A Principal Investigator's (PI) Guide to Responsibilities, Qualifications, Records and Documentation of Human Research

University of Kentucky

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I. Compliance with IRB and Applicable Federal Requirements

A. Investigators are responsible for ensuring that research is conducted according to sound research design, the terms of the grant, contract and/or signed agreement and applicable laws and regulations for protecting the rights, safety, and welfare of subjects. This includes identifying, describing, and adhering to applicable local regulations, laws, and/or ethics requirements for international research.

B. Investigators are responsible for ensuring that research involving humans conforms to generally accepted scientific principles, and that it is based on a thorough knowledge of the scientific literature and other relevant sources of information. The methods to be used should be appropriate to the objectives of the research and the field of study.

C. Investigators are responsible for providing the IRB with sufficient information and materials to facilitate required determinations.

1. Before initiating research, the investigator is responsible for obtaining written and dated approval from the IRB for the research protocol, written consent form (if the consent signature requirement is waived, the script of the orally presented consent material), subject recruitment procedures and materials (e.g., advertisements, scripts of orally presented materials), and any other written information to be provided to subjects.

2. During the course of the research, investigators are responsible for maintaining IRB approval, and keeping the IRB informed about the research.

D. Investigators are responsible for conducting research in compliance with the investigative plan (protocol) as approved by the IRB.

1. Investigators are responsible for complying with the eligibility criteria as specified in the approved protocol.

2. Investigators are responsible for complying with the recruitment plan as specified in the approved protocol/application. See the Principal Investigator's Guide to Identification and Recruitment of Human Subjects for Research for guidance.

3. Investigators are responsible for adhering to the procedures as specified in the approved protocol, including randomization procedures, if any.

4. Investigators may not make any changes in the research without prior IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

5. Investigators conducting research involving use of an investigational device must adhere to the plans as approved by the IRB for control, storage, and accountability of the device.

6. Investigators are responsible for promptly reporting to the IRB any deviation from, or a change to the protocol, which was made to eliminate immediate hazards to subjects without prior IRB approval. The report should include a description of the deviation or change and the reasons for implementation. If appropriate, a proposed amendment to the research should be submitted:

   (i) to the IRB for review and approval, and
   (ii) to the funding agency.

7. If the research is blinded, the investigators are responsible for only breaking the code in accordance with the protocol and promptly document and explain to the IRB any unblinding due to unanticipated problems involving risks to a subject.

8. Investigators are responsible for obtaining prior IRB approval for all payments, reimbursements and medical services to be provided to research subjects.

E. Investigators are required to submit written continuation/final review reports to the IRB at least annually, or more frequently, if requested by the IRB.

F. Investigators are responsible for complying with the applicable IRB and the federal regulatory requirements related to the reporting of unanticipated problems/adverse events.

G. Upon completion of the research, investigators are responsible for providing the IRB with a summary of the outcome, and the funding and regulatory agencies with any required reports.

H. When a Principal Investigator (PI) leaves the University of Kentucky (UK), he/she must close out his/her protocol(s) to another PI who will take responsibility for the research.

I. If the investigators close out a study, investigators are responsible for promptly informing the IRB.

II. Informed Consent/Assent Process and Documentation

A. Investigators are responsible for ensuring that informed consent/assent/HIPAA authorization, if applicable, is obtained and when applicable, documented, unless a waiver of the requirement has been approved by the IRB prior to a prospective subject's participation in a research study. The process includes providing subjects with sufficient information so they can make informed choices on beginning and continuing participation and this dialog should be documented throughout the study. When vulnerable populations are involved in research, investigators must comply with the additional safeguards as required for IRB approval. (See the ORI Informed Consent Website)

1. Prior to involvement of subjects, investigators are responsible for obtaining written IRB approval of the recruitment and informed consent/assent process including, if applicable, the written consent/assent or form (if the consent signature requirement is waived, the script of

the orally presented consent material) and other oral or written information to be provided to subjects.

2. Investigators must ensure the form and process begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research.

3. If individuals other than the principal investigator are to obtain consent/assent/authorization, investigators are responsible for designating only qualified individuals. Investigators must identify the individuals in the IRB application and specify whether they are authorized to obtain informed consent/assent/authorization. Individuals designated to act on behalf of the investigators must be approved by the IRB prior to involvement in the consent/assent/authorization process.

