In this chapter:

15.1 **Investigator Attestations**

15.2 **Qualification of Principal Investigators and Research Staff**
- Training in the Protection of Human Subjects and HIPAA
- Knowledge of Applicable Federal, State and Local Laws
- Knowledge of the Definition of Human Subject Research

15.3 **Events Reportable to the IRB**
- PI Responsibilities for Reporting Unanticipated Problems involving Risks to Subjects or Others
- Assessment by Principal Investigator

15.4 **Research Oversight**
- Oversight of Research Staff during Recruitment
- Selection of Study Participants
- Informed Consent
- Study Conduct
- Compliance with the IRB
- Progress Report and Continuing Review Application
- Closure Report (amendment)
- Confidentiality of Records and Personal Data
- Privacy Rule (HIPAA)
- Delegation of Research Responsibilities
- Special Considerations for the Oversight of Research Protocols in FDA-Regulated Drug or Device Studies

15.5 **Data Monitoring Plan (DMP)**
- Sponsor Responsibilities

**15.1 Investigator Attestations**
The protection of human participants in research is the shared responsibility of PIs, sponsors, and the IRBs; and the PIs are ultimately responsible for the safety and welfare of participants. When conducting research with human participants, the PI attests that the following statements are true, as part of the electronic submission of the IRB application:

1. The information provided in this application is correct.
2. If relevant, the grant document that I have forwarded to my funding agency is attached to this IRB submission and it accurately and completely reflects what is contained in the submission.
3. I will not begin my research until I have received written or electronic notification of final IRB approval.
4. I will not begin my research until I have received any other written or electronic notification of additional compliance approvals I may need (e.g., administrative approvals from sites or facilities, Industry Contracts, Institutional Biosafety Committee, Radiation Safety Committee, Jefferson County Public Schools, etc.)
5. I will maintain records of this research according to Federal and institutional requirements.
6. I will seek and obtain prior written or electronic approval from the IRB for any modifications in the proposal, including any changes in procedures, any changes in study personnel, and changes in informed consent language, applicable HIPAA documents, funding agencies, etc.
7. I will utilize the most recently approved (and stamped when required) IRB/Privacy Board document(s) for this study.
8. I will promptly report to the IRB any unexpected or otherwise significant adverse events or unanticipated problems or incidents that may occur in the course of this study.
9. I will report in writing to the IRB any significant new findings which develop during the course of this study which may affect the risks and benefits to participation.
10. I will comply with all IRB requests to report on the status of the study. This includes filing Progress Reports 8 weeks in advance of the study approval expiration.
11. If appropriate, I certify to the Privacy Board that I will not reuse/disclose PHI, to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which use/disclosure would be permitted by the HIPAA privacy regulations.
12. If appropriate, I certify to the IRB/Privacy Board that I will maintain, store, and/or transmit any sensitive information, including PHI, obtained during this study, on any electronic media (server, desktop computer, laptop, PDA/Smart phone, USB drive, DVD/CD or any other electronic storage media) in a manner consistent with the University of Louisville Information Security Policies and Standards.
13. If this is an industry sponsored study, I certify to the IRB that the research related injury language in the contract and the language included in the informed consent are consistent.
14. If this is an industry sponsored study, I agree to pay, or ask the sponsor to pay the initial and continuing review fees in a timely manner. I accept that my final approval letter will not be provided until the required fees are paid.
15. If these conditions are not met, I understand that the IRB can rescind its approval of this research and the research could be suspended or terminated.

15.2 Qualification of Protocol Directors and Research Staff

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<th>AAHRPP Std./Element</th>
<th>Description</th>
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<tr>
<td>III.2.A</td>
<td>Researchers and Research Staff are qualified by training and experience for their research roles, including knowledge of applicable laws, regulations, codes, and guidance; relevant professional standards; and the Organization’s policies and procedures regarding the protection of research participants.</td>
</tr>
</tbody>
</table>

Training in the Protection of Human Subjects and HIPAA

University of Louisville requires that PIs and other personnel involved in the design or conduct of a project confirm completion of training in the protection of human research participants. Individuals involved in the design or conduct of a project include co-PIs, research coordinators, professional staff, persons administering informed consent or surveys, post-docs, and students. Collaborating individuals operating under the University of Louisville’s FWA and third party (subcontract) research personnel or consultants must also comply with this education requirement.

