# Human Research Protection Program:

## Research Investigator Q & A Guide

UK UNIVERSITY OF KENTUCKY
Office of Research Integrity

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## UK Human Research Protection Program

Investigators are familiar with the institutional Human Research Protection Program, regulatory framework and ethical standards for protecting human subjects.

1. **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 enough resources to support it.

2. **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: https://www.research.uky.edu/uploads/2018-university-kentucky-human-research-protection-program

3. **What rules or guidelines are investigators 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. Health Insurance Portability Accountability Act (HIPAA), Family Educational Rights and Privacy Act (FERPA) or General Data Protection Regulation (GDPR)

   Funding Agency Requirements:

   - Department of Defense (DoD)
   - US Department of Education (DoED)
   - Environmental Protection Agency (EPA)
   - US Department of Justice (DOJ); National Institute of Justice (NIJ); Bureau of Prisons (BOP)
   - Department of Energy (DOE)

   **State Law**

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      - AR 7:1 Research Misconduct
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      - 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
      - ✶ IRB SURVIVAL HANDBOOK – Guidance Documents by Topic

**4. What ethical standards or guides do investigators 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. The Belmont Report outlines three ethical principles that are 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.

Click to read→ THE BELMONT REPORT
*Ethical Principles and Guidelines for the Protection of Human Subjects of Research*

***Remember/Consider….***

*Proposed research that is compliant with the regulations may still have ethical concerns.*

*Researchers should apply ethical principles and standards appropriate for their discipline when designing and conducting human research studies.*

**5. 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, medical interventions in a participant's home)?**

Prior to IRB review, the PI is responsible for determining applicable state laws relative to the conduct of their research. Contact the Office of Legal Counsel UKOfficeofLegalCounsel@uky.edu 859 257-2936 and ask to be connected with a research attorney if assistance is needed.

**6. 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.

**7. 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?**

**Identify Applicable Requirements/Protections:** For research conducted at an international location, the investigator identifies local regulations, laws, or ethics review requirements for human subject protection. they may refer to the annual International Compilation of Human Research Standards or the National Institutes of Health ClinRegs 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.

**Cultural Consultation:** In addition, the investigator informs the IRB of any relevant cultural norms or customs particularly regarding 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 protocols involving non-English speaking subjects, and/or subjects from a foreign culture.

8. **To receive federal funds for research, an agreement is submitted to follow federal regulations, review human research, monitor on-going studies and report to federal agencies. What is the title of the agreement and the name of the agency?**

   Agreement: Federal-Wide Assurance (FWA)

   Agency: Office for Human Research Protections (OHRP)

9. **How does UK ensure the rights and welfare of participants are protected when the investigator is operating at a non-UK facility, is conducting collaborative research, or when oversight is shared with or deferred to another organization or IRB?**

   In the IRB application, investigators include letters of support approving the conduct of research at non-UK facilities.

   If research involves collaboration with any sites and/or personnel outside UK, then it is considered multisite research and IRB reliance issues will need to be addressed.

   UK has procedures to define the responsibilities of collaborating institutions and to coordinate communication among responsible IRBs. UK IRB requires a written agreement to be completed between organizations involved in a reliance relationship. A Reliance (or Authorization) Agreement identifies and describes the respective authorities, roles, responsibilities, and methods of communication between an institution/organization providing the IRB review of research and a participating site relying on the institution/organization.


   Federal policies require review by a single IRB for select multi-site research. Studies using an external IRB **must** register with the UK IRB. The ORI Single IRB Reliance website provides tools, checklists, forms, sample agreements and guidance for navigating single IRB review.

   Prior to allowing investigators to cede research to an external IRB, the IRB (with assistance from OR) is required to:

   a. Verify initial and continuing Human Subjects Protection training of investigators.
   b. Verify the external IRB is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). UK may agree to defer responsibility for IRB review to a non-AAHRPP accredited institution's IRB for research that is not greater than minimal risk. To defer responsibility, the non-UK IRB must have an OHRP-registered IRB.

10. **Does UK research have an emergency preparedness and response plan?**

    Yes, the Emergency Preparedness Response Plan [PDF] provides guidance for initiating a response to an emergency/disaster situation impacting the UK Human Research Protection Program (HRPP). The Emergency Preparedness Response Plan includes policies to enable sustainability of the HRPP and continuing protection of participants in research during emergencies. It is located on the ORI IRB homepage.

## What Needs Institutional Review Board (IRB) Review?

Investigators understand the definition of human research and seek guidance when determining if an activity requires IRB review.

1. **What is the process for determining whether an activity is under the purview of the IRB?**

1. See **What Needs IRB Review** website for resources. Contact ORI with questions about regulations or UK policy
2. If not sure, submit a **Not Human Research (NHR)** determination form in REDCap
3. The ORI Director or IRB Chair provides an official determination on whether an activity meets applicable regulatory definitions of human subject research. ORI communicates the decision to the investigator.

The PI may use "What Needs Review" resources to make a preliminary decision; they may contact ORI staff or IRB Chair/Vice Chair or other member for advice on application of the federal regulations and UK policy.

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

The ORI What Needs IRB Review Website includes, Guidance, Videos, Tables, Forms, and other resources.

For quick reference, see the brief video *What Needs IRB Review*? [HTML Video, 05:10 minutes]

If unsure, Submit the Not Human Research (NHR) determination form or send an e-mail requesting a determination to IRBSubmission@uky.edu to obtain a formal written IRB determination regarding need for review.