4. Investigators are generally expected to use only written information approved by the IRB, and/or consent documents containing the “IRB Approval” stamp unless circumstances do not accommodate use of version containing an IRB stamp (e.g., use of an electronic system). Regulations do not mandate consent stamps and IRB policy permits exceptions where uploading a stamped version may not be feasible.

5. Neither investigators nor others involved in the research should coerce or unduly influence a subject to participate or to continue to participate. Investigators should be cognizant of any potential environmental or situational influence and distinguish between clinical research and standard treatments to avoid therapeutic misconception.

6. When subjects are to be paid or otherwise rewarded for inconvenience and time spent, investigators are responsible for proposing a payment for IRB approval that is not so large as to unduly influence prospective subjects to consent to participate in the research.

7. Investigators, or a person(s) designated by the investigators, are responsible for informing the subject or the subject's legally authorized representative of all pertinent aspects of the research.

8. Investigators are responsible for ensuring that the language used in the oral and written information about the research, including the consent form, is in non-technical and practical language that is understandable to the subject or the subject's legally authorized representative.

9. Investigators, or a person(s) designated by the investigators, are responsible for providing accurate written and verbal information about the research unless the IRB grants a waiver of the informed consent process. All questions about the research should be answered to the satisfaction of the subject or the subject's legally authorized representative. Investigators must provide potential subjects sufficient opportunity and ample time to decide whether or not to participate in the research study during the consent process.

10. Investigators are responsible for ensuring the subject or legally authorized representative (LAR) sign and date the consent document and other appropriate signatures are obtained, if applicable. Only individuals authorized by the investigators to obtain informed consent should participate in the consent process and/or print their name on the line provided for “Name of [authorized] person obtaining informed consent”.

11. Investigators are responsible for ensuring that each person or LAR signing a consent or assent form is given a copy of the signed form and, if applicable, the signed authorization form.

12. For Food and Drug Administration (FDA)-regulated research, investigator or designee document in the subject's case history, that the subject provided consent prior to participation.

13. Investigators are responsible for informing the subject or the subject's legally authorized representative in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation. The communication of this information may include re-consent/assent of active subjects and should always be documented.

III. Monitoring and Oversight of Research

A. Investigators are required to permit and facilitate monitoring and auditing by the IRB, applicable funding agencies and, at reasonable times, inspection by federal and state regulatory agencies as appropriate.

B. For research that collects data through intervention or interaction with individuals, the investigator is responsible for ensuring that each subject is appropriately monitored and that the research itself is monitored for subject safety and scientific considerations. Investigators must develop procedures for promptly reporting any noncompliance or unanticipated problems to the IRB, appropriate institutional officials, and/or funding agency representative.

1. For all research involving intervention or interaction with individuals, investigators are responsible for having a thorough understanding of the intervention including potential risks, interactions, and precautions and are responsible for monitoring each subject's experience and taking steps to safeguard their individual rights and welfare.

2. For investigator-initiated research involving administration of drugs, devices or biologics, investigators are responsible for complying with all FDA sponsor requirements.

3. For research requiring administration of drugs or devices, the investigators, or a person designated by the investigators are responsible for explaining the correct use of the product(s) to each subject and should check at appropriate intervals that each subject is following the instructions properly.

4. For greater than minimal risk research or NIH funded/FDA regulated clinical investigations, investigators are responsible for establishing a data and safety monitoring plan (DSMP) and for implementing the plan as approved by the IRB. (See Resources for data and Safety Monitoring)

   a. If the DSMP includes a data and safety monitoring board (DSMB), the PI is responsible for submitting documentation regarding DSMB activities (i.e., summary report, meeting minutes) to the IRB as provided to the PI by the sponsor or as prepared by the PI. It is the PI's responsibility to acquire documentation that DSMB activities have occurred if not provided by the sponsor.

   b. At the time of continuation review of the study, the PI is responsible for submitting documentation representing DSMP or DSMB activities not previously submitted to the IRB.

