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University of Louisville policies, procedures, and education programs help Principal Investigators (PIs) and all University of Louisville investigators carry out research studies in an ethical manner. In addition to following applicable federal, state, and local regulations, investigators follow ethical principles and standards appropriate for their discipline. In designing and conducting clinical trials, PIs follow Good Clinical Practice (GCP) guidelines defined by the Food and Drug Administration, and have the protection of participants’ rights and welfare as their primary concern.

The University of Louisville will allow faculty and staff of the University to act as a Principal Investigator (PI)/Program Director (PD) on an extramurally funded project.

If an individual is not a permanent employee of the University of Louisville, the term of appointment must be sufficient in length to complete the proposed project. Such individuals must obtain formal approval by the appropriate chair and/or dean to submit the application in the name of the University with assurances that adequate resources and supervision will be available for the project to be successful should it be funded. Gratis Faculty with research appointments who wish to conduct Human Subjects Research and act as a PI on a study may also require EVPRI approval. This is determined on a case by case basis and the final decision is made by the EVPRI.

In most circumstances, all paid and gratis faculty with research gratis appointments of the University, who conduct human subjects research associated with their appointment, must utilize the University's IRBs for review, approval and continued oversight of the research. In certain circumstances, individual or institutional conflicts of interest may require the utilization of an independent IRB. Requests for use of an independent IRB must be made to the EVPRI or the University IRB and approved by the EVPRI.

For additional information, OHRP has a list of Frequently asked questions (FAQs) about investigator responsibilities.
14.1 Identification and Management of Conflict of Interest

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<tr>
<td>III.1.B</td>
<td>Researchers and Research Staff identify and disclose financial interests according to organizational policies and regulatory requirements and, with University of Louisville, manage, minimize, or eliminate financial conflicts of interest.</td>
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PIs and research staff are expected to follow University of Louisville policies addressing the disclosure of conflicts of interest as described in Chapter 3.2 and the policies referenced therein.

Disclosures of potential conflicts of interest are reviewed and resolved by the Conflict of Interest Office. The IRB has the final authority to decide whether the potential conflict of interest and its management, if any, allows the research to be approved. See Chapter 3.3 and Chapter 6.1.

14.2 Sound Study Design

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<tr>
<td>III.1.C</td>
<td>Researchers employ sound study design in accordance with the standards of the discipline.</td>
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The significance of the research depends upon the validity of the results. It is unethical to put subjects at risk or to inconvenience them through participation in a study that may produce little or no reliable information. Regardless of the source of funding, it is the PI’s responsibility to judge the research design to be sound enough to meet its objectives before submitting the protocol for IRB review. The Protocol Application provides questions addressing the various considerations for sound study design. The Protocol Application also includes a description of the provisions for monitoring the data and reporting to the IRB and other entities (see Chapter 14.3 below).

In developing, or in evaluating the adequacy of, a research design involving investigational drugs or biological products, the PI should refer to the FDA Guidance Documents representing the Agency's current thinking on good clinical practice (GCP) and the conduct of clinical trials, and including selected guidelines of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (“ICH”), as published in the Federal Register on May 9, 1997.

The PI should also be familiar with the various types of control groups, their relative advantages and disadvantages, and the ethical issues associated with each control type, as outlined in the FDA guidance Choice of Control Group and Related Issues, published May 2001. Although directly applicable to FDA-regulated trials involving investigational drugs or biological products, many of the principles can be applied to clinical trials in general.

14.3 Detection of Harm, Minimization of Risks and Mitigation of Potential Injuries through Study Design and During the Course of the Research

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<tr>
<td>III.1.C</td>
<td>Researchers design studies in a manner that minimizes risks to participants.</td>
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Risks may affect physical, psychological, social, legal or economic well-being, including loss of privacy or breach of confidentiality. The PI must minimize risks at all times by using procedures that are consistent with sound research...
design and that do not expose participants to unnecessary risks, and whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.

When submitting a Protocol Application to the IRB, the PI must:

- Describe the potential risks.
- Include, where possible, a scientific estimate of their frequency, severity, and reversibility. If statistical incidence of complication and the mortality rate of proposed procedures are known, this data should be included.
- Explain how risks will be minimized.
- Justify the level of risk.
- Describe adequate provisions for monitoring the data during the conduct of the research to minimize risk to participants (see Chapter 9).

For proposed changes to the research, including any change to mitigate potential harm to participants, the PI must submit a protocol amendment to the IRB describing any resulting changes in the level of risk to participants, and explaining the risk level and potential benefits.

At Continuing Review, the PI must indicate whether there has been an increase, no change, or a decrease in the level of risk of the study. If the risk assessment has changed the PI must update the information in the Risks section of the protocol (if applicable) and informed consent document(s).