University of Louisville employs the Collaborative Institutional Training Initiative (CITI) course as its training program. Required CITI training for investigations includes, but is not limited to, modules on the history and ethical principles of human subject research, basic IRB regulations and review process, informed consent, HIPAA regulations, and research with vulnerable participants. University of Louisville requires a refresher training course to be completed every four years. Completion of the required training is a condition for IRB approval of protocols, regardless of the project’s source of funding.
Knowledge of Applicable Federal, State and Local Laws

The HSPPO disseminates and makes available to the University of Louisville research community, via the Human Subjects Website and education programs, the following resources to promote knowledge about applicable Federal, State and organization policies for human subjects research:

- Guidances on topics affecting the conduct of research, such as informed consent, vulnerable populations, conflict of interest, reporting requirements, etc.
- Template consent forms and instructions that include federal, state and local requirements
- Electronic protocol submission system - with application questions intended to address required considerations
- Information and instructions on submitting protocols to the IRB
- References and links to federal, state and organizational requirements
- Contact information for IRB staff for assistance
- The University of Louisville Research Policy Handbook (RPH) is also available online

Where applicable, Kentucky State laws have been included in the HSPP Policy Manual and document templates. When University of Louisville investigators conduct research in states other than Kentucky, they are expected to be knowledgeable of and adhere to the laws of the state in which research is being conducted, as well as those of Kentucky. Investigators are advised to seek guidance from the IRB staff or Legal Counsel if they have questions as to the applicable laws.

Knowledge of the Definition of Human Subject Research

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<th>AAHRPP Std./Element</th>
<th>Description</th>
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<tbody>
<tr>
<td>III.1.A</td>
<td>Researchers and Research Staff know which of the activities they conduct are overseen by the Human Research Protection Program, and they seek guidance when appropriate.</td>
</tr>
</tbody>
</table>

Prior to submitting a protocol for IRB review investigators are instructed to consider whether their project meets the statutory definition of human subject research or clinical investigation contained in Guide-025-Is my Project Research? This provides guidance based on DHHS- (OHRP) and FDA specific requirements.

IRB staff is also available to assist investigators in determining if a project needs to be submitted for IRB review. If the proposed activity clearly does not involve "research" or “clinical investigation” and "human subjects", it does not require submission to the IRB. If there is any doubt as to whether an activity is human subject research, the investigator should contact the HSPP office, or submit a Non-Human Subjects Application to the IRB through the Electronic Submission System (ESS). See Chapter 3.1 and 3.2 for additional information on the definition of human subject research.

15.3 Events Reportable to the IRB

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<tr>
<th>AAHRPP Std./Element</th>
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<tr>
<td>III.2.D</td>
<td>Researchers and Research Staff follow reporting requirements during a research study in accordance with applicable laws, regulations, codes, and guidance; University of Louisville policies and procedures; and the IRB’s requirements.</td>
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</tbody>
</table>
**PI Responsibilities for Reporting Unanticipated Problems involving Risks to Subjects or Others**

PIs are responsible for reporting unanticipated problems involving risks to subjects or others (UPIRTSOS) and other reportable information to the IRB. For industry sponsored projects, PIs are responsible for maintaining contact with the sponsor, and receiving reports from the sponsor, and if applicable, the monitoring entity (e.g., DSMB, DMC) and reporting suspected UPIRTSOS and other reportable information to the IRB. For sponsor-investigator projects, the PI is solely responsible for reporting UPIRTSOS and other reportable information to the IRB. Routine, periodic reports (e.g., Data Monitoring Committee reports, annual progress reports) should be submitted to the IRB at Continuing Review.

**Assessment by Principal Investigator**

The PI is responsible for the initial assessment of whether an event is a UPIRTSO or other reportable information. PIs must assess each adverse event, whether received from a sponsor, monitoring entity or occurring on a sponsor-investigator project, and promptly report to the IRB, UPIRTSOS and other reportable information according to the guidance [Events that Require Prompt Reporting to the IRB (Guide-023)](https://example.com/).  

