# Human Research Protection Program: Research Investigator Q & A Guide

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**Office of Research Integrity**  
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University of Kentucky (UK) Human Research Protection Program

Who is ultimately responsible for the UK Human Research Protection Program (HRPP)?

How is that authority communicated to the research community?

What rules or guidelines are you expected to follow?

- Federal Regulations that Apply to All UK Human Subject Research
- University of Kentucky Policies and Procedures and Regulations
- Regulations that are applicable to select protocols
- Funding Agency Requirements
- State Law

What ethical standards or guides do you follow?

What do you do when you need assistance determining applicable laws either in state or when conducting research in other states (i.e. age of majority, emancipated minors, Legally Authorized Representatives)?

Does UK follow International Conference on Harmonization (ICH) Good Clinical Practice guidelines?

If you propose research be conducted at an international location what do you inform the IRB regarding applicable local regulations, ethics review requirements, or cultural norms?

In order to receive federal funds for research, UK submits an agreement to follow federal regulations, review human research, monitor on-going studies and report to federal agencies. What are the title of the agreement and the name of the agency?

What Needs Intuitional Review Board (IRB) Review?

What is the process for when determining whether an activity is under the purview of the IRB?

What resources are available for investigators and IRB members for determining what activities require IRB review?

When you have consulted the guidance and are still not certain or need an official determination regarding an activity’s need for IRB review, what do you do?

What is the difference between protecting the privacy interests of participants and maintaining the confidentiality of data?

What is the minimum IRB requirement for maintenance of research records?

IRB Submission & Review Types

Where should I start to determine what type of IRB review will be required?

How do I find out general information about IRB submission?

Where can I find general Frequently Asked Questions?

Scientific Design & Minimizing Risk

How do you judge sound scientific design in your own or a sponsor’s study?

Who is involved in conducting scientific review at UK?

What is minimal risk?

What are the kinds and levels of risk?

To what vulnerable population do the federal regulations apply a slightly different definition of “minimal risk”?

What procedures do you employ to minimize risk or mitigate potential injuries?
What additional safeguards can you consider to reduce risk or enhance benefit other than those pertaining to informed consent?

### Conflict of Interest

- What is UK’s policy on Conflict of Interest (COI)?
- What is a Conflict of Interest?
- Who must disclose financial conflict of interest (COI)?
- What are the Significant Financial Interests (SFI) that must be disclosed?
- How is researcher COI managed?
- Who has the final authority regarding management of investigator conflict of interest?
- What is the importance of disclosing financial conflicts of interest in the conduct of human research?
- Does the institution (University of Kentucky) have a Conflict of Interest Policy?

### Qualifications, Training, & Oversight

- What experience and qualifications do you/your research staff members have for conducting research?
- What human research education opportunities does the institution provide?
- What functions have you delegated to study staff or may ask what tasks you DON’T delegate to staff?
- How often do you talk with or observe study staff?
- How much time do you devote to oversight of protocol process, activity, staff and subjects?

### Feasibility & Resources

- How do you assess and ensure availability of resources required to conduct research in a way that will protect the rights and welfare of participants?

### Data & Safety Monitoring

- When is a Data and Safety Monitoring Plan required?
- What Data and Safety Monitoring information are you required to report to the IRB?

### Recruitment & Study Population

- What recruitment methods do you use?
- What practices may place subjects at risk for coercion or undue influence?
- What additional provisions do you employ for protection of vulnerable populations, groups vulnerable to undue influence, or populations with cultural considerations?
- What must the Principal Investigator (PI) consider when applying Subpart D regulations to FDA regulated pediatric research involving a placebo arm?

### Informed Consent Process & Documentation

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- What are requirements for the informed consent document?
- What guidance and consent language is provided for research with specimens or tissues?
- Can informed consent be altered or waived?
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How do you determine an appropriate assessment and adequate safeguards for enrollment of subjects with impaired consent capacity?
What items may need to be addressed in the informed consent form for FDA regulated investigations?

Complaints, Concerns, Suggestions, Questions, Requests

Who do you call with a complaint, concern, question or suggestions?
What provisions do you have in place for receiving and handling a subject complaint or request for information?
Who may a subject call outside of the study personnel regarding their rights and welfare?

Monitoring & Event Reporting Requirements

When do you begin collecting, recording and reporting adverse event and unanticipated problems for a research subject?
What problems/events are you required to report to the IRB?
What is considered a Serious Adverse Event (SAE) for FDA regulated research?
What is the IRB reporting requirement if a non-serious adverse event occurs that is not related to the study?
What other activities on an approved protocol require reporting by the PI to the IRB?

Food & Drug Administration (FDA) Regulated Research

What is the IRB’s role in reviewing FDA regulated research?

FDA Regulation Drug Research:
What process do you to make sure that investigational drugs are controlled so that they are used only in approved research protocols under your direction?
Does the IRB ask for information about how you will control the study drug?
Does UK require study drug to be managed by an Investigational Drug Unit?
(If applicable) Are you knowledgeable about the additional regulatory requirements you are responsible for as the Sponsor-Investigator (hold the IND) of the drug investigation?

FDA Regulated Medical Device Research:
What process do you to make sure that investigational devices are controlled so that they are used only in approved research protocols under your direction?
Does the IRB ask for information about how you will control the study device?
Does the IRB ask about qualifications or training needed to use or administer the device the study device?
(If applicable) Are you knowledgeable about the additional regulatory requirements you are responsible for as the Sponsor-Investigator (hold the IDE or Abbreviated IDE) of the device investigation?

FDA Emergency Use:
What happens when you plan an emergency use of a test article in a life-threatening situation?
Is a patient receiving a test article in an emergency situation considered to be in research?
What is the difference between single subject emergency use and Planned Emergency Research?

Community Engaged Research (CER)/Community Based Participatory Research (CBPR)

What resources are available to facilitate the approval and conduct of Community Engaged Research (CER) or Community Based Participatory Research (CBPR)?

Outreach & Education for the Public and Potential Research Participants

Who is responsible for ensuring a local research participant outreach program that educates the public and potential participants?
Who hears concerns from research participants?
UK Human Research Protection Program
Investigators are familiar with the institutional Human Research Protection Program, regulatory framework and ethical standards for protecting human subjects.

Who is ultimately responsible for the UK Human Research Protection Program (HRPP)?

Vice President for Research, Dr. Lisa Cassis is the designated institutional official responsible for oversight and management of all aspects of UK research. The VPR establishes the mechanisms and framework for the HRPP and ensures sufficient resources to support it.

How is that authority communicated to the research community?

The Human Research Protection Program (HRPP) Comprehensive Plan establishes the authority and independence as well as the level and scope of responsibility for the IRBs and describes the organizational structure for human research protection. Located on the VPR webpage www.research.uky.edu/vpresearch/documents/A1-UK_HRPP_Comprehensive_Plan.pdf

What rules or guidelines are you expected to follow?

Federal Regulations that Apply to All UK Human Subject Research
Department of Health and Human Services (DHHS) 45 CFR 46:
Subpart A – “Common Rule” IRB Operations, Approval Criteria, Informed Consent
Subpart B - Fetuses/Pregnant Women/Neonates
Subpart C - Prisoners
Subpart D - Children

Regulations that are applicable to select protocols
A. Food and Drug Administration regulations
B. If applicable to the research, UK applies: Health Insurance Portability Accountability Act (HIPAA)

Funding Agency Requirements
If applicable to research, UK applies:
• Department of Defense (DoD)
• US Department of Education (DoED)
  Family Educational Rights and Privacy Act
  National Institute on Disability and Rehabilitation Research
  Protection of Pupil Rights Amendment
• Environmental Protection Agency (EPA)
• US Department of Justice (DOJ)
  National Institute of Justice (NIJ)
  Bureau of Prisons (BOP)
• Department of Energy (DOE)

State Law

University of Kentucky Policies and Procedures and Regulations
A. President Level Administrative Regulations (AR):
  • AR 7:1 Research Misconduct
  • AR 7:2 Research Conflict of Interest and Financial Disclosure Policy
  • AR 7:4 Human Research Subject Protection and Institutional Review Boards
  • AR 7:9 Institutional Conflict of Interest
B. Vice President for Research (VPR): University of Kentucky Human Research Protection Program Comprehensive Plan
C. IRB/ORI:

- **Standard Operating Procedures**
- **Application Forms**
- **Guidance Documents (See IRB SURVIVAL HANDBOOK).**

**What ethical standards or guides do you follow?**

The above research regulations are based on the ethical principles set forth in the Nuremberg Code, Declaration of Helsinki, and the Belmont Report issued by the National Commission for the Protection of Human Subjects 1979. Belmont outlines three ethical principles that are considered to be central to human subject protection.