3. **Does secondary research with specimens or data require IRB review?**

Secondary research with specimens or data may or may not require IRB review. It depends on whether the specimens or data meet the definition of human subject. Considering only whether data or specimens are "identifiable" may result in a wrong determination. Consult the guidance For Determining When Protocols Involving Coded Private Information or Biological Specimens Meet the Federal Definition of "Human Research"

***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.

Private information is considered a human subject if you:
>can see identifiers
>have access to a code linking identifiers
>know who provided the private information
>can readily figure out who provided the private information

# IRB Submission & Review Types

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

ORI has a Getting Started website for individuals new to human subject research. The ORI IRB Review Types webpage provides resources for determining which type of review a protocol will require.

Exempt and Expedited review is designed for minimal risk research. However, each category has conditions and limitations. Research that cannot meet the criteria for exempt or expedited review must be submitted for full review by a convened board.

In addition to checking the ORI guidance, researchers are encouraged to contact ORI for consultation and a preliminary interpretation of the most appropriate application type. Ultimately, the IRB will choose the type of review based on the full application relative to the regulatory and ethical framework.

***Remember/Consider….***

*Use Chrome or Firefox browsers to access E-IRB.*

*Review the IRB Review Types webpage and contact ORI for help determining the appropriate review before creating a new IRB application.*

*E-IRB has a "Copy Protocol" function that allows you to copy an IRB-approved application to use as a template.*

| Review Type | Risk/Initial Review Categories | Initial Review by: | Guidance |
|---|---|---|---|
| Exempt | Minimal Risk/ 6 Categories | 1 IRB member (consultant if necessary) | UK ORI Common Rule Exemption Categories Tool [PDF] |
| Expedited | Minimal Risk/ 7 Categories | 1 IRB member (consultant if necessary) | Issues to be Addressed when conducting Expedited Review [PDF] |
| Convened | Greater Than Minimal Risk or doesn't fit in above categories | Full Board Meeting with Investigator Invited  | Research Risk Assessment Guidance [PDF] |

**2. How do I find out general information about the IRB and human research?**

The IRB Membership Website provides general information on IRB review types, IRB meeting dates, IRB membership rosters, etc.


The IRB FAQs answer common questions regarding review operations, Medical vs. Nonmedical IRB, informed consent, terminology, etc. Categories include General IRB, Need for IRB Review, Informed Consent, and Continuing/Annual Administrative Review.

An interactive New to the UK Institutional Review Board (IRB) Process provides answers to select questions for researchers or faculty new to the UK IRB Process.

3. **Where can I learn how to use the E-IRB submission?**

   The Electronic IRB System E-IRB website includes FAQs, tips, features, news, and updates.

   View video tutorials using your Link Blue ID to access the private E-IRB Video Library using your Link Blue ID and password to see video tutorials.

4. **How do I request IRB approval for changes while conducting the research?**

   **Modification Requests (MR)** – submit a MR for any change to a protocol from what was previously approved. This 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 or Deviation)

   - **Exception** - *one-time enrollment of a research subject in a protocol that fails to meet current IRB approved*
   - **Deviation** - *one-time departure from the current IRB approved protocol once a subject has been enrolled*

   **★Changes may not be initiated without IRB review and approval, except where necessary to eliminate immediate hazard.**

   - **Continuing Review (CR) or Annual Administrative Review (AAR)**– changes may also be requested as part of the annual or continuing review submission.

## 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.

1. **What criteria would you consider in evaluating whether your research or a sponsored study is scientifically sound?**

- potential risk/benefit ratio
- potential contribution to generalizable knowledge
- demographic illustrative of real patient/subject population
- enrollment criteria to rule out 'at risk' participants
- specific indicators for diagnostic criteria
- study design, (e.g., intervention or outcomes; comparative or placebo)
- controls, blinding, deception
- statistical plan & methods to minimize bias
- certificate of confidentiality to protect sensitive information against compulsory legal demands
- subject safety monitoring

***Remember/Consider….***

*Reasons you may have turned down a sponsored study.*

*An example of how you have minimized risk in a study.*

*How you determine if you have enough study personnel?*

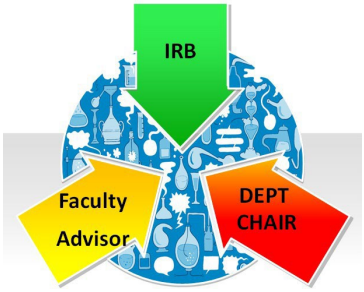
*Do you have protected time for research activities?*

*Any ethical issues specific to the study design.*

2. **Who is involved in conducting scientific review at UK?**

The Department Chairperson/Faculty Advisor and the IRB.

- Department Chairperson/Faculty Advisor attest (Assurance Signature) 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; and
  - ✓ provision of ongoing mentoring and guidance




- The IRB 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. When needed, the IRB seeks consultation from content experts.

3. **How do IRB regulations define 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)].

4. **How does the definition of minimal risk differ in the regulations for prisoners?**

For research involving prisoners, the definition of minimal risk requires reference to physical or psychological harm, as opposed to harm or discomfort, to risks normally encountered in the daily lives, or routine medical, dental or psychological examination of healthy persons. See Guidance on

Prisoner Involvement in Research.