C. Qualified investigators are responsible for personally conducting or supervising the research.

1. Investigators are responsible for clearly describing, in the investigational plan, involvement of others in the conduct of research.

2. Investigators are responsible for maintaining a list of appropriately qualified study personnel to whom he/she has delegated significant research-related duties.

3. Investigators are responsible for ensuring that all associates, colleagues, and employees assisting in the conduct of the research have been notified that they are listed on the protocol, have completed necessary training, and are informed about their obligations in meeting the investigators' commitments.

4. Investigators are responsible for maintaining appropriate oversight of research and research staff, and for delegating research responsibilities, functions, and activities appropriately.

IV. Qualifications of Investigators

A. Investigators must be qualified by education, training and experience to assume responsibility for the proper conduct of human subject research.

1. Investigators are responsible for being able to provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the IRB, funding agencies, and/or regulatory agencies.

2. Investigators are responsible for being thoroughly familiar with the appropriate use of proposed investigational procedures, techniques, and products as described in the current literature, product information, investigator's brochure, and other available information sources.

3. Investigators are responsible for reviewing and complying with professional practice standards, ethical codes, applicable regulatory requirements, IRB guidance documents, and Office of Research Integrity/IRB standard operating procedures.

4. Investigators are responsible for disclosing, eliminating, or appropriately managing, to the satisfaction of the University, any conflicts of interest that might bias or appear to bias the research and the reporting of results in accord with University policy.

5. Qualified physicians (or dentists, when appropriate) who are investigators or sub-investigators are responsible for all research-related medical (or dental) decisions. For additional guidance on medical oversight and delegation, see the Investigator Qualifications and Provision of Medical Oversight.

6. Investigators who are also serving as FDA-regulated sponsors are responsible for being knowledgeable about the additional regulatory requirements of sponsors and for ensuring that the requirements are followed by all study personnel. See FDA-Regulated Research for guidance.

V. Resources

A. As part of their qualification to conduct research, investigators are responsible for ensuring adequate resources are available.

1. Investigators are responsible for being able to demonstrate (e.g., based on retrospective data) potential for recruiting the required number of eligible subjects.

2. Investigators are responsible for having sufficient time committed to properly conduct and complete the research project within the proposed time period

3. Investigators are responsible for having an adequate number of qualified staff and adequate facilities to conduct the research properly and safely for the duration of the research.

VI. Investigator Records and Documentation

A. Investigators are responsible for the accuracy, completeness, legibility, and timeliness of the data recorded and reported in research and in publications about the research.

B. As appropriate to the research and as specified by applicable regulations, investigators are responsible for maintaining documents, which individually and collectively permit evaluation of the conduct of the research and the quality of the data produced. At a minimum, these documents include the following:

1. the investigational plan (protocol) and amendments, as approved by the IRB;
2. the grant, contract and/or signed agreement between the investigator and the funding agency;
3. form(s) used to obtain and document consent/assent;
   (i) current IRB approved form(s);
   (ii) signed consent/assent for each subject, if applicable;
4. any written recruitment materials and other written information given to subjects;
5. data collection form(s) including source documents and case report forms;
6. accountability records of investigational products;
7. correspondence from the IRB including approval letter(s);
8. any reports from monitoring and auditing bodies;
9. reports of unanticipated problems/serious adverse events;
10. approvals from regulatory authorities, if applicable.

C. Investigators are responsible for maintaining signed documents and IRB records for at least six years after study closure and should take measures to prevent accidental or premature destruction of these documents. Investigators are responsible for storing records consistent with IRB policy and the plan approved by the IRB in a secured fashion to prevent breaches of confidentiality.

D. For research which falls under the authority of the FDA or other regulatory or funding agency, investigators are responsible for retaining the signed documents and IRB records for the period specified in the applicable regulations if the requirements are longer than six years after completion of the study. For multi-site studies, investigators consult the study sponsor

regarding retention requirements, but must maintain records for a minimum of six years after study closure.