- **Respect for persons** involves recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy.
- **Beneficence** entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm.
- **Justice** requires that the benefits and burdens of research be distributed fairly.


**What do you do when you need assistance determining applicable laws either in state or when conducting research in other states (i.e. age of majority, emancipated minors, Legally Authorized Representatives)?**

Prior to IRB review, the PI is responsible for determining applicable state laws relative to the conduct of their research. If assistance is needed, the PI may consult Katherine Adams, Office of Legal Counsel, kadams@email.uky.edu, 859 257-2936.

**Does UK follow International Conference on Harmonization (ICH) Good Clinical Practice guidelines?**

UK does not apply International Conference on Harmonization/Good Clinical Practice (ICH/GCP) requirements to all human research. It is the PI’s responsibility to request that the IRB apply ICH GCP. In most cases we can provide the sponsor with the “Extent of Compliance Statement” indicating the IRB is compliant with Food and Drug Administration regulations and ICH guidelines relating to GCP, except where ICH GCP conflicts with FDA or DHHS.

**If you propose research be conducted at an international location what do you inform the IRB regarding applicable local regulations, ethics review requirements, or cultural norms?**

If research is to be conducted at an international location, the investigator identifies local regulations, laws, or ethics review requirements for human subject protection. He/she may refer to the annual [International Compilation of Human Research Standards](https://ohrp.osirroup.edu) on the OHRP website or the [National Institutes of Health ClinRegs](https://clinicaltrials.gov) website. If the project has been or will be reviewed by a local Ethics Committee or IRB, the investigator provides the UK IRB with a copy of that review.

In addition, the investigator informs the IRB of any relevant cultural norms or customs particularly in regard to recruitment or informed consent. The IRB obtains a cultural consultant to assist in the review of issues which require expertise beyond or in addition to that available on the IRBs. Cultural consultants provide comments, concerns, translations, in writing to the IRB on all protocols involving non-English speaking subjects, and/or subjects from a foreign culture.
In order to receive federal funds for research, UK submits an agreement to follow federal regulations, review human research, monitor on-going studies and report to federal agencies. What are the title of the agreement and the name of the agency?

Agreement: Federalwide Assurance (FWA)
Agency: Office for Human Research Protections (OHRP)

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<td>Investigators understand the definition of human research and seek guidance when determining if an activity requires IRB review.</td>
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What is the process for when determining whether an activity is under the purview of the IRB?

The PI may use available resources to make a preliminary decision; he/she may contact ORI staff, IRB Chair/Vice Chair or member for advice on application of the federal regulations and UK policy. If unclear, the investigator may submit Not Human Research (NHR) determination form to obtain an IRB decision or send an e-mail. The ORI Director or IRB chair (or designee “Research Compliance Officer”) makes the final determination using a stepwise process to determine if the activity meets applicable regulatory definitions of human subject research. The ORI communicates the decision to the investigator via phone, email or hard copy memo.

What resources are available for investigators and IRB members for determining what activities require IRB review?

a. GUIDANCE TABLE: When do activities involving human subjects need Institutional Review Board (IRB) review and approval?  
   www.research.uky.edu/ori/ORIForms/1-When_IRB_review_needed_guidance.pdf
b. Form for requesting a need for IRB review determination:  
   NOT HUMAN RESEARCH (NHR) DETERMINATION FORM:  
   www.research.uky.edu/ori/ORIForms/F0-9999-NHRdeterminationE-form.pdf
c. Guide For Determining When Protocols Involving Coded Private Information or Biological Specimens Meet the Federal Definition of “Human Research”  
d. Determination of What Activities Need IRB Review SOP

e. Guidance from ORI director, Ada Sue Selwitz, ORI Research Compliance Officer, Helene Lake-Bullock, or an IRB Chair.

When you have consulted the guidance and are still not certain or need an official determination regarding an activity’s need for IRB review, what do you do?

While some determinations are clear cut, other situations may be more complicated to apply (i.e. is the investigation “systematic”; what constitutes “generalizable” knowledge, etc.).

The investigator may contact ORI staff, the IRB Chair/Vice Chairs, or IRB members for an authoritative decision and/or advice on the application of the federal regulations and UK policy. Contact us directly or complete and submit the Not Human Research (NHR) Determination Form. ORI can provide an official IRB determination on letterhead.

Remember/Consider…

Food & Drug Administration (FDA) and the Department of Defense (DoD) have different definitions which can alter a determination. Consult the UK What Needs IRB Review website for applicable definitions.  

Considering only weather data or specimens are “identifiable” may result in a wrong determination regarding need for IRB review. Be sure to consult the Guide For Determining When Protocols Involving Coded Private Information or Biological Specimens Meet the Federal Definition of “Human Research”

When unsure, use the Not Human Research (NHR) Determination Form:  
http://www.research.uky.edu/ori/ORIForms/F0-9999-NHRdeterminationE-form.pdf
IRB Submission & Review Types

Where should I start to determine what type of IRB review will be required?

Before determining the applicable review type, ensure the activity requires IRB review. See the section above for resources for determining if the activity requires IRB review by meeting the federal definitions of “research” or “human subject”.

Resources for determining which type of review a protocol will require as well as links to the respective IRB Submission Forms are available on the IRB Review Types webpage.

The preliminary determination that a research project is eligible for exemption certification or expedited review is made by the investigator. The Issues to be Addressed when conducting Exempt Review and Issues to be Addressed when conducting Expedited Review documents explain the categories of research and conditions that must be met to qualify for these review mechanisms. Questions of interpretation may be directed to the Office of Research Integrity at 859-257-9428.

Exempt Review involves the IRB’s review and determination that the research activity is eligible for “exemption” from certain ongoing IRB review requirements. These are research activities that involve little to no risk and in which the only involvement of human subjects will be in one or more of six federally designated categories. Certain activities cannot be exempt because of additional protections granted to vulnerable populations. Be aware that exemption is for IRB regulations only and other regulations (e.g., HIPAA) still apply. See the Issues to be Addressed when conducting Exempt Review document for additional guidance.

Expedited Review may be used for initial review of studies that are no greater than minimal risk and meet one or more of the DHHS or FDA Expedited Categories and may be used to review minor revisions of previously approved research. The process may be carried out by an IRB Chair or his/her designee or by sub-committee review. Expedited reviewers may approve or recommend revisions to research however they do not have the authority to disapprove a study. If the study does not meet the Expedited Criteria or the reviewer(s) are unable to approve, the study would be shifted to the full convened IRB for review. See the Issues to be Addressed when conducting Expedited Review for details.

Research that cannot meet the criteria for exempt or expedited review must be submitted for full review by a convened board. Ultimately the IRB will choose the mechanism for review based on regulatory and ethical requirements.

How do I find out general information about IRB submission?

Where can I find general Frequently Asked Questions (FAQ)?

Answers to many FAQs regarding IRB review operations, Medical vs. Nonmedical IRB, informed consent, terminology, etc. may be found at http://www.research.uky.edu/ori/humanFAQs.htm.

What is the difference between protecting the privacy interests of participants and maintaining the confidentiality of data?