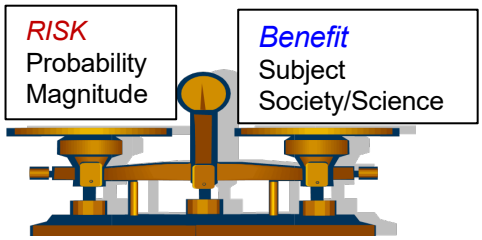
5. **What are the kinds and levels of risk?**


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.

Ultimately the IRB designates the risk-benefit category. 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

To approve research, the IRB must determine that risks to subjects are 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.



6. **What procedures do you employ to minimize risk or mitigate potential injuries?**

   Potential protections include:

   - Using procedures already being conducted for non-research reasons
   - Incorporating criteria to exclude “at risk” subjects
   - Choosing least intrusive design that yields valid data (outcomes vs. randomized intervention; comparative drug vs. placebo)
   - Conducting safety monitoring including safety labs and other assessments
   - Planning for responding to clinically significant abnormalities including withdraw of study product and re-challenge with product if appropriate
   - Including provisions for medical services or professional intervention (e.g., counseling) in the event of adverse events
   - Adopting strategies for research with a focus on, treatment for, or potential for suicidal ideation or behaviors. See the ORI Guidance on Suicidality and Research Ethics
   - Ensuring protections to secure confidential or private identifiable information
   - Establishing data and safety monitoring
   - Obtaining a Certificate of Confidentiality to protect against compulsory legal demands such as subpoena


7. **What additional privacy regulations apply to select protocols?**

   - Health Insurance Portability and Accountability Act (HIPAA) is a federal regulation designed to protect the use and disclosure of Protected Health Information or PHI. PHI is defined as any of the 18 HIPAA identifiers in combination with health information transmitted or maintained in any form (electronic, paper, or oral) that relates to the past, present or future physical or mental health or conditions of an individual.
   - Family Educational Rights and Privacy Act (FERPA) is a federal law that protects the privacy of personally identifiable information contained within a student’s educational record.
   - General Data Protection Regulation (GDPR) is a regulation affecting the way data is processed in the European Economic Area (EEA)*. This regulation increases the rights afforded to research participants and reshapes the way organizations handle and process personal data from individuals located in the EEA.

8. **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 Study Closure SOP.

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

Privacy concerns people. 

The following are considerations and strategies for respecting the privacy of potential participants.

- Consider the methods used or setting where potential participants are identified. What is the targeted study population's expectation of privacy, both in person and online?
- Only approach individuals known to you or make contact on behalf of someone the individual knows.
- Comply with privacy guidelines of applicable professional associations and scholarly disciplines (e.g., oral history, anthropology, psychology).
- Access the minimum amount of information necessary.

Confidentiality concerns data. 

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 application, 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*
- safeguards to protect identifiable research information (*e.g., coding, 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 or sharing information or tissue/specimens/data for use in current or future research.

## 10. What information or resources are available for conducting survey research?

The ORI Survey Website [HTML] includes survey guidance and tools developed to meet the diverse needs of survey researchers. It includes identifiable and anonymous consent templates, resources for advertising, survey platforms, fraud prevention, and regulations applicable to school-based surveys.

## 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.

1. **What is UK's policy on Conflict of Interest (COI)?**

   UK has two policies on conflict of interest, one for researchers and one for the institution:

   Financial COI related to research of individual investigators is covered in **Administrative Regulation (AR) 7.2 - Financial Conflicts of Interest in Research**. The AR outlines procedures for defining, identifying, disclosing, managing, reporting and training regarding COI.

   Institutional COI is covered in **Administrative Regulation (AR) 7.9 – Institutional Conflict of Interest**. *A potential or actual* 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.

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

   **See the OSPA COI website for guidance.**

   If you have questions or need assistance with a specific situation, contact Conflict of Interest Administrator Emily Bradford at 257-9420 or emily.bradford@uky.edu.

   ORI & OSPA coordinate handling of Investigator COI for both funded and unfunded human subject research. Details are outlined in the COI coordination SOP.

2. **How is researcher COI managed?**

   The IRB application asks if any investigators or key study personnel have a SFI requiring disclosure if the interests are related to the proposed research.


1. If a financial COI exists and cannot be eliminated, the investigator works with Emily Bradford **Assistant Director/Research Compliance in the Office of Sponsored Projects Administration.** to complete the UK template management plan and obtain approval from their Associate Dean for Research (ADR).
2. All management plans are referred to the Research Conflict of Interest Committee (RCOIC) for review. ORI Reliance IRBReliance@uky.edu represents human research on the RCOIC.
3. The RCOIC recommends a plan to the Institutional Official who makes the final decision on approval of the plan.
4. 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.

***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".*

*Initial and periodic COI training informs investigators regarding thresholds, SFI disclosure, management, and reduction of financial COI.*

3. **Who has the final authority regarding management of investigator COI?**

   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. The IRB may also add requirements such as disclosing a conflict in the informed consent document.

4. **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). Medical Center investigators must disclose all SFI, regardless of value. Other investigators disclose SFI related to their institutional responsibilities.

5. **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. Investigators may be asked to include additional safeguards in the management plan.

6. **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**
   - 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)

## 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.

1. **What Responsibilities and Qualifications are required for research investigators?**

   The Principal Investigator's Guide to Responsibilities, Qualifications, Records and Documentation of Human Research list responsibilities and basic qualifications for conducting human subject research. A link to this guide is provided in IRB approval letters. It is a succinct guide to enhance compliance and includes institutional responsibilities for research reviewed by an external, non-UK IRB.