All studies considered more than minimal risk must include a data and safety monitoring plan which describes how the PI will oversee the participants’ safety and welfare and how unanticipated problems involving risks to participants or others, and adverse events will be characterized and reported.

### 14.4 Recruitment

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<tr>
<td>II.3.C</td>
<td>The IRB has and follows written policies and procedures to evaluate the equitable selection of participants.</td>
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<td>II.3.C.1</td>
<td>The IRB has and follows written policies and procedures to review proposed participant recruitment methods, advertising materials, and payment arrangements and determines whether such arrangements are fair, accurate, and appropriate.</td>
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<tr>
<td>III.1.E</td>
<td>Researchers and Research Staff recruit participants in a fair and equitable manner.</td>
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Pls are referred to the University of Louisville recruitment policies and procedures set forth in Chapter 10. The PI must provide all necessary information on the protocol application to allow meaningful review by the IRB of the recruitment process.

The PI is instructed to follow the guidance on recruitment, telephone screening (which includes phone script samples), and advertisements.

In selecting a population from which to draw participants for a particular research protocol, the PI must consider whether the choice of population results in an equitable distribution of the burdens and benefits of research. The PI must provide appropriate justification in the protocol application when recruiting participants among vulnerable...
Populations such as prisoners, pregnant women, economically and educationally disadvantaged, decisionally impaired, and homeless people. (45 CFR 46.111(a)(3); 21 CFR 56.111(a)(3))

University of Louisville students and employees
While employees and students are not vulnerable subpopulations per se, they may perceive that they are under some pressure from their superiors to agree to participate.

Investigators should detail any extra precautions taken to safeguard the rights and welfare of subject populations. In the case of using employees or a student “subject pool,” the IRB should ensure that consent for participation is sought only under circumstances, which minimize the possibility of coercion or undue influence, and that genuinely equivalent alternatives to participation are available.

Students
It is not uncommon for research projects to involve students, either those enrolled in a specific course or those enrolled in university programs. For instance, it is common practice for medical students to serve as subjects in biomedical research or for psychology students to serve as subjects in behavioral research. The obvious concern is that their participation may not be truly voluntary, because of a desire to appear particularly cooperative or highly motivated, or because participation in research is a course requirement.

Various procedures have been suggested to reduce the possible unintended coercion, while still permitting students to participate as subjects in research. These include:

- Posting IRB approved advertisements throughout the university to recruit subjects from a broad base of students.
- Offering students the opportunity to participate in “mass screenings” with follow-up with those who meet research criteria. It should be clearly stated that participation in the screening, as well as participation in the research is voluntary.
- Avoiding any personal solicitations by students, faculty, GTAs or RAs for fellow students or faculty.
- Providing a number of research projects from which to choose, if participating as a research subject is a course requirement.
- Providing alternative and equal methods for meeting course credit (or extra credit) requirements, such as attending a series of research presentations by faculty, writing a brief paper, conducting one’s own research.

Researchers need to exercise special caution when they desire students in a class to participate in research at the same time. Unintended coercion must be avoided by (1) ensuring that participation is voluntary, (2) that no one knows who is and is not participating, and (3) a time and effort equivalent alternative is provided for those who wish not to participate. Course grades should not be based on research participation. Basing grades on research participation is coercive and should be avoided.

A researcher should not have access to the data collected until after the class grades have been posted. Researchers often ask a colleague not affiliated with the research or class to administer the evaluation and hold the data until after the grades are posted.
Employees
University employees, such as faculty, office staff, lab technicians, and postdoctoral fellows, are similar to students in that they are vulnerable to perceived, even if not intended, pressures to appear cooperative and supportive of their supervisor’s work. Accordingly, many of the same procedures described above to reduce the likelihood of coercion in recruiting student volunteers apply equally to university employees.

Including Children as Participants
Children should be included in research, along with adults, unless there is a compelling rationale for their exclusion. Research that limits enrollment to children is generally not appropriate unless:

i. The condition or disease is limited to children, or

ii. The research seeks to obtain information on a test article or procedure that previously had been studied only in adults.

Appropriate Payment
Payments to research participants may not be of such an amount as to result in coercion or undue influence on the participant’s decision to participate.

Payments may not be provided to participants on a schedule that results in coercion or undue influence on the participant’s decision to continue participation. For example, payment may not be withheld as a condition of the participant completing the research. If the participant withdraws early, payment must be prorated to reflect the time and inconvenience of the participant’s participation up to that point.