Privacy concerns people, whereas confidentiality concerns data. In developing strategies for the protection of subjects’ privacy, consideration should be given to:

• The methods used or setting where potential participants are identified.
• Privacy guidelines developed by relevant professional associations and scholarly disciplines (e.g., oral history, anthropology, psychology); and
• How to access the minimum amount of information necessary to complete the study.

**Confidentiality** refers to the researcher’s agreement with the participant about how the participant’s identifiable private information will be handled, managed, and disseminated. In the IRB research description, investigators describe their plan to preserve the confidentiality of identifiable data, including:

• controls on storage, handling, and sharing of data
• physical security measures (e.g., locked facility, limited access);
• data security (e.g., password-protection, data encryption) see IRB Data Security Guidance for electronic data at [http://www.research.uky.edu/ori/ORIForms/D105-Electronic-data-policies.pdf](http://www.research.uky.edu/ori/ORIForms/D105-Electronic-data-policies.pdf)
• safeguards to protect identifiable research information (e.g., coding, links, certificate of confidentiality);
• procedures employed when sharing material or data, (e.g., honest broker (if applicable), written agreement with recipient not to re-identify); and
• measures that you will take to secure and safeguard confidentiality if protocol involves storing material or tissue/specimens/data for use in current or future research (how material will be destroyed or rationale for perpetual maintenance.

**What is the minimum IRB requirement for maintenance of research records?**
At a minimum, research records should be maintained for **six (6) years** after completion of the study. Longer retention may be required by sponsors or for studies that fall under the authority of other agencies. For more information see the “ORI/IRB Recordkeeping SOP” at [http://www.research.uky.edu/ori/SOPs_Policies/C4-0250-IRB-ORI_Record_Keeping.pdf](http://www.research.uky.edu/ori/SOPs_Policies/C4-0250-IRB-ORI_Record_Keeping.pdf)

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### Scientific Design & Minimizing Risk

Investigators design scientifically sound research that is likely to develop or contribute to generalizable knowledge. Investigators judge the design and validity of sponsored research before participating or enrolling subjects.

Investigators understand and apply procedures to minimize risk.

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**How do you judge sound scientific design in your own or a sponsor’s study?**

• potential risk/benefit ratio
• potential contribution to generalizable knowledge
• demographic illustrative of real patient/subject population
• specific indicators for diagnostic criteria
• study design, (e.g., cluster randomization, standard of care comparison)
• controls, blinding, deception
• statistical plan & methods to minimize bias
• subject safety monitoring

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<td>Reasons you may have turned down a sponsored study.</td>
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<td>An example of how you have minimized risk in a study.</td>
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<td>Any ethical issues specific to the study design.</td>
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Who is involved in conducting scientific review at UK?

The Department Chairperson/Faculty Advisor and the IRB.

- Department Chairperson/Faculty Advisor attest (signing form Z) that the science is meritorious and deserving of conduct in humans by considering the:
  - validity and utility of science;
  - availability and qualifications of personnel;
  - potential subject population; facilities and equipment;
  - ongoing mentoring and guidance; and
  - resolves issues prior to the IRB’s receipt of the submission.

- The IRB review considers the scientific study design within context of human subject protection. IRB members draw on their own knowledge and disciplinary expertise to determine if research procedures are consistent with sound research design and the protocol has potential to yield the expected knowledge.

What is minimal risk?

- The Department of Health and Human Services defines *minimal risk* to mean “the *probability* and *magnitude* of harm or discomfort anticipated in the research *are not greater* in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” [45 CFR 46.102(2)(i)].

What are the kinds and levels of risk?

- A risk is a potential harm or injury associated with the research that a reasonable person in the subject’s position would likely be considered injurious. Risks can be categorized as physical, psychological, sociological, economic, and legal. Risks to subjects must be reasonable in relation to anticipated benefits, if any, to subjects and to the importance of knowledge that may reasonably be expected to result from the research.

- The four categories for level of risk are:
  - Not greater than minimal risk
  - Greater than minimal risk, but presenting the prospect of direct benefit to individual subjects
  - Greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition
  - Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of subjects

- During review of a proposal, the IRB may refer to a document providing guidance on Assessing the Research Risk. See the PDF document: [http://www.research.uky.edu/ori/SOPs_Policies/8-Risk_Assessment.pdf](http://www.research.uky.edu/ori/SOPs_Policies/8-Risk_Assessment.pdf)

To what vulnerable population do the federal regulations apply a slightly different definition of “minimal risk”?

- See Department of Health and Human Services (DHHS) 45 CFR 46 Subpart C on Prisoners: [http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc)

For research involving prisoners, the definition of minimal risk refers to “the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental or psychological examination of healthy persons”.
What procedures do you employ to minimize risk or mitigate potential injuries?

Potential protections include:

- Utilize procedures already being conducted for non-research reasons
- Safety monitoring including safety labs and other assessments
- Consider a plan for responding to clinically significant abnormalities including withdraw of study product and re-challenge with product if appropriate
- Protections to secure confidential or private information

What additional safeguards can you consider to reduce risk or enhance benefit other than those pertaining to informed consent?

- Additional limitations on inclusion/exclusion criteria or screening tests to rule out potential subjects at greater risk of physical or emotional harm
- Provisions for ensuring necessary medical services or professional intervention (e.g., counseling) in the event of adverse events
- Employ data security measures
- Increased oversight
- Establish a data and safety monitoring plan or board http://www.research.uky.edu/ori/QIP/DSMP.htm

Conflict of Interest

Investigators and research staff should understand the organization’s conflict of interest policy in order to follow it. For example, investigators should know what interests the organization requires to be disclosed. Investigators and research staff should know how, when, and to whom to disclose interests.

What is UK’s policy on Conflict of Interest (COI)?

UK actually has two policies on conflict of interest; one for researchers and one for the institution itself.

Financial COI related to research of individual investigators is covered in Administrative Regulation (AR) 7.2 - Financial Conflicts of Interest in Research http://www.uky.edu/regs/files/ar/ar7-2.pdf. The AR outlines procedures for defining, identifying, disclosing, managing, reporting and training regarding COI.

It is under the authority of the Institutional Official, Vice President for Research, Dr. Lisa Cassis. Administered by the Office of Sponsored Projects Administration (OSPA).

See the OSPA COI website http://www.research.uky.edu/ospa/coi.html

If you have questions or need assistance with a specific situation, contact Conflict of Interest Administrator Kelley Davis at 257-0579 or kelley.king@uky.edu.

The AR was updated to comply with 2012 Public Health Service (PHS) regulations. The AR requires investigators to complete an online financial disclosure Statement (FDS) to identify significant financial interests (SFI) related to institutional responsibilities.

ORI & OSPA coordinate handling of Investigator COI for both funded and unfunded human subject research.

Remember/Consider….

UK has Conflict of Interest Policies for researchers and the institution itself.

Research staff may be covered by the COI requirements as the definition for investigator is tied to responsibilities and not “title”.

What is the financial threshold for disclosing if you do not own holdings in a company but serve a consultant or on their board of directors?
What is a Conflict of Interest?

A potential or actual Conflict of Interest (COI) exists when a significant financial interest (as defined below) of an Investigator or a family member of the Investigator could directly and significantly affect the design, conduct, or reporting of research.

Who must disclose financial conflict of interest (COI)?

Disclosure is required for investigators – defined as project director or principal investigator/program director, co-investigator, collaborator, senior/key personnel, faculty associate, and any other person, regardless of title or position, who is responsible for the design, conduct, reporting, or proposing of research. Therefore, research staff performing any of the above functions would be included in the scope of the administrative regulation.

Both funded investigators and unfunded investigators who disclose a conflict on an IRB protocol application, complete an online financial disclosure Statement (FDS) to identify significant financial interests (SFI) related to institutional responsibilities. 

What are the Significant Financial Interests (SFI) that must be disclosed?