***Remember/Consider….***

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

*PI's describe staff qualifications in the IRB Research Description.*

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

***How do you communicate with and supervise study personnel?***

2. **What experience and qualifications do investigators and study personnel have for conducting research?**

   - It is the PI's 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 in the IRB application, they are attesting that everyone 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, regardless of funding source, must complete initial HSP training and refresher HSP training every 3 years. 💻 For details, see the Human Subject Protection (HSP) Training FAQ

3. **What human research education opportunities does the institution provide?**

   Ongoing education opportunities are provided by multiple departments including ORI, Society of Postdoctoral Scholars (SOPS), Research Scholars Program, Center for Clinical and Translational Sciences (CCTS), Healthcare Bioethics Program, and others. ORI offerings include monthly office hour sessions, guest speaker seminars, webinars, videos, annual human research protection updates, departmental and class presentations, and a regional human subject protection conference. In addition to resource websites such as Getting Started and the IRB Survival Handbook, the ORI Education Team has built an Education Resource **[HTML]** library of topic-specific videos, recordings, and interactive tools. These resources aim to provide clear and accurate content, in a brief and engaging format.

4. **What are the IRB's expectations regarding oversight and delegation for medical intervention studies and clinical trials?**

   Unless a study submitted to the Medical IRB is non-interventional, (e.g., survey, record review, or purely outcomes research), some form of medical oversight may be necessary. However, the degree and level of expertise needed can vary depending on risk level, condition, study population, applicable regulations, and external oversight (e.g., sponsor monitor; mentor). The Investigator Qualifications and Provision of Medical Oversight guide provides regulatory guidance on oversight, supervision, and delegation.

   Inappropriate delegation is frequently cited in FDA warning letters. The FDA Guidance, Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects clarifies FDA's expectations on delegation and oversight.

5. **What functions have you delegated to study staff; what is the process for task delegation; or what tasks do investigators not delegate to staff?**

   Prior to describing delegation, the PI should indicate their 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 if the tasks are within their scope of practice. Anyone delegated a task must be qualified by education, training, and experience (and state licensure where relevant). In addition, the investigator would need to ensure that the delegation is consistent with any specifications in the research protocol or stipulations by the IRB.

***Remember/Consider….***

*In FDA Regulated clinical studies, a qualified physician (or dentist) serving as the PI or Sub-Investigator, 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 and Device sections of the application include specific questions regarding training and qualifications required to administer the test product.*

*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 responsibilities.*

Medical procedures and assessments (including adverse event causality, un-blinding, treatment decisions) should not be inappropriately delegated to unqualified staff. Using task delegation logs is a best practice for clinical research, to define roles and indicate who serves in the PI's absence.

Investigators designate which study personnel should be authorized to obtain informed consent on the IRB application for review by the IRB. The investigator must ensure that the study personnel are informed regarding their obligations and commitments.

6. **How often do you talk with, observe, and provide oversight to study staff?**

   Investigators are responsible for having enough time committed to properly conduct and supervise the conduct of the research. Some investigators hold weekly meetings with staff to discuss study status.

   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. www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf.

## Feasibility & Resources

Investigators assess feasibility and ensure adequate resources to perform research

1. **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.
   - **Potential Subject Population -** the CCTS provides biostatistics and informatic consultation, as well as a query tool (i2b2) for searching clinical data based on inclusion criteria to determine adequacy of a potential patient population. CCTS Participant Recruitment Services assist in developing a recruitment plan, creating recruitment materials, and promoting IRB-approved studies.

## Data & Safety Monitoring

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

1. **Which studies require a Data and Safety Monitoring Plan (DSMP) at UK?**

   A DSMP is required at Initial IRB Review for:

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

   Monitoring the progress of the research and the safety of participants are key components to a DSMP.

   The IRB recognizes that the elements of a monitoring plan may vary depending on the potential risks, complexity, and nature of the research. After reviewing the plan, the IRB may determine that a formal DSMP is not necessary or find that monitoring by the investigator as proposed is adequate or could determine that the study requires an independent individual or independent body (i.e., Data and Safety Monitoring Board) for monitoring.

   The ORI DSMP website provides guidance for developing a plan and guidance for when a DSMP is warranted or required. NOTE: If relying on an independent agent or committee for DSMB services, (e.g., Center for Clinical and Translational Science DSMB), it is the PI's responsibility to establish the services with the agent or committee.

***Remember/Consider….***

*DSMP required for:*
- *> minimal risk research*
- *NIH Funded Clinical Trial*
- *FDA Regulated Clinical Investigation*

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

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

   Reporting status and outcomes from Data and Safety Monitoring is essential for the IRB to decide if the criteria for approval is met at continuing review. The PI is responsible for reporting on the status of the studies' data and safety monitoring plan. If the study has an independent Data and Safety Monitoring Board (DSMB) the PI should submit activity reports to the IRB upon receipt, through modification requests or continuing review (CR) submission.

   ORI staff will contact the PI at CR, if a report is expected and not submitted.

**Recruitment & Study Population**

Investigators employ fair and equitable recruitment and avoid undue influence or coercion.

Investigators should have a justifiable rationale for inclusion of vulnerable populations.

If vulnerable populations are to be recruited, investigators comply with regulatory requirements and apply additional safeguards for protecting the subjects' rights and welfare.

1. **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.).