14.5 Human Subjects Protection Resources

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<td>III.1.D</td>
<td>Researchers determine that the resources necessary to protect participants are present before conducting each research study.</td>
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Principal Investigators (PIs) are required to indicate in the Protocol Application whether they will have access to adequate resources to carry out the research. Resources, including space, personnel, services and equipment required for conducting the proposed research properly and safely, must remain available as needed throughout the research. The PI must provide information about the qualifications and number of study staff, personnel training, available facilities, and the time available to conduct and complete the research, and must demonstrate sufficient access to a population allowing recruitment of the required number of participants.

PIs should continually monitor the resources allocated for their research and notify the IRB if any change in the availability of resources may adversely impact the rights and welfare of participants.

In addition to IRB approval of the protocol, human participant research (including recruitment and enrollment) which is sponsored cannot begin until a contract has been finalized, or a grant award activated.

The principal investigator is also responsible for obtaining all additional approval(s) required, such as facility approval, before beginning their research.
A Review of Scientific and Scholarly Merit and a review by the PIs Department Chair are also required at the time of initial submission. This “sign off” is completed through the electronic submission system.

14.6 Consent Process

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<td>III.1.F</td>
<td>Researchers employ consent processes and methods of documentation appropriate to the type of research and the study population, emphasizing the importance of comprehension and voluntary participation to foster informed decision-making by participants.</td>
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Also see Chapter 12 on informed consent and assent.

Informed Consent is a Continuing Process

Informed consent is a continuing process whereby the investigator and research participant have an on-going dialogue about all aspects of a research study that might inform a participant’s decision to take part in the study, and their decision to continue their involvement as a participant. Although consent is given it may be withdrawn at any point. The informed consent process should be regarded as continuing throughout the duration of the research. The purpose of the consent process is to assure knowledgeable decision-making and voluntary participation.

This process generally includes:

- Bringing the research study to the notice of potential participants.
- Presentation and explanation by the investigator or delegate of the study and study activities to the participant or their legally authorized representative (LAR).
- Documentation of informed consent via a signed and dated written consent document.
- Ongoing discussions between the investigator and the participant regarding continued participation in the study.

The PI is expected to be familiar with:

- The informed consent policies in Chapter 12, including the criteria for a legally effective informed consent process, and any additional federal, state, and institutional requirements.
- The consent process information and consent form templates provided on the Human Subjects Research website.

The basic and possible additional consent requirements, and those specific to certain types of research activity (such as genetic testing, data and tissue repositories, and xenotransplantation), are addressed in Chapter 12.

Consent requirements for research involving vulnerable and other special populations - including consent from a legally authorized representative (LAR) – are described in Chapter 12.2. This addresses adults with impaired decision-making capacity, prisoners, children, pregnant women, fetuses and neonates, and University of Louisville employees and students.

The Consent Document

The Human Subjects Website provides consent form templates, which address the required elements of informed consent, as well as providing language for other situations, in which certain additional information may need to be disclosed to participants. For research involving children, an Assent Template is also provided.
To assist PIs in preparing consent documents comprehensible to lay persons (i.e., at approximately 8th grade level) a glossary of lay terms is also available on the website.

The IRB encourages and recommends the use of a full consent form, translated into the participant’s language whenever possible. In certain situations, the use of a ‘short form consent process’ may be permitted by the IRB, incorporating the use of a short form consent document translated into the participant’s language.

If the research involves extensive screening procedures, the PI may wish to develop a separate consent document that explains the screening procedures in detail and provides a brief summary of the underlying research. In such circumstances, screening could begin after the individual signed the screening consent form but before the signing of the main consent document, which would be signed only if the individual satisfied the screening criteria and was actually enrolled in the study.

See Chapter 12.1 for detailed information on consent documents, the long form, and the use of the short form consent process.

Providing Consent Process Information to the IRB
In the Protocol Application, the PI must:

- Describe the consent process in enough detail to allow for meaningful review by the IRB,
- Include the proposed written informed consent document(s) that address each of the elements of informed consent in the context of the research (unless the IRB waives the documentation requirement – see below), and
- Include any written material to be given to prospective participants to explain the nature of the research.

The PI is responsible for making all revisions to the proposed consent document as requested by the IRB. Any other change to the consent document must be submitted to the IRB for prior review and approval.

Requesting Waivers or Alteration of Consent Requirements
Under specific circumstances, the PI may request that the IRB grant a:

- Waiver or alteration of the consent process – i.e., the requirements for obtaining informed consent, or
- Waiver of documentation – i.e., the requirement to obtain a signature on a written consent document.

The requirements for these two options differ. Refer to Chapter 12.5 for explanation.

Obtaining Informed Consent
The PI is responsible for obtaining and documenting the informed consent of individuals who participate in research, unless the requirement to obtain and document informed consent is altered or waived by the IRB. No research procedures, including screening procedures to determine if an individual is eligible to enroll in the research, may begin until after the participant has signed the consent form, unless the IRB has approved a waiver or alteration of consent. Retroactive consent – i.e., consent obtained or documented after the participant has undergone one or more research procedures – is not acceptable.