In all cases, UPIRTSOS that are deaths or life-threatening experiences (at University of Louisville or when University of Louisville is the coordinating institution in a multi-site study), must be reported within 5 working days from when the PI learns of the event.

**Reporting Assessed Events and Information**

For events required to be reported to the IRB, PIs should submit reports using the appropriate ESS Form (e.g Serious Adverse Event, UPIRTSO, Deviation/Violation/Misc.).
### Reporting Timeframes

<table>
<thead>
<tr>
<th>Reporting Category</th>
<th>When to Report</th>
<th>iRIS Form</th>
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<tbody>
<tr>
<td><strong>Local Adverse Events</strong></td>
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<tr>
<td>Local Adverse Event PI determines to be:</td>
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<tr>
<td>• Definitely, Probably, or Possibly related to the research intervention,</td>
<td>Report within 5 working days of UofL site awareness</td>
<td>Complete the Serious Adverse Event (SAE) Reporting Form within the iRIS system</td>
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<tr>
<td>• Serious, and</td>
<td></td>
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<tr>
<td>• Unexpected</td>
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<tr>
<td><strong>Unanticipated Problems (UPIRTSOs)</strong></td>
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<tr>
<td>Local Event PI determines to be:</td>
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<tr>
<td>• unexpected (in terms of nature, severity, or frequency), and related or possibly related to a subject’s participation in the research, and suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.</td>
<td>Report within 5 working days of UofL site awareness</td>
<td>Complete the UPIRTSO Reporting Form within the iRIS system</td>
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<tr>
<td><strong>Deviations/Violations/Misc.</strong></td>
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<td></td>
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<tr>
<td>Major Deviations/Violations/Misc.</td>
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<td></td>
</tr>
<tr>
<td>• The PI and/or study sponsor is responsible for determining if a deviation is major or minor</td>
<td>Report within 5 working days of UofL site awareness</td>
<td>Complete the Deviation/Violation/Misc. form in iRIS. Attach notification of deviation to the study sponsor (if applicable) in iRIS</td>
</tr>
<tr>
<td>• Note: Intentional deviation from the inclusion/exclusion criteria should be submitted prospectively and include a copy of the sponsor’s approval.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Minor Deviations/Violations/Misc.</strong></td>
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<tr>
<td>• The PI and/or study sponsor is responsible for determining if a deviation is major or minor</td>
<td>Report with the next continuation review application</td>
<td>Attach documentation with the continuation review application: These can be combined on one document (e.g. an excel file)</td>
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<tr>
<td><strong>External Safety Reports</strong></td>
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<tr>
<td>The majority of IND Safety Reports, MedWatch Reports do not need to be reported to the UofL IRB. The only reports that must be reported are those that reveal an unanticipated problem involving risks to participants and others. Some sponsors require submission of all reports to the board regardless of the nature of the event reported. If you are submitting to fulfill such a requirement, please indicate this in your submission.</td>
<td>Not Required</td>
<td>Other-Amendment</td>
</tr>
</tbody>
</table>

### Additional Examples Of Events That Require Reporting to the IRB

The following are additional examples of events that require reporting to the IRB:

- a) Changes made to the research without prior IRB approval in order to eliminate apparent immediate harm.
- b) Any accidental or unintentional change to the IRB approved research protocol or plan that involved risks or has the potential to recur.
- c) Any publication in the literature, safety monitoring report, interim result, or other finding that indicates an unexpected change to the risks or potential benefits of the research.
d) Any complaint of a participant that indicates an unanticipated risk or that cannot be resolved by the research staff.


f) Any other event appropriate to the local context.

**When Modifying the Protocol is Indicated**

An event or new information might prompt a protocol modification (amendment) – either initiated by the PI, Sponsor, or specified by the IRB after reviewing a report. When an event or new information requires a modification to a previously approved protocol (e.g., new side-effect in the consent form or suspension of enrollment) a modification must be submitted for IRB review, and must be approved by the IRB prior to implementation of the proposed changes. The only exception to pre-approval is for modifications necessary to eliminate apparent immediate hazard to the research participants; in this case, the PI must submit the modification to the IRB within 5 days following its implementation.