Review ORI's PI Guide to Identification and Recruitment of Human Subjects for Research.

**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 emphasize 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.

See the IRB recruitment guidance video for additional information: Institutional Review Board (IRB) Review: Research Recruitment and Advertising [YouTube Video]

See Use of Gender-Inclusive Language [html video]. Also, the UK ORI Guidance for Use of Gender Inclusive Language.

***Remember/Consider….***

*Describe recruitment and enrollment plans including any contingency plans in the IRB Research Description so that all recruitment strategies have prospective IRB approval.*

*Do not target or exclude populations based on convenience.*

*The IRB reviews final copies of all advertisements including paper, video, etc.*

***UK prohibits finder's fees and recruitment bonuses.***

2. **What practices may place subjects at risk for coercion or undue influence?**

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.

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

3. **Can faculty enroll their University Students in research?**

   With adequate safeguards, faculty may enroll students. The IRB considers the faculty researcher's recruitment plan on a case-by-case basis. Additional approval is required to enroll students from select medical education programs. See the key points below and the ORI Guidance for Enrolling University Students as Subjects for details.

   🗝**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 consent 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 is 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 federal human subject protection regulations.

4. **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:

   - Adults with Impaired Consent Capacity Policy
   - UK IRB Policy on Children in Research
   - Protection of Human Subjects in Research Involving HIV Testing
   - Summary on Prisoners Regulations – OHRP Video Series Prisoner Review
   - Guidance for Enrolling Students as Research Subjects
   - Guidance for Enrolling K-12 Students as Research Subjects
   - Research Involving Economically or Educationally Disadvantaged Persons

5. **What concerns should investigators consider when a study involves economically or educationally disadvantaged populations?**

   Economically or educationally disadvantaged persons may be subject to undue influence in participating in research due to limited understanding and/or unfair level of benefit in exchange for study participation (perception of free treatment, access to treatment, or compensation). As with all research, the benefits and risks must be weighed and evaluated to ensure the ethical conduct of a study.

   For the inclusion of economically or educationally disadvantaged persons, the benefits must not be so great that the subjects disregard the risks. Alternatively, the benefits of participation in comparison to the risk, must not be so minimal such that only those who are economically or educationally disadvantaged want to participate. Studies should not be skewed toward either extreme.

   The Research Involving Economically or Educationally Disadvantaged Persons addresses the following concepts:

   - Subjects enrolling in research without fully understanding study risks;
   - Rewards/services or compensation that is unduly influential; and
   - Unfair benefit in exchange for participation.

6. **What must the investigator consider when applying children's regulations to FDA regulated pediatric research involving a placebo arm?**

The regulations protecting children as vulnerable subjects, requires investigators to categorize children's studies 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 adopted the children's regulations; however, they have a specific interpretation of the categories relative to use of a placebo.

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.

**1. Describe your informed consent process?**

- 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 informed consent. Investigators indicate in the IRB application, which study personnel will obtain consent and describe the proposed process in the research description.
- Describe what techniques you use to ensure comprehension and voluntary participation, such as:
  - plain language documents; visuals, graphics;
  - steps to minimize coercion or undue influence; &
  - teach back questions to assess understanding.
- Potential subjects must be allowed ample time to read, review, discuss and consider 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.

***Remember/Consider….***

*Informed consent a PROCESS; not just a form!*

*KEY INFORMATION defines what the study is about and includes the main reasons a potential subject would & would not choose to participate.*

*KEY INFORMATION* is presented FIRST during the consent process and in the form.

**2. What general requirements from the revised Common Rule are intended to enhance informed consent?**

The revised Common Rule requires subjects be provided with the information that a reasonable person would want to have to make an informed decision about whether to participate.

Informed consent must begin with a concise and focused presentation of the Key Information that is most likely to assist a prospective subject in understanding the reasons why one might or might not want to participate.

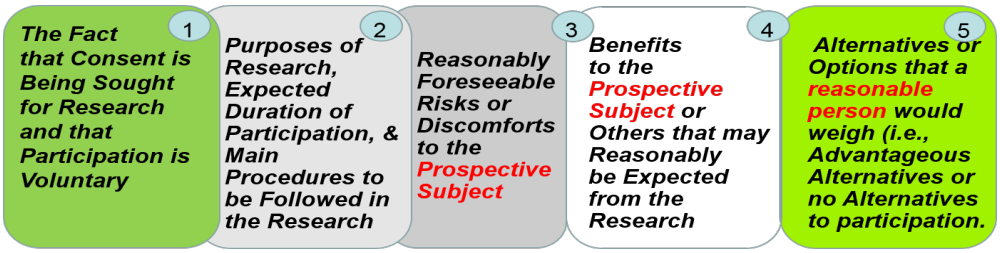
It must present information in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates understanding.

## 3. What is Key Information?

| | |
|---|---|
| ø Is not a summary of a full protocol (like an abstract) | ✓ Is about a page or less |
| ø Does not need to include all required elements | ✓ Is presented first vs. being dispersed in the document |
| ø Doesn't have to look identical to our template | ✓ Should include the information that is most crucial to a participant's decision whether to or whether not to participate |
| ø Typically does not include exclusions unless the exclusion involves restrictions that would affect someone's decision to participate | ✓ May or may not be risks & benefits; could be other pros and cons that a prospective participant would weigh |

## 4. What is included in Key Information?

Although not defined in the Common Rule regulation, Key Information is described in the preamble to include:




**Key Information Samples** for Simulated Studies are available on the Sample Applications and Protocol Development Resources webpage. The format is flexible and may be tailored to the needs of the specific study population.