Each Investigator must disclose all significant financial interests {SFI} that are related to his/her institutional Responsibilities. Financial interests are aggregated for the Investigator, his/her spouse, and dependent children.

a) For a publicly traded entity, remuneration and equity interest exceeding $5000 in value received in the 12 months preceding disclosure.

b) For a non-publicly traded entity, remuneration exceeding $5000 in value received in the 12 months preceding disclosure OR any equity interest.

c) Any intellectual Property Income (e.g., patents, copyrights), excluding royalties paid by University of Kentucky.

d) Certain travel reimbursement for Public Health Service (PHS) funded projects.

If “Yes” to a, b, or c, indicate specific activities where Employee, Spouse, Dependent Children serve:

- Serve as corporate officer
- Serve on governing board, board of directors, trustee
- Serve on scientific advisory board, peer review panel
- Serve as consultant, whether paid or unpaid
- Own equity interest (e.g., stock, stock options)
- Receive royalties for inventions, copyrights,
- Receive authorship fees
- Speaking fees or honoraria
- Gifts, benefits

How is researcher COI managed?

The IRB application asks if any investigators or key study personnel have a Significant Financial Interest requiring disclosure and if the interests related to the proposed research?

If a financial COI exists and cannot be eliminated, the investigator and his/her dean or director propose a management plan.

All management plans are referred to the Research Conflict of Interest Committee (RCOIC) for review.
The RCOIC recommends a plan to the Institutional Official who makes the final decision on approval of the plan.

IRB does not complete its review and approval of the IRB application until it receives the final VPR approved management plan. The IRB may not change the approved plan, but, it may impose further restrictions/conditions on the protocol or disapprove the protocol.

Who has the final authority regarding management of investigator conflict of interest?

For human subject research, the IRB has the final authority to decide whether the conflict of interest and approved management plan, if any, allows the research to be approved by the IRB.

What is the importance of disclosing financial conflicts of interest in the conduct of human research?

The concern is that significant financial conflicts of interest may interfere with an Investigators’ objectivity in recruitment of subjects (coercion), conduct of the research, evaluation of the research design or research data, and/or reporting research activities. Additional safeguards may be indicated.

Does the institution (University of Kentucky) have a Conflict of Interest Policy?

Yes, the Institutional COI policy is covered under Administrative Regulation (AR) 7.9 Institutional Conflict of Interest (COI) Involving Research [www.uky.edu/regs/files/ar/ar7-9.pdf](http://www.uky.edu/regs/files/ar/ar7-9.pdf)

- It is under the authority of the Institutional Official, Vice President for Research, Dr. Lisa Cassis. Administered by the Office of Sponsored Projects Administration (OSPA).
- The institution requires select administrators to disclose significant financial interest (SFI).
- Review is conducted by the Institutional Conflict of Interest Committee (ICOIC) chaired by Lisa Tannock, M.D.
- IRB Chair Terry Malone serves as liaison between IRB and ICOIC.
- Numerous ways beyond disclosures to identify and inform the IRB of an ICOI involving a human subject protocol.

If you are aware that institution has a COI related to your research, let the IRB know.

Qualifications, Training, & Oversight

Investigators and research staff are qualified by training and experience for their research roles, including knowledge of applicable federal, state, and local regulations; relevant professional standards; and the Organization’s policies and procedures. Investigators appropriately delegate tasks that are commensurate with staff qualifications and provide oversight throughout the study.

What experience and qualifications do you/your research staff members have for conducting research?

- It is the Principal Investigator’s (PI) responsibility to ensure that each member of the research team is adequately qualified with training and expertise to safely perform their designated research role.
- Consider how tasks are delegated, how staff are trained on protocol-specific tasks and to whom responsibility is delegated when the PI is unavailable.
When the PI signs the signature assurance sheet ("Form Z") in the IRB application, (s)he is attesting that each individual listed as study personnel in the application possesses the necessary experience for conducting research activities in the role described for this research study. The PI indicates which study personnel will be involved in the informed consent process.

UK has initial and continuing human research mandatory education requirement for human subject protection (HSP). All investigators/study personnel conducting research involving human subjects, or data or biological specimens derived there from, regardless of funding source, must complete initial HSP training and refresher HSP training every 3 years. For details on how this training requirement can be met, see the ORI Mandatory Training FAQ page at http://www.research.uky.edu/ori/human/Human_Research_Mandatory_Education.htm

What human research education opportunities does the institution provide?

For a list of training opportunities see the UK Human Research Education Options available at http://www.research.uky.edu/ori/ORIForms/48-UKHumanResearch_EducationOptions.pdf


What functions have you delegated to study staff or may ask what tasks you DON’T delegate to staff?

Prior to describing delegation, the Principal Investigator should indicate his/her direct involvement in the conduct of the study including recruitment, obtaining consent, assessing eligibility criteria, events, and protocol procedures.

An investigator may delegate many tasks to study staff provided that they are qualified to perform the task and it is within their scope of practice. Investigators designate which study personnel should be authorized to obtain informed consent on the IRB application for review by the IRB. The investigator must assure that the study personnel are informed regarding their obligations and commitments. Medical procedures and assessments (including adverse event causality, unblinding, treatment decisions) should not be inappropriately delegated to unqualified staff.

How often do you talk with or observe study staff?
Site visitors will want to know that the Principal Investigator has provided adequate supervision and oversight.

How much time to you devote to oversight of protocol process, activity, staff and subjects?
Investigators are responsible for having sufficient time committed to properly conduct and supervise the conduct of the research.

Remember/Consider....

ALL study personnel are required to complete initial Human Subject Protection (HSP) training and re-certify every 3 years.

Staff qualifications are described on the IRB Research Description (Form B).

While tasks may be delegated, responsibility ultimately remains with the Principal Investigator.

In FDA Regulated clinical studies, a qualified physician (or dentist) should be responsible for all trial-related medical decisions and care including for example:

- physical examinations
- evaluation of adverse events
- assessment of primary endpoints

IRB Drug (Form O) and Device (Form P) forms include specific questions regarding training and qualifications required to administer the test product. They also include a section on the additional regulatory responsibilities for Sponsor-Investigators.

Individuals who serve as Sponsor-Investigators for FDA regulated products (hold investigational new drug [IND] or investigational device exemption [IDE]) are required to complete additional training regarding their regulatory requirements.
FDA provides guidance regarding appropriate task delegation, supervision, and oversight responsibilities with respect to protecting human subjects and ensuring data integrity for FDA regulated clinical research.


### Feasibility & Resources

Investigators assess feasibility and ensure adequate resources to perform research.

**How do you assess and ensure availability of resources required to conduct research in a way that will protect the rights and welfare of participants?**

- **Protocol considerations** include valid research question, risk vs. potential benefit, realistic inclusion/exclusion criteria, appropriate facilities, sufficient time, appropriate staff credential or expertise, adequate potential subject population, safety considerations such as placebo or washout, etc. personnel, space, equipment, and time.

- **Facility Considerations** - consider proximity or availability of other resources. For example, the proximity of an emergency facility for care of participant injury, or availability of psychological support after participation. Investigators should not commence a research study without adequate resources to protect participants, and should stop a research study if resources become unavailable.

### Data & Safety Monitoring

The Investigator designs and carries out research studies with adequate data and safety monitoring during the research, when appropriate.

**When is a Data and Safety Monitoring Plan required?**

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 take steps to, safeguard their individual rights and welfare.

A Data and Safety Monitoring Plan is required for:

- Greater than minimal risk research
- NIH Funded Clinical Trial
- FDA Regulated Clinical Investigation

The ORI website provides guidance for developing a DSMP at http://www.research.uky.edu/ori/QIP/DSMP.htm.

**Remember/Consider….**

<table>
<thead>
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<th>DSMP required for:</th>
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<tr>
<td>• Greater than minimal risk research</td>
</tr>
<tr>
<td>• NIH Funded Clinical Trial</td>
</tr>
<tr>
<td>• FDA Regulated Clinical Investigation</td>
</tr>
</tbody>
</table>

For studies with DSMPs, the PI is responsible for reporting DSMP activities, findings, or reports to the IRB.

