IRB decisions to industry sponsors and other holders of INDs or IDEs (University of Louisville sponsor-investigators excepted). For FDA-regulated research, clinical investigators generally serve as the link between the IRB and the sponsor, and are required to do so by the FDA in compliance with their obligations as clinical investigators. This relationship is agreed to by investigators when they sign FDA Form 1572 (for drug and biologic studies) or an investigator agreement for device studies.

There are occasions when direct communication between the IRB and the sponsor may facilitate resolution of concerns about study procedures or specific wording in an informed consent document. The IRB staff may engage in such direct communication on behalf of the IRB when the IRB Chair or the HSPPO Director considers it desirable. The clinical investigator will be kept apprised of such communication.

The FDA indicates that direct communication between the sponsor and the IRB may be appropriate when the IRB does not accept a sponsor's Non-significant Risk (NSR) designation of a medical device (21 CFR 812.66). Direct communication between the sponsor and the IRB is required for the waiver of informed consent in planned emergency research relative to (a) the public disclosures required under 21 CFR 56.109(a)(7)(ii),(iii); or (b) disapproval of such a waiver under 21 CFR 50.24(e). See Chapter 5.11**.**

6.13 Chapter Definitions

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