## 5. What are the Nine Basic Elements of Informed Consent?

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject/others that may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and

(9) One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies

without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

(ii) A statement that the subject's information or biospecimens collected as part of the research, identifiers are removed, will not be used or distributed for future research studies.

**6. What are the Nine Additional Elements of Informed Consent (include if applicable)?**

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject;

(6) The approximate number of subjects involved in the study;

(7) A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

(8) A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and

(9) For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)

Use the ORI Consent/Assent Checklist to ensure all elements are included and requirements are met in the document and process.

**7. What templates are provided for guiding development of the document?**

The E-IRB submission system provides a variety **of informed consent templates** (all contain required elements of informed consent). Templates are tools for creating informed consent; but their use is not mandatory or prescriptive. Investigators are encouraged to tailor documents and process to the needs of the potential subject population. Samples Include

- Nonmedical Informed Consent Template [English & Spanish]
- Medical Informed Consent/HIPAA Combined [English & Spanish]
- Sample Repository/Registry/Bank Consent Template
- Nonmedical Assent Form Template [English & Spanish]
- Medical Assent Form Template [English & Spanish]; and
- Survey Templates (for survey/questionnaire research) [English & Spanish].
- Short Form in 10 languages for use with a verbal short form process [*when a non-English speaking person who may benefit from study participation is incidentally encountered]*

**8. Does E-IRB have a consent template for establishing a research bank, registry, or biorepository?**

The Sample Repository/Registry/Bank Consent Template may be used

Because there is extensive variation in the way banks and repositories operate, a “one size fits all” template is not feasible. The template includes sample language for many different bank/registry operations, so researchers will need to tailor the consent to fit the procedures.

Bank operators must also consider how information will be shared and whether additional consent will be needed. Investigators are encouraged to first review the following guidance when developing plans,

preparing the IRB submission and creating the informed consent document:

- UK Research Biosample Bank Guidance
- UK Research Registry Guidance

**9. What is the difference between the IRB waiving informed consent and waiving the informed consent signature requirement?**

An informed consent waiver involves altering some or all the elements of informed consent or waiving the requirement to obtain informed consent. Waiver of signatures involves waiving the requirement to obtain the participant's signature on a consent document. 🎬See the Waiver vs. Waiver of Signatures video for a detailed comparison.

The conditions for altering or waiving informed consent and options for waiving the informed consent signature requirement are outlined below.

**10. Under what conditions can informed consent be altered or waived?**

Some research projects would not be possible if informed consent were required. The IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent, or may waive the requirements to obtain informed consent, if it finds and documents that the research meets all **five conditions below:**

a) The research involves no more than minimal risk to the subject.
b) The rights and welfare of subjects will not be adversely affected.
c) The research could not practicably be carried out without the requested waiver or alteration.
d) Whenever possible, the subjects or legally authorized representatives will be provided with additional pertinent information after they have participated in the study.
e) If the research involves using or accessing identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format. Private information/specimens are "identifiable" if the investigator may ascertain the identity of the subject or if identifiers are associated with the information (e.g., medical records). This could be any of the 18 HIPAA identifiers including dates of service.

**11. Under what circumstances can the informed consent signature requirement be waived?**

IRB regulations allow the IRB to waive the requirement to obtain a signed consent document for some or all the subjects if any one of the following 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. Under this option, each participant (or legally authorized representative) must be asked whether they want to sign a consent document; if the participant agrees to sign a consent document, only an IRB approved version should be used.
b) The research presents no more than minimal risk and involves no procedures for which written consent is normally required (i.e., consent on a mailed survey or phone script)
c) Subject or a Legally Authorized Representative (LAR) is a member of a distinct cultural group or community in which signing forms is not the norm. The research is no greater than minimal risk and there is an alternative mechanism for documenting that informed consent was obtained.

**12. What else may be involved in the process of documenting the informed consent?**

- Informed consent is documented using a written consent form approved by the IRB and signed and dated by the subject or the subject's Legally Authorized Representative (LAR).

  💻 To determine **who may serve as an LAR**, see the ORI/IRB Informed Consent SOP

  💻 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 [or Nonmedical research.

- 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 document their consent by signing and dating** the IRB approved informed consent form **prior to** study participation.
- Regulations do not require that investigators sign consent forms. The UK consent templates do not include an investigator signature line; however, researchers may add one if desired or required by sponsoring agencies.
- Investigators are responsible for ensuring that each person or LAR signing a consent or assent form is **given a copy** of the signed form or, if applicable, the signed HIPAA authorization form. The form 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.
- Inclusion of a detailed chart note may be necessary to inform other caregivers regarding participation clinical or interventional trials.