**What Data and Safety Monitoring information are you required to report to the IRB?**

The PI is responsible for confirming that all reports were previously submitted (via modification review) or providing a DSMP report, or if study is monitored by a DSMB, obtaining a report or confirmation that no activities have occurred since the previous continuation review.

ORI staff contact the PI if a report is expected and not submitted.
The IRB would request the missing report as a revision if a report was available, but not submitted with the CR or ORI staff could not obtain the report.

If a DSMP/DSMB is required for the protocol and activities had occurred but not been shared with the IRB, the IRB could withhold approval for research as it would be unable to determine if the criteria for approval is met.

<table>
<thead>
<tr>
<th>Recruitment &amp; Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigators employ fair and equitable recruitment and avoid undue influence or coercion.</td>
</tr>
<tr>
<td>Investigators should have a justifiable rational for inclusion of vulnerable populations.</td>
</tr>
<tr>
<td>If vulnerable populations are to be recruited, investigators comply with regulatory requirements and apply additional safeguards for protecting the subjects' rights and welfare.</td>
</tr>
</tbody>
</table>

What recruitment methods do you use?

Methods of recruitment should:

- be applied equally among all groups (gender, race, age) to ensure each group receives the potential benefit;
- not exclude any group without adequate justification;
- involve sound plans to protect the subject's identity (e.g., approach a potential subject at appropriate times and settings which would not compromise subject's privacy; allowing only those having legitimate access to the subjects' identity and information to make first contact and subsequently communicate with potential subjects);
- involve sound plans to protect the confidentiality of the research records (e.g., limited access to only authorized individuals; secure storage; timeline for destruction of data with identifiers, etc.).


Key points:

- No cold call contacts to potential subjects identified in private records; contact through care giver with established relationship.
- Consistent with state law, the UK IRB does not approve finder’s fees in research studies.
- Advertising is limited to information needed to determine interest and does not imply favorable outcome, claims of superiority, and does not list dollar amount of any compensation.
- Proposed compensation should be appropriate and method and timing of disbursement should not be coercive or present undue influence. Payment should not be contingent upon completion of the entire study.
- Compensation should not include any discount for the study product once approved for marketing.
- Recruitment bonuses paid to the organization or research staff is prohibited.

View a quick guide to ad development and approval by downloading ORI’s “Research Advertising” document:  [http://www.research.uky.edu/ori/ORIForms/89-research-advertising-for-web.pdf]
What practices may place subjects at risk for coercion or undue influence?

Appropriate provisions should be in place to ensure a potential subject does not feel coerced to participate, or experience undue influence when making a decision on whether or not to participate.

Being directly approached by an authority figure such as a boss, teacher or physician may make a potential subject feel coerced or unduly influenced to participate in research. Students may volunteer to participate in the belief that doing so will place them in a favorable situation with faculty.


Key Points:

- Students should be of age to consent (18 years +).
- Graduate Medical Education Committee approval is required to enroll Medical Center residents/house officers as subjects.
- Obtain permission to access student records even if you have access in your academic role.
- If in a perceived authority position, use a 3rd party to seek participation & consent.
- If extra credit offered, provide alternative opportunities for credit.
- If in a perceived authority position, use a 3rd party to seek participation & consent.
- If extra credit offered, provide alternative opportunities for credit.
- Per Office of Human Research Protection January 2010 notice, imposing penalty credits on students who fail to show up for scheduled appointments with investigators without cancelling by a specified deadline violates the requirement of Department of Health and Human Services (HHS) regulations at 45 CFR part 46.116(a)(8).

What additional provisions do you employ for protection of vulnerable populations, groups vulnerable to undue influence, or populations with cultural considerations?

There are additional provisions for protection of vulnerable populations and potential participants who are vulnerable to coercion or undue influence. See the following Guidance/Policy Documents:

What must the Principal Investigator (PI) consider when applying Subpart D regulations to FDA regulated pediatric research involving a placebo arm?

In completing the IRB Form W, investigators categorize the study into one of four categories based on potential risk and benefit. The category corresponds to the level of safeguards and protections that will be required. FDA has indicated that administration of a placebo would not meet Category 2, *(research involves greater than minimal risk but presents the prospect of direct benefit to the individual subjects 21 CFR 50.52)*, because it would not offer a prospect of direct benefit. The placebo arm of a pediatric clinical trial should be categorized under either Category 1, 3, or 4. Should the research fall under Category 4, a report must be sent to the applicable federal agency for review and the IRB may not independently approve the research.

**Informed Consent Process & Documentation**

The investigator develops an informed consent process appropriate to the research and population emphasizing comprehension and voluntary participation. Investigators understand the difference between consent process (which is ongoing) and consent documentation.

What is the process of informed consent?

- In addition to meeting regulatory requirements for informed consent, the process involves the “who”, “what”, “when”, “where”, and “how” that result in a valid, effective, and ongoing comprehension and voluntary participation.
- While the informed consent process is prospective and takes place prior to any research activity, consent should also be an ongoing educational interaction between the investigator and the research subject that continues throughout the study.
- The process of consent should ensure that potential subjects are provided with information about the research project that is understandable by them, and permits the subject to make an informed and voluntary decision about whether or not to participate.
- Potential subjects should be allowed ample time to read, review, discuss and consider participation.
- Steps used to minimize coercion, undue influence, and therapeutic misconception.
- Use of visuals, aids, verbal concepts, demos, or learning tools.

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**Remember/Consider....**

Describe the "who, what, when, where" of your consent process in the IRB application (Form B)

Informed consent a PROCESS; not just a form!

The UK ORI/IRB Informed Consent SOP is a comprehensive resource for questions regarding consent process.
**What are requirements for the informed consent document?**

- **There are eight federally mandated elements** of informed consent and additional elements required by the UK IRB as applicable to the research. An Investigator may use the ORI Informed Consent template to ensure she/he has included the required elements.

  The amount of information and the manner of presentation is generally related to the complexity and risk involved in the research study. The IRB provides a variety of informed consent templates (all contain required elements of informed consent and most include Spanish versions):

  - IRB Application “Form C” (Informed Consent Template) [Medical & Nonmedical];
  - Informed Consent/HIPAA Combined Template [Medical & Nonmedical];
  - Sample Consent to Participate in a Research Repository or Individual Study Banking Material for Future Use;
  - IRB Application “Form D” (Assent Form Template) [Medical & Nonmedical];
  - Single-Subject Consent to Receive or Refuse Result or Incidental Finding - Sample Consent; and
  - Cover Letter Template (for survey/questionnaire research).


**What guidance and consent language is provided for research with specimens or tissues?**

Because there is extensive variation in the way banks and repositories operate, a “one size fits all” template is not feasible.

The guidance document entitled, *“Issues to be Addressed and Sample Consent Language for Tissue/Specimen Repositories or Individual Studies Banking Material for Future Use”* addresses considerations when designing an informed consent document for a research repository or a study that involves specimen banking for future use. Each issue category is followed by sample consent language that may be used to customize a consent document to fit the unique characteristics of the specimen/tissue repository or study involving specimen banking.

Studies that involve greater than minimal risk or invasive procedures to collect specimens specifically for research are directed to use the injury and compensation language from the standard UK Medical Consent Template.

**Can informed consent be altered or waived?**

Only under certain conditions can the IRB waive the requirement for the informed consent process. The IRB may waive the requirement for informed consent if it finds and documents that the research meets certain conditions:

- **a)** no more than minimal risk involved,
- **b)** rights and welfare of subjects not adversely affected,
- **c)** research **COULD NOT** be practicably done without the waiver or alteration, and
- **d)** when possible, subject is provided with additional pertinent information after participation.