15.4 Research Oversight

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<tr>
<td>III.2.B</td>
<td>Researchers maintain appropriate oversight of each research study, as well as Research Staff and trainees, and appropriately delegate research responsibilities and functions.</td>
</tr>
</tbody>
</table>

The general principles stated here apply to all research, including behavioral/social science research.

**Oversight of Research Staff during Recruitment**

The PI is responsible for ensuring recruitment activities, whether undertaken by research staff or the PI, are via methods set forth in the protocol application and approved by the IRB. The PI must ensure that informed consent is obtained from each research participant before that individual participates in the research study. The PI may delegate the task of obtaining informed consent to another individual knowledgeable about the research, while retaining ultimate responsibility over the conduct of the study.

**Selection of Study Participants**

The PI must ensure selection of study participants is equitable and appropriate to the goals of the study. Adequate safeguards for the protection of participants during the recruitment and conduct of research must be set forth in the protocol application. See:

- Chapter 10.1 (Equitable Selection)
- Chapter 7.2 (Equitable Selection)
- Chapter 10.4 (Recruitment)

**Informed Consent**

PIs are responsible for assuring the quality of the informed consent process and for making sure that consent is obtained and documented before subject participation, unless waivers are granted by the IRB. For a detailed discussion of the informed consent process requirements and description of available templates and guidance, see Chapter 12-Informed Consent and Assent.
Study Conduct

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<th>AAHRPP Std./Element</th>
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<tr>
<td>III.2.C</td>
<td>Researchers and Research Staff follow the requirements of the research protocol or plan and adhere to University of Louisville policies and procedures and to the requirements or determinations of the IRB.</td>
</tr>
</tbody>
</table>

The PI is responsible for conducting the study in a manner that is scientifically and ethically sound and for ensuring the use of appropriate methods and correct procedures, according to the approved protocol. Any new information, modification, or unanticipated problem involving risks to participants or others must be promptly reported to the IRB (Chapter 15.3), and research participants must be informed of any change that may affect their willingness to participate.

The PI must assure that all personnel under his or her supervision are adequately trained and supervised and that research duties are delegated to individuals qualified to perform the assigned tasks. Any non-compliance must be reported promptly to the IRB as required in Chapter 3.6-Internal and External Report of Findings.

The PI is also responsible for the timely and proper administration of the research project. Beyond the scientific and clinical conduct of the study, responsibilities include:

- Compliance with federal, state, and local laws and University of Louisville policies, including disclosure of any potential conflict of interest
- Fiscal management of the project
- Training and supervision of postdoctoral candidates, students, and residents
- Compliance with the sponsor’s terms and conditions (e.g., non-disclosure of sponsor confidential information)
- Submission of modification and continuing review applications in a timely manner
- Obtaining approval for changes prior to implementation.

Compliance with the IRB

Federal regulations require that any research study involving human subjects be reviewed and approved by an IRB. IRB approval must be obtained before any recruitment or screening can take place.

It is the PI’s responsibility to submit a written protocol to the IRB for review. At submission, the obligations of the PI with respect to oversight of their research protocols and research staff during recruitment, selection of study participants, and conduct of the study according to the protocol as approved by the IRB are stated in the Protocol Application and must be agreed to by the PI for the submission to be accepted. The PI is responsible for ongoing adherence to the determinations and requirements of the IRB for the duration of the research.

The documents required for protocol submission are listed in Chapter 7. A detailed discussion of the roles and responsibilities of IRBs is presented in Chapter 6.

Progress Report and Continuing Review Application

PIs must submit protocols (other than those subject to 45 CFR 46.101(b) - Exempt research) for continuing review by the IRB before the expiration date of the protocols, and in sufficient time to ensure the non-interruption of studies.
Closure Report (amendment)
At the conclusion of the study, PIs involved in research approved under regular review (including student research with a faculty advisor) must submit a closure amendment to the IRB. This should be submitted to the IRB within 30 days of closure.

When a Principal Investigator terminates employment or association with UofL, he or she is obligated to submit a closure amendment to the IRB or transfer the protocol to another Principal Investigator via amendment.

Confidentiality of Records and Personal Data
PIs working with human subjects must safeguard the privacy of participants and protect the confidentiality of personal information:

- Safeguard mechanisms must be established, maintained, and documented throughout the research process.
- Sustained attention must be paid to maintaining confidentiality of research data in the design, implementation, conduct, and reporting of research.
- Full information about the privacy and confidentiality of data must be provided to prospective participants through the informed consent process.
- Unintentional breaches must be avoided by taking additional precautions in communication, administration and storage of information.