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

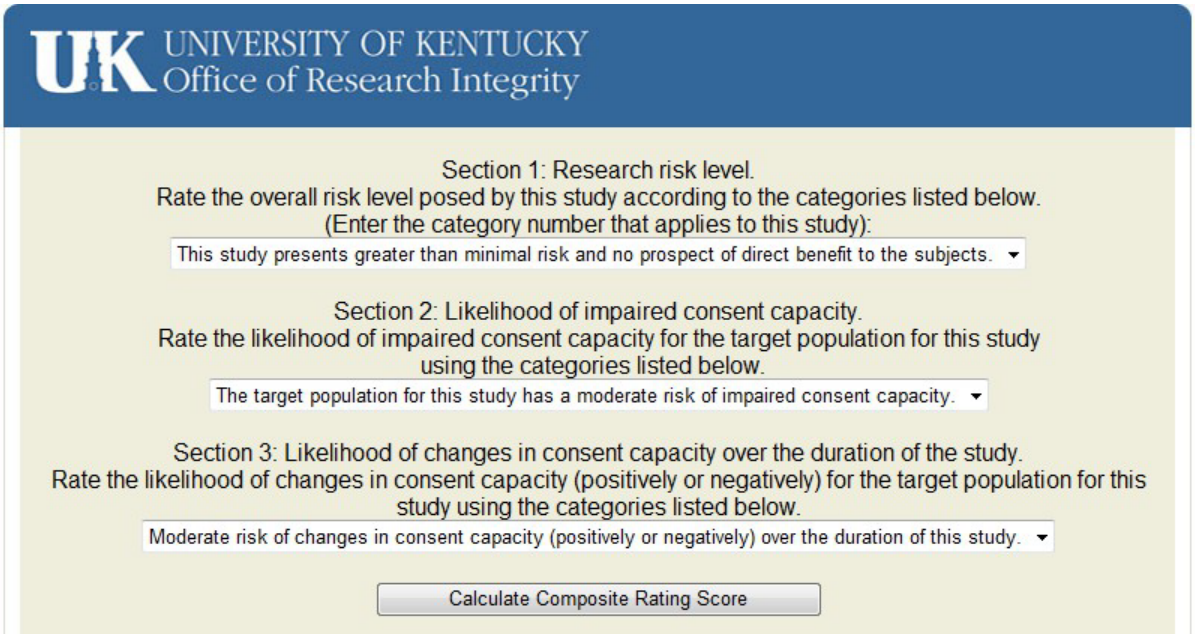
- Because children and some adults with impaired consent capacity are not legally considered capable of providing consent, regulations do allow a parent or LAR give "permission" for the individual to participate when **assent or "affirmatively agreement"** to participate is obtained from the child (or adult with impaired consent capacity). Depending on the risk level of the study, provisions may be necessary for permission of both parents.
- For guidelines on when assent needs to be documented based on age and maturity, as well as parental permission requirements for research involving children, see the **UK IRB Policy on Children in Research**.

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

Consent capacity is not merely absent or present but exists along a continuum. Investigators consider how they will assess the abilities of potential participants and provide safeguards to respect autonomy when present and protect the rights and welfare of the participant.

An LAR may also be needed to consent on behalf of adults with complete impaired consent capacity (e.g., comatose). ORI provides brochures to help LARs consider both what is in the best interest of the participant, balanced with what the participant would likely have chosen if able. Form T (pictured below):

- Prompts investigators to consider a more comprehensive list of conditions with potential to encounter a prospective subject with impairment;
- Allows 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 and methods for assessing dissent;
- Encourages fair and equitable recruitment; and
- Promotes use of safeguards and enhancements to the consent process to enable individuals who otherwise have limitations, to make competent decisions.




**15. What are the regulations on re-consent?**

The regulations do not reference "re-consent". However, enrolled participants must be informed of information arising during the study, which may affect their willingness to continue to participate. Modification requests to revise consent documents include questions to assess whether the change increases risk to study participants, is due to an Unanticipated Problem or Adverse Event (UP/AE), or could involves information that might relate to a subject's willingness to continue to take part in the research.

If so, the researcher is asked to state how information will be communicated to subjects (i.e., re-consent, letter, etc.).

UP/AE reports include questions to assess need for consent revision and/or notification of active enrolled subjects.

**16. What consent forms need to be posted on Clinicaltrials.gov?**

The OHRP Posting Clinical Trial Consent only applies to clinical trials conducted or supported by a Common Rule department or agency (e.g., NIH). One copy of the consent must be posted on a publicly available federal website (e.g., Clinicaltrials.gov).

The consent form must:

- have been used in enrolling participants;
- be posted by the awardee on the Federal website (Clinicaltrials.gov) after the clinical trial is closed to recruitment; and
- be posted no later than 60 days after the last study visit by last subject, as required by the protocol.

Federal agency supporting the trial may permit redactions of proprietary information.

Emily Bradford, PhD, OSPA Clinical Trial Compliance Administrator provides guidance and assistance with consent registration as well as other Clinicaltrials.gov requirements.

## Complaints, Concerns, Suggestions, Questions or Requests for Information

Investigators respond to participants' complaints or requests for information.

**1. Who do you contact with a complaint, concern, or suggestions?**

Concern regarding ORI and IRB administrative procedures -
ORI Director Helene Lake-Bullock

(859) 257-2978 or
helene.lake-bullock@uky.edu


Concern regarding an IRB Decision:

- Contact the applicable IRB Chair
- Submit a written appeal that includes a justification for changing the IRB decision. The convened IRB reviews the appeal. The appeal determination is final.

2. **What provisions do you have in place for receiving and handling a subject complaint or request for information?**
   - Your protocol-specific plan described in the IRB Research Description.
   - The procedures to satisfy this should offer a safe, confidential, and reliable channel for current, prospective, or past research subjects (or their designated representative) allowing them to discuss problems, concerns and questions, or obtain information.
   - For **greater than minimal risks studies**, the IRB recommends the consent document(s) include a reliable, dedicated pager or phone number for after-hours emergencies.
3. **Who may a subject call outside of the study personnel, about their rights and welfare?**

   Each IRB approved informed consent document should include the **ORI toll-free phone number** (1-866-400-9428) as a subject's primary contact point about their rights and welfare.