The PI may delegate all or a portion of the informed consent process to others on the research team, such as sub-investigators or research coordinators. However, it is ultimately the responsibility of the PI to ensure that those individuals carry out their tasks properly and in accordance with regulatory and IRB requirements.
The PI must use the consent document currently approved by the IRB. The IRB approval stamp must appear on the consent document.

No participants should be involved in research prior to the IRB approval date, and no participants should be involved in research using a consent document whose approval period has expired.

The PI or their delegate should plan to discuss research with potential participants at a time when they are not under duress, and to allow sufficient time and opportunity to ask questions and to consider whether or not to participate in the research before agreeing to participate.

In discussing research with potential participants, the PI or their delegate:

- May not describe items or procedures under investigation as if they were known to be safe and effective as a treatment for the potential participant’s disease or condition, or as if they present a known advantage,
- May not understate the risks of the research, as there may be no countervailing benefits to participants.

The PI or their delegate is responsible for giving the participant a copy of the signed informed consent document, and for maintaining the original form.

**Obtaining Informed Consent in the Clinical Research Context - Special Considerations**

The distinction between treatment and research is especially important if the PI is also the potential participant’s attending physician, a situation that increases the risk of confusion. Thus, it must be clearly stated to the participant that they will be involved in research and that if randomization is involved, that this is also described.

The purpose of medical or behavioral treatment is to provide interventions designed solely to enhance the well-being of the patient or client. By contrast, research is designed primarily to develop generalized knowledge rather than to benefit each participant in the research. Research involves activities to test a hypothesis and draw conclusions, and any therapeutic benefit to the participants is secondary to the objectives of the research.

Research involving randomization of participants, whether to proven or experimental procedures, raises further issues. In these circumstances, the PI should ensure that each participant understands that the assignment will not be based upon the attending physician's clinical judgment as to which treatment may prove more beneficial to that participant, and may involve additional testing that would not be performed as clinical care.

**Consent Situations Requiring Prompt Reporting to the IRB**

Situations where informed consent is not properly obtained or not documented, and no corresponding waiver or alteration of the consent process has been granted by the IRB, may constitute noncompliance. Such circumstances may require reporting to the IRB. These include, but are not limited to:

- Involving an individual in research without first obtaining their informed consent and a signed informed consent document (unless the IRB has explicitly waived these requirements).
- Involving an individual in research using a consent form other than the current IRB-approved form.
- Situations where the PI believes informed consent documents have been lost, misplaced, or destroyed.

See also:

- Chapter 15.3 for information on reporting to the IRB
- **Guide-023-Events that Require Prompt Reporting to the IRB**
14.7 Response to Participants’ Requests for Information and Complaints

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<td>III.1.G</td>
<td>Researchers and Research Staff have a process to address participants’ concerns, complaints, or requests for information.</td>
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Requests for information
The PI and members of the research staff are required to respond promptly and adequately to all requests for information received from participants, prospective participants and their family members or designated representatives. In addition to providing information and answering questions that arise as part of the informed consent process, the PI must inform the participant that he/she is available to answer any questions that arise about the research in the future. The consent form must list the full name and contact information for the PI, sub-investigators, and other research study staff as appropriate. The consent form must also inform participants how to reach the IRB if they have any questions about their rights as research subjects (see University of Louisville consent form template for contact information language).

Complaints
The PI is expected to investigate and respond promptly to complaints, and to follow the proper procedure for addressing and reporting complaints to the IRB. A complaint is a formal or informal, written or oral, expression of dissatisfaction by the participant or the participant’s representative. Complaints that are not resolved promptly by the PI or member of the research staff must be reported to the IRB as follows:

- Complete and submit a Deviation/Violation/Misc Form to the IRB
- Include with the Form a brief description of the complaint and the circumstances in which the complaint was made and any action taken to date in addressing the complaint. Complaints are handled in accordance with the policies described in Chapter 3.7.

If the complaint is not directly related to the conduct or design of the research, the IRB staff may refer the complaint to the appropriate University of Louisville institutional official or committee. In circumstances in which the complaint is referred, the IRB staff should provide the participant with the name and contact information for the referral. On Continuing Review, investigators are required to list all complaints received about the research in the past year, whether or not they were previously reported to the IRB.

Privacy issues
If the complaint involves University of Louisville privacy practices, all documentation relating to the complaint must be retained for at least six years from the date of creation. If such a complaint cannot be handled promptly, the appropriate University of Louisville Privacy Officer should be notified.