For example, if you are conducting research involving deception, or conducting medical record reviews, your research may meet the conditions for waiving informed consent. See IRB Application “Form E” instructions and “Form E” [http://www.research.uky.edu/ori/MedicalFullReviewApplication.htm#ICA](http://www.research.uky.edu/ori/MedicalFullReviewApplication.htm#ICA)
What does documenting the informed consent process entail?

- Informed consent is documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative (LAR).
- The subject/LAR must document their consent by signing and dating the IRB approved informed consent form prior to study participation.
- Investigators are responsible for ensuring that each person or legally authorized representative (LAR) signing a consent or assent form is given a copy of the signed form or, if applicable, the signed HIPAA authorization form.
  - To determine who may serve as an LAR, see the ORI/IRB Informed Consent SOP [http://www.research.uky.edu/ori/SOPs_Policies/]
  - To educate the LAR regarding his/her responsibility to consider substituted judgment and best interest for a subject, see the Advice to Legally Authorized Representatives brochure for Medical [http://www.research.uky.edu/ori/ORIForms/87-Form-T-MED-brochure.pdf] or Nonmedical [http://www.research.uky.edu/ori/ORIForms/88-Form-T-NonMED-brochure.pdf] research.
- Only the investigator should sign on the line provided for “Investigator” (may be PI or Sub-I). Only individuals authorized by the investigators to obtain informed consent should participate in the consent process and/or sign on the line provided for “Name of [authorized] person obtaining informed consent”.
- The subject/LAR must receive a copy of the signed consent form, as this document serves as a reference for study information and study contact information.
- Once a signed consent form is obtained, the original should be retained in the PI’s study records. For studies conducted at a UK hospital or clinic, the PI places a copy of the signed consent form or, if applicable, assent form in the medical record unless the IRB waives the requirement.
- 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.
- During the course of the study, protocol changes may be implemented or study results shared, which may affect the subject’s willingness to continue to participate. These must be reported to the IRB so a determination can be made about whether to re-consent the enrolled subjects.

What is the difference between the IRB waiving informed consent and waiving documentation of informed consent?

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<th>Brief Description</th>
<th>IRB Request Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waiver of the requirement for informed consent</td>
<td>If the conditions outlined on Form E are met, the IRB may waive the requirement for some or all elements of the informed consent process (i.e. medical record review, deception research).</td>
<td>Form E</td>
</tr>
<tr>
<td>Waiver of documentation of informed consent</td>
<td>Waiver of the requirement for obtaining documentation of informed consent means the subject does not put in writing/document his/her agreement to participate in the study (signature). The subject is still informed through informed consent process and is given the opportunity to decide whether to participate (i.e. internet research, mail survey, telephone survey).</td>
<td>Form F</td>
</tr>
</tbody>
</table>

Under what circumstances can documentation of informed consent be waived?

DHHS regulations (45 CFR 46.117c) allow the IRB to waive the requirement to obtain a signed consent document for some or all of the subjects if certain conditions are met.
a. The only record linking the subject and the research would be the consent document and the principal risk would be harm resulting from breach of confidentiality

b. The research presents no more than minimal risk and involves no procedures for which written consent is normally required

The FDA will accept condition b to be applied to FDA regulated research, but not condition a. While condition a may be useful in highly sensitive social science research, common examples for condition b include mail surveys, telephone surveys, internet research, or international research where recruitment of subjects would be inhibited based on cultural beliefs. See IRB Application “Form F” instructions and “Form F”. [http://www.research.uky.edu/ori/MedicalFullReviewApplication.htm#ICA]

When might you need to employ additional safeguards?

Many situations may apply; however, anytime vulnerable populations or individuals vulnerable to coercion are involved in research, investigators must employ additional safeguards are required for IRB approval.

What is the difference between Informed Consent, and the process of obtaining Assent and Parental Permission?

- Only a person can provide consent for themselves. However, because children and some adults with impaired consent capacity are not legally considered capable of providing consent, regulations do allow a parent or legally authorized representative (LAR) to give “permission” for the individual to participate when assent or “affirmatively agreement” to participate is obtained from the child (or adult with impaired consent capacity).
- For details on when assent needs to be documented, when assent is not required, and parental permission requirements for research involving children, see the UK IRB Policy on Children in Research [http://www.research.uky.edu/ori/SOPs_Policies/22-Children_in_Research_Policy.pdf] and the recently revised “Form W”.
- For the UK IRB policy on research involving adults with impaired consent capacity, see the document: UK Impaired Consent Capacity Policy [http://www.research.uky.edu/ori/ORIForms/62-Impaired-Consent-Capacity-Policy.pdf] and the recently revised automated “Form T”.

How do you determine an appropriate assessment and adequate safeguards for enrollment of subjects with impaired consent capacity?

The UK IRB impaired consent capacity policy and tools are designed to enable investigators to ethically include subjects who have limited or impaired consent capacity in research.

The policy and automated Form T [www.research.uky.edu/ori/ORIForms/FormT/Scale.asp]:
- Prompt investigators to consider a more comprehensive list of conditions with potential to encounter a prospective subject with impairment;
- Allow investigators to develop a plan of assessing capacity with a tool that offers options based on consideration of study risk, likelihood of impairment and potential for fluctuations in impairment;
- Encourage fair and equitable recruitment; and
- Promote use of safeguards and enhancements to the consent process to enable individuals who otherwise have limitations, to make competent decisions.

Consent enhancements include adult assent, LAR information pamphlet, methods for assessing dissent, study overview summaries.
For the UK IRB policy and sample enhancements for research involving adults with impaired consent capacity see the Impaired Consent Capacity documents at http://www.research.uky.edu/ori/IRB-Survival-Handbook.html#Impaired.

What items may need to be addressed in the informed consent form for FDA regulated investigations?

The UK Informed Consent template includes language reference FDA including:

- In the IRB approved consent form and HIPAA authorization, the investigator must inform the subject that his/her health information may be shared with FDA;
- In the IRB approved consent form, the investigator must inform the subject in the purpose that the study includes evaluation of both safety and effectiveness of the test article and state the test article is investigational, and, if applicable, not approved by the FDA;
- Applicable FDA regulated clinical trials: In the IRB approved consent form, the investigator must inform the subject that the clinical trial will be entered into a national clinical trial registry data bank; and
- Early withdrawal from FDA regulated clinical trials: In the IRB approved consent form, the investigator informs the subject that data collected to the point of withdrawal, remains part of the study database and may not be removed.

The ORI/IRB Informed Consent SOP has additional information including:

- use of the short form consent process;
- FDA required language;
- Assent process;
- who may serve as LAR in adults/minors;
- non-English speaking subjects,
- emancipated minors; and
- consent waivers.
Complaints, Concerns, Suggestions, Questions or Requests for Information
Investigators respond to participants’ complaints or request for information.

Who do you call with a complaint, concern, question or suggestions?
- ORI and IRB administrative procedures:
  ORI Director Ada Sue Selwitz (859) 257-2978 or email selwitz@uky.edu
- Disagree with IRB Decision:
  Contact the IRB Chair or Reviewer
Submit anonymously to ORI's online customer service form
https://redcap.uky.edu/redcap/surveys/?s=jB2Nfm

What provisions do you have in place for receiving and handling a subject complaint or request for information?
- The procedures to satisfy this should offer a safe, confidential, and reliable channel for current, prospective, or past research subjects (or their designated representative) permitting them to discuss problems, concerns and questions, or obtain information. [Your protocol specific plan described in the IRB Research Description “Form B”.]
- For greater than minimal risks studies, the IRB recommends the consent document(s) include a reliable, dedicated pager or phone number.

Who may a subject call outside of the study personnel regarding their rights and welfare?
- Each IRB approved informed consent document should include the ORI Research Compliance Officer's toll-free phone number (1-866-400-9428) as a subject's primary contact point regarding their rights and welfare. The RCO serves the role of an informed individual who is unaffiliated with the specific research protocol.

Monitoring & Reporting Requirements
Investigators assess and report unanticipated problems occurring during a research study in accordance with applicable federal, state, and local regulations and the Organization’s policies and procedure.