VII. Investigator Responsibilities as PI for Multi-Site research under UK Single IRB Review [Reliance]

A. The UK PI is responsible for complying with the UK IRB's policies and procedures when UK is the reviewing IRB for a multi-site research protocol as well as ensuring that sites included in the protocol do so as well. These responsibilities include, but are not limited to:

1. Coordinating with Human Research Protection Program (HRPP) personnel to determine whether this UK's IRB can act as the single IRB for all or some institutions participating in the study or if an external (non-UK) IRB will assume oversight.
2. Identifying all sites that will be engaged in human research and requiring oversight by the reviewing IRB.
3. Ensure that all sites receive a request to rely on UK IRB and that all institutional requirements for the reviewing and relying sites are satisfied before a study is activated at a relying site.
4. Collaborating with the reviewing IRB to document roles and responsibilities for communicating and coordinating key information from study teams and the IRB or HRPP at relying sites.
5. Responding to questions or information requests from study teams or the IRB or HRPP staff at relying sites.
6. Providing the relying site investigators with the policies of the reviewing IRB.
7. Providing the relying site investigators with the IRB-approved versions of all study documents.
8. Preparation and submission of IRB applications on behalf of all sites. This includes initial review, modifications, personnel updates, reportable new information and continuing review information for all sites.
9. Establishing a process for obtaining and collating information from all sites and submitting this information to the reviewing IRB. This includes site-specific variations in study conduct, such as the local consent process and language, subject identifications and recruitment processes and local variations in study conduct.
10. Ensuring that consent forms used by relying sites follow the consent template approved by the reviewing IRB and include required language as specified by the relying sites.
11. Providing site investigators with all determinations and communications from the reviewing IRB.
12. Submitting reportable new information from relying sites to the reviewing IRB in accordance with the terms outlined in the authorization agreement or communication plan.
13. Reporting the absence of continuing review information from relying sites if they do not provide the required information prior to submission of the continuing review materials to the reviewing IRB. Notifying the relying site of their lapse in approval and applicable corrective actions.
14. Providing study records to the relying institution, reviewing IRB or regulatory agencies upon request.

VIII. Investigator Responsibilities for Research Reviewed by an External (Non-UK) IRB [Reliance]

A. The UK PI is responsible for complying with the reviewing IRB's policies and procedures as well as the terms of reliance agreements and other UK research requirements outside of the IRB review (e.g., HIPAA, Conflict of Interest). These responsibilities include, but are not limited to:

1. Comply with the reviewing IRB's procedures for initial and continuing review, record keeping, reporting requirements, and that all information requested by the reviewing IRB is provided in a timely manner. (See Reliance Communication Plan)
2. Disclose conflicts of interest and comply with any conflict of interest management plans that may result in coordination with the relying organizations and reviewing IRB. (See Investigator Conflict of Interest/OSPA/IRB Coordination SOP)
3. Promptly report to the reviewing IRB proposed changes to the research. The UK PI cannot implement changes to the research without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to subjects.
4. Do not enroll participants in research prior to review, approval, and other applicable requirements by the reviewing IRB. (See Relying Investigator Guidance and Checklist)
5. Obtain, document, and maintain records of consent for each participant or each participant's legally authorized representative. (See Relying Investigator Guidance and Checklist) Compliance may be monitored through random UK Quality Assurance reviews or in cooperation with the reviewing IRB.
6. Promptly report to the reviewing IRB any unanticipated problems according to the requirements specified in the reliance agreement and/or Reliance Communication Plan.
7. Provide all data safety monitoring reports to the reviewing IRB in accordance with the requirements specified in the reliance agreement and/or Reliance Communication Plan.
8. Report non-compliance, subject complaints, protocol deviations, and/or other events in accordance with the requirements specified in the reliance agreement and/or Reliance Communication Plan; this may include reporting to both the reviewing IRB and the UK IRB.
9. Have appropriate qualifications and expertise to conduct the research, are knowledgeable about laws, regulations, codes and guidance governing their research, and are knowledgeable about both the reviewing IRB's and UK's policies and procedures. Notify the reviewing IRB when local policies that impact the IRB review are updated or changed.
10. Conduct monitoring in addition to or in cooperation with the reviewing IRB, when appropriate.

[Reliance] sections adapted from Harvard University's Investigator Manual, Appendix D

Guidance adapted by University of Kentucky Office of Research Integrity from "Statement Regarding Investigator Responsibility" by Gary L. Chadwick, Pharm.D., MPH, CIP
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