Privacy and confidentiality are addressed in Chapter 11.

Privacy Rule (HIPAA)
When conducting research that involves the use and disclosure of protected health information (PHI), the PI must abide by the applicable HIPAA policy of the University of Louisville and facilities where the research is being conducted in order to account for disclosures of PHI when an individual requests such accounting. See Chapter 11.3

Delegation of Research Responsibilities
PIs may delegate research responsibility. However, PIs maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility. The conduct of a study usually requires the involvement and contribution of other individuals under the direction of the PI, based on their qualifications and capabilities. In delegating study-specific tasks and responsibilities to other members of the research team, the PI must ensure that those assuming a duty are well trained and competent.

Special Considerations for the Oversight of Research Protocols in FDA-Regulated Drug or Device Studies
FDA regulations and guidance specify the responsibilities of sponsors (and their investigators) using FDA test articles. [21 CFR 31 Subpart D; 21 CFR 812 Subparts C,E]. The FDA requirements are summarized in Guide-012 - Special Considerations for the Oversight of Research of FDA-regulated Drug or Device Studies.

In sponsor-investigator research, the PI assumes all of the responsibilities in overseeing the research normally assumed by sponsors in industry-sponsored projects.
15.5 Data Safety Monitoring Plan (DSMP)

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<tbody>
<tr>
<td>III.2.D</td>
<td>Researchers and Research Staff follow reporting requirements during a research study in accordance with applicable laws, regulations, codes, and guidance; University of Louisville policies and procedures; and the IRB’s requirements.</td>
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</table>

When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects (45 CFR 46.111(a)(6); 21 CFR 56.111(a)(6)). See also Chapter 9.2.

The extent of monitoring varies by the risk/benefit ratio of the study and by the size, complexity and nature of the study. The IRB requires a data safety monitoring plan (DSMP) for all studies greater than minimal risk. For externally sponsored studies, the DSMP is normally incorporated into the protocol. For an investigator-sponsored study greater than minimal risk, the principal investigator is responsible for creating and implementing a data and safety monitoring plan. The IRB will review the proposed level of risk and monitoring plan and will accept or amend the DSMP. Any proposed change to the IRB approved DSMP must be reviewed and approved by the IRB. The responsibility for human participant protection in human subject research is shared among the IRB, PI, trial sponsors and oversight boards or committees. The safety of participants must be considered in study design.

**Studies that are greater than minimal risk** to participants must include a data safety monitoring plan (DSMP) to evaluate whether the character, incidence, and severity of expected harms match those expected, and to evaluate the causality of unexpected harms. Additionally, a description of the DSMP is required in the Application submitted to the IRB. In order to approve research, the IRB determines that when appropriate, there will be adequate monitoring of data to protect the safety and well-being of participants.

Monitoring may be conducted by the PI, or a Monitoring Entity (ME). In all studies, the PI has ultimate responsibility for identifying potential risks and identifying adverse events occurring in the study population and reporting the events to the sponsor and to the IRB as required in Chapter 3.10.

**Sponsor Responsibilities**

Sponsor responsibilities may include (but are not limited to), as appropriate to the scope and complexity of the research:

- Establishing procedures to assure that interim data remains confidential
- Notifying all participating IRBs of unanticipated problems involving risks to participants or others
- Notifying FDA and the responsible IRBs of any recommendations or requests made by a Monitoring Entity to the sponsor that address safety of participants.

If there is a Data Safety Monitoring Committee, sponsor responsibilities may include:

- Appointing a Chair
- Establishing procedures to assess potential conflicts of interest of proposed members
- Establishing Standard Operating Procedures (SOPs) for statistical analyses, report format, and meeting schedules
- Submitting SOPs to the FDA prior to interim data analyses, optimally before the initiation of the trial.

In sponsor-investigator research, the PI assumes all of the responsibilities in overseeing the research normally assumed by sponsors in industry-sponsored projects. This includes the responsibility if registering all “applicable clinical trials” on the clinicaltrials.gov registry.