When do you begin collecting, recording and reporting adverse event and unanticipated problems for a research subject?

Upon subject enrollment into the study.

What problems/events are you required to report to the IRB?

The UK IRB has three reporting categories for unanticipated problems/adverse events that occur internal or external to the university.
1. **Prompt Reporting** of problems/events that are serious(or) life-threatening(or) involves risk to subjects or others, **AND** unanticipated, **AND** related to the research; also, anticipated or unanticipated related deaths;
2. **Non-Prompt Reporting** include:
   - anticipated problems or adverse events whether or not serious or life-threatening (including external IND safety reports)
   - unanticipated or anticipated death not related to the research (e.g., due to underlying disease) (including external IND safety reports)

3. **Continuation Review Reporting** if any problems/adverse events occurred within 12 months prior to the continuation review (CR) request, with a written summary of all problems/adverse events involving subjects since the study was initiated, whether anticipated or unanticipated, serious or not serious, life-threatening or not life-threatening, or related or not related.

   If the study is monitored by a Data Safety Monitoring Board (DSMB), submit with the continuation review, any DSMB report issued within 12 months prior to the continuation review (CR) request.

<table>
<thead>
<tr>
<th>Prompt Reporting Timelines</th>
<th>Life Threatening</th>
<th>Unanticipated</th>
<th>Related</th>
<th>7 calendar days</th>
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<tr>
<td>Serious</td>
<td>Unanticipated</td>
<td>Related</td>
<td>14 calendar days</td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>Unanticipated or Anticipated</td>
<td>Related</td>
<td>Immediately (within 48 hours of receipt)</td>
<td></td>
</tr>
</tbody>
</table>

For additional information, see the “Policy on Prompt Reporting for Unanticipated/ Anticipated Problems/Events” [http://www.research.uky.edu/ori/SOPs_Policies/2-AE_policy.pdf].
What is considered a Serious Adverse Event (SAE) for FDA regulated research?  
http://www.fda.gov/Safety/MedWatch/HowToReport/ucm053087.htm  
An adverse event is considered an SAE when the patient outcome is:  
- Death  
- Life threatening  
- Hospitalization (initial & prolonged)  
- Disability  
- Congenital anomaly  
- Requires intervention to prevent permanent impairment  

What is the IRB reporting requirement if a non-serious adverse event occurs that is not related to the study?  
This would be collected and included in the investigator’s summary assessment submitted with the continuation review.  

What other activities on an approved protocol require reporting by the PI to the IRB?  

- **MODIFICATIONS** – any change to a protocol from what was previously approved.  
  Includes proposed changes to the current IRB approved protocol or changes which impact an individual subject but does not change the overall protocol (i.e., **exception** - one-time enrollment of a research subject in a protocol that fails to meet current IRB approved or **deviation** - one-time departure from the current IRB approved protocol once a subject has actually been enrolled).  
  ★Changes may not be initiated without IRB review and approval, except where necessary to eliminate immediate hazard.  
- **VIOLATIONS** – a protocol deviation or protocol exception occurs without prior IRB review and approval, the Principal Investigator submits a [Protocol Violation Reporting Form](http://www.research.uky.edu/ori/ORIForms/D109-UK-Investigator-Quick-Guide-to-IRB-Reporting-Requirements.pdf) within 14 days of the occurrence.  
- **DATA AND SAFETY MONITORING REPORTS**  
- **FOOD AND DRUG ADMINISTRATION CORRESPONDENCE**  
- **UNRESOLVED SUBJECT COMPLAINT** that requires IRB involvement  
- **SUBJECT INCARCERATION**  
- **AUDIT, INSPECTION, OR INQUIRY BY A FEDERAL OR EXTERNAL AGENCY**  

[See the one-page Investigator Quick Guide to IRB Reporting Requirements at](http://www.research.uky.edu/ori/ORIForms/D109-UK-Investigator-Quick-Guide-to-IRB-Reporting-Requirements.pdf)
Food & Drug Administration (FDA) Regulated Research

Investigators are responsible for ensuring that studies testing FDA regulated products are conducted under a valid Investigational New Drug (IND), Investigational Device Exemption (IDE), meets Abbreviated IDE requirements or is exempt from IND/IDE requirements.

Investigators are responsible for the control and accountability of FDA regulated investigational products.

Investigators follow FDA regulations and UK procedures for emergency use of a test article.

What is the IRB’s role in reviewing FDA regulated research?

In addition to conducting the IRB and informed consent review according to FDA regulations, the IRB has been given specific responsibilities for:

- reviewing the qualifications of investigators,
- assessing the adequacy of research sites, and
- verifying the sponsor’s or sponsor-investigator’s determination of whether an Investigational New Drug (IND) or Investigational Device Exemption (IDE) is required.

These responsibilities were detailed in the FDA Guidance for IRBs at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM328855.pdf.

If the IRB is unsure regarding the sponsor or sponsor-investigator’s determination regarding need for an IND/IDE, investigators may be required to consult the FDA for a ruling.

FDA Regulated Drug Research:

What process do you do to make sure that investigational drugs are controlled so that they are used only in approved research protocols under your direction?

Research that involves the use of a drug other than a marketed drug in the course of medical practice must have an investigational new drug (IND), unless the research meets one of the exemptions from the requirement for an IND.

If your study involves collecting data on a drug*, complete IRB Form O to document sponsor or sponsor investigator’s determination that the study is:

1. Exempt from IND requirements; or
2. Subject to IND requirements and being conducted under a valid IND.

*The term drug includes FDA approved drugs, unapproved use of approved drugs, investigational drugs, biologics, other compounds intended to affect structure of function of the body, and in some cases dietary supplements, or substances generally recognized as safe (GRAS) when used to diagnose, cure mitigate, treat or prevent disease.

IRB Application “Form O” (Use of Any Drug Being Tested in Research http://www.research.uky.edu/ori/ORIfoms/10900-Form_O-Investigational_New_Drug.doc

Does the IRB ask for information about how you will control the study drug?

Yes, the IRB Form O asks where the study drug will be housed and managed. If drug will not be managed by the Investigational Drug Service (IDS), the investigator describes how the drug will be managed including policies and procedures for receipt, storage, control, dispensing, accountability, and procedures in place to prevent drug dispensing and/or administration errors.
Does UK require study drug to be managed by an Investigational Drug Unit?

Inpatient studies are required by Hospital Policy to utilize the Investigational Drug Service (IDS). Use of IDS is highly recommended, but optional for outpatient studies. Outpatient studies not using IDS services are subject to periodic inspection by the IDS for compliance with good clinical practices. If using the IDS, have a process for communicating applicable changes in the protocol/intervention, and actions such as protocol suspension.

(If applicable) Are you knowledgeable about the additional regulatory requirements you are responsible for as the Sponsor-Investigator (hold the IND) of the drug investigation?

The IRB Form O asks sponsor-investigators this question and asks if any responsibilities have been transferred to a commercial sponsor, contract research organization, or other entity. Links are provided to a Summary of FDA Requirements for Sponsor Investigators [http://www.research.uky.edu/ori/human/44-Revised_IND_Document.pdf]. The form also asks how monitoring the conduct of the clinical investigation, and reviewing and evaluating safety information will be performed, and by whom.

To ensure investigators who assume sponsor functions are knowledgeable about the regulatory and institutional requirements IRB policy requires sponsor-investigators to successfully complete a one-time mandatory training before final IRB approval is granted.

FDA Regulated Medical Device Research:

What process do you to make sure that investigational devices are controlled so that they are used only in approved research protocols under your direction?

Research that is conducted to determine the safety or effectiveness of a device must have an Investigational Device Exemption (IDE) issued by the FDA, unless the device meets the requirements for an abbreviated investigational device exemption (IDE) or the research meets one of the exemptions from the requirement for an IDE.

If your study is designed to determine the safety or efficacy of a medical device**, complete IRB Form P to document the sponsor or sponsor investigator’s determination that study is:

1. Exempt from IDE requirements; or
2. A NONSIGNIFICANT RISK (NSR) DEVICE STUDY [subject to “Abbreviated” IDE requirements without a formal IDE issued by FDA]; or
3. A Significant Risk (SR) device study [conducted under a formal IDE issued by FDA].

**Device may include a component, part, accessory, assay, software, or computer/phone application if intended to affect the structure or function of the body, diagnose, cure, mitigate, treat or prevent disease.

IRB Application Form P (Use of Any Device Being Tested in Research
http://www.research.uky.edu/ori/ORIForms/11100-Form_P-Investigational_New_Device.doc

New 11/4/14 FDA Printable Slides IDE BASICS

Does the IRB ask for information about how you will control the study device?

Yes, The IRB Form P asks how the device will be controlled including policies and procedures for control, dispensing, and accountability. It also asks where the device will be stored and how access to the device(s) will be limited to prevent unauthorized access (e.g., secure, locked storage; signage).

TIP: The ORI Quality Improvement Resources website provides a Device Accountability SOP
In addition, the IRB requires periodic quality improvement reviews (QIR) for investigational device accountability. If selected for a device accountability QIR, ORI conducts an on-site evaluation of policies and procedure for storage, control, dispensing, accountability, and monitoring.

Does the IRB ask about qualifications or training needed to use or administer the device the study device?
Yes, The IRB Form P asks specific qualifications or training is required to use or administer the device and any plans to obtain or augment applicable qualifications or expertise.

(If applicable) Are you knowledgeable about the additional regulatory requirements you are responsible for as the Sponsor-Investigator (hold the IDE or Abbreviated IDE) of the device investigation?
The IRB Form P asks sponsor-investigators this question and asks if any organization or entity will assist in meeting the responsibilities.

Links are provided to a Summary of FDA Requirements for Device Sponsor-Investigators http://www.research.uky.edu/ori/human/45-Revised_IDE_Document.pdf. The form also asks how monitoring the conduct of the clinical investigation, and reviewing and evaluating safety information will be performed, and by whom.

To ensure investigators who assume sponsor functions are knowledgeable about the regulatory and institutional requirements IRB policy requires sponsor-investigators to successfully complete a one-time mandatory training before final IRB approval is granted.


FDA Emergency Use:

What happens when you plan an emergency use of a test article in a life-threatening situation?

Under the Food and Drug Administration (FDA) regulations, "emergency use" is defined as the use of a test article (e.g. investigational drug, biologic, or device) on a human subject in a life-threatening or severely debilitating situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain Institutional Review Board (IRB) approval.

Although the FDA may exempt the requirement for prospective review by the full IRB in emergency use cases, it is the policy of the University of Kentucky Medical IRB that in these situations prior review by the IRB Chair or designee is required.

Unless the healthcare provider determines that immediate use of the test article is required to preserve a patient’s life, the UK IRB requires confirmation that the article meets the FDA emergency use criteria by the IRB Chair or designee. The provider or Principal Investigator (PI) submits the following information directly to the IRB Chair:
1. Written memo, email or phone call of explanation which justifies administration of the test article.
2. Copy of the informed consent form.
3. Completed General Information Sheet with title including the words "EMERGENCY USE" and the name of the investigational product.

This notification is not considered to be prospective IRB approval. It simply allows the IRB Chair to concur with the emergency use (as opposed to compassionate or other use situation) and initiates tracking to ensure
the PI submits a report of the use within the five working day time frame required by FDA regulation [21 CFR 56.104(c)].

Informed consent from the individual or the legally authorized representative is required. The only exception to this policy requires a corroborative evaluation by an independent physician as described in the Emergency Use Standard Operating Procedure (SOP) and FDA regulations [21 CFR 50.23(a)]. See the Emergency Use SOP for required elements.

In accord with federal regulations, any subsequent use of the test article in another subject should first receive full IRB review.

See the Emergency Use SOP for detailed IRB submission and review procedures.

Is a patient receiving a test article in an emergency situation considered to be in research?

If the activity involves emergency use of an FDA regulated test article in a life-threatening situation, the activity is research and the patient is a subject under FDA regulations. The FDA may require data from an emergency use of a test article in a life-threatening situation to be reported in a marketing application.

What is the difference between single subject emergency use and Planned Emergency Research?

The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB in order for an investigational drug or device to be used in a human in a life-threatening situation where time is not sufficient to obtain IRB approval. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval.

FDA regulations for planned emergency research [21 CFR Subpart B 50.24 ] provide a narrow exception to the requirement that the investigator obtain informed consent from each subject, or the subject’s legally authorized representative, prior to enrollment in research conducted in an emergency setting. The regulations also provide additional protections for subjects enrolled in these studies. For example, the regulations require consultation with representatives of and public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation. They also require public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study. As well, the regulations require that an independent data monitoring committee exercises oversight of the clinical investigation. NOTE: On rare occasions the UK IRB has applied this rule which requires extensive community consultation.

Community Engaged Research (CER)/
Community Based Participatory Research (CBPR)

Resources to facilitate CER/CBPR.

What resources are available to facilitate the approval and conduct of Community Engaged Research (CER) or Community Based Participatory Research (CBPR)?

Community-based participatory research is one type of community-engaged research and is conducted as an equal partnership between researchers and members of a community. CBPR is defined as an applied collaborative approach that enables community residents to more actively participate in the full spectrum of research (conception, design, conduct, analysis, interpretation, conclusions, and communication of results) with a goal of influencing change in community health, systems, programs or policies.

While CER/CBPR may involve unique ethical and regulatory challenges, the Office of Research Integrity, Center for Clinical and Translational Science, investigators, and the Institutional Review Board members developed a list of frequently asked questions (FAQs) intended to assist researchers design and implement research in the community and facilitate Institutional Review Boards' review of CER/CBPR.
The IRB has members with experience with community-engaged research. The IRB application request that the investigator describe strategies for involvement of community members in the design and implementation of the study, and dissemination of results from the study. In preparing the application, Investigators are encouraged to describe operational procedures that are general or include a range of procedures to allow flexibility, while including enough details to allow the IRB to apply the federal criteria for approval.

The Center for Clinical and Translational Services (CCTS) Community Engagement Program provides a network of resources, facilities, consultation, training, and funding opportunities for community engaged research. www.ccts.uky.edu/ccts/community-engagement

Implicit Human Research Protection Guidance Frequently Asked Questions: Community-Engaged Research (CER) and Community-Based Participatory Research (CBPR)
www.research.uky.edu/ori/ORIForms/D115-CBPR-FAQs.pdf

### Outreach & Education for the Public and Potential Research Participants

*Investigators are aware of public education and potential research participant outreach efforts.*

**Who is responsible for ensuring a local research participant outreach program that educates the public and potential participants?**

The Participant Recruitment/Marketing core of the Center for Clinical and Translational Science (CCTS) works with UK Healthcare, UK Marketing, the ORI, and research investigators to provide education, outreach, and research opportunities to the general public. The CCTS spearheads community outreach events and delivers patient/subject education via numerous outlets including social media, dedicated research wall mounts, and traveling exhibits. CCTS Marketing has collaborated with Public Relations to host a series of live Twitter feeds (#AskaCat) as a forum for participants and the public to submit questions, or suggestions regarding participation in research or specific research related topics. Representatives from the IRB/ORI are invited to participate in these events. www.ccts.uky.edu/ccts/participant-recruitmentmarketing

**Who hears concerns from research participants?**

The ORI Research Compliance Officer, Helene Lake-Bullock, serves as the primary contact for current, prospective, or past research participants. Each IRB approved informed consent document as well as CCTS outreach materials include the ORI’s toll-free phone number (1-866-400-9428) as a subject’s primary contact point to obtain information, offer input or discuss problems, concerns, or questions about research participant rights. ORI Participant website www.research.uky.edu/ori/human/participants.html.