## 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.

1. **What events/issues do you report to the IRB?**
   - Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO)
   - Violations – Any change (deviation or exception) which occurred without prior IRB review and approval, the PI submits a Protocol Violation Report within 14 days of the occurrence.
   - Protocol Non-Compliance, Suspension, or Termination
   - Data and Safety Monitoring Report
   - Food and Drug Administration (FDA) correspondence
   - Unresolved subject complaint that requires IRB involvement
   - Subject Incarceration
   - Audit, Inspection, or inquiry by a federal or an external agency.

**Download the one-page Investigator Quick Guide to IRB Reporting Requirements.**

2. **When do you begin collecting, recording, and reporting an adverse event and an unanticipated problem for a research subject?**

   Upon subject enrollment into the study. The PI or qualified sub-investigator determines which events meet the following criteria for reporting to the IRB. The PI also will consider and assess the collective information as part of the Continuing or Annual Administrative review safety reporting.
3. **What safety-related reporting is required at Continuation Review (CR) or Annual Administrative Review (AAR)?**

The PI submits a written summary of both unanticipated problems and available information regarding adverse events since the last IRB initial, continuing, or annual administrative review. For multisite studies, the written summary should describe external events that meet the UPIRSO criteria.

The amount of detail provided in such a summary will vary depending on the type of research being conducted; in many cases, such a summary could be a brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and the investigator's brochure (if applicable). The summary must include the PI's assessment whether the problems/adverse events warrant changes for the protocol, consent process, or risk/benefit ratio.

In addition, the PI provides information regarding Data and Safety Monitoring activities as part of the Continuing Review **(CR**) for greater than minimal risk research.

**4. What unanticipated problems or adverse events are you required to promptly report to the IRB?**

The UK IRB Policy on Unanticipated Problems and Safety Reporting requires investigators to promptly report UPIRSO as well as other safety related information important to human subject protection or study integrity (FDA 483 issued, FDA Clinical Hold). The **Prompt/NonPrompt Reporting [PDF] guide was developed to** help research teams understand the differences between an internal prompt event and an internal non-prompt event, based on the first three prompt reporting criteria in the UK UP Policy.

## Prompt Reporting

***An Unanticipated problem involving risks to subjects or others (UPIRSO)-*** includes any incident, experience, or outcome that meets the following criteria:

1. ***Unexpected*** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. ***Related or possibly related*** to participation in the research; and
3. ***Suggests that the research places subjects or others at a greater risk of harm*** (including physical, psychological, economic, or social harm) than was previously known or recognized.

An adverse event (AE) or unanticipated adverse device effect (UADE) could be considered an "unanticipated problem involving risks to subjects or others".

***All Research-Related Deaths*** (whether anticipated or unanticipated)

***Other event that in the PI's judgment, warrants reporting or is in the best interest of the subject(s)*** (e.g., because it may affect the safety and/or welfare of subjects; it changes the risk level of the study; or the frequency of the same event significantly increases)

***Other unanticipated problems that impact the conduct of the study or integrity of the human research protection program*** (e.g. FDA Clinical hold or recall, published literature or data and safety monitoring board report impacting risk-benefit ratio, FDA Form 483 or warning letter, investigator medical license restriction or suspension, participant is incarcerated)

***Allegations or compliance actions including:***
1. Negative actions by a government oversight office, including, but not limited to, FDA 483 inspection report, FDA Warning letter, OHRP Determination letter, or other agency compliance action related to human research protections.
2. Lawsuits related to human research protections.
3. Press coverage (including, but not limited to radio, TV, Newspaper, Online) of a compliance allegation or negative nature regarding UK Human Research Protection Program.

| 🕘 Prompt Reporting Timelines 🕘 | | | |
|---|---|---|---|
| Life Threatening | Unanticipated | Related | 7 calendar days |
| Other UPIRSO | Unanticipated | Related | 14 calendar days |
| Deaths | Unanticipated **or** Anticipated | Related | Immediately (within 48 hours of receipt) |

### 3. What other allegations or compliance actions do researchers report to ORI immediately (within 24 hours of becoming aware)?

- Any negative actions taken by a government oversight office including but not limited to OHRP Determination Letters, FDA Warning Letters, and FDA restrictions;
- Any lawsuits (i.e., litigation, arbitration, or settlements initiated) related to human subject research protections; or
- Press coverage (including but not limited to radio, TV, newspaper, online publications) of negative nature regarding the UK HRPP.

### 4. What are the "Big 3" findings that are reportable to federal and regulatory agencies?

- IRB determination of**:**
  - **Continuing Noncompliance or Serious Noncompliance;**
  - **Unanticipated Problems Involving Risk to Subjects or Others**; or
  - **Suspension or Termination** of IRB approval in response to above determinations.

***Continuing noncompliance*** is defined as persistent failure to adhere to the laws, regulations, or policies governing human research.

***Serious noncompliance*** is defined as a failure to adhere to the laws, regulations, or policies governing human research that may reasonably be regarded as:

1. Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or
2. Substantively compromising the effectiveness of a facility's human research protection or human research oversight programs.

***Unanticipated problem involving risk to subjects or others (UPIRSO)*** see above

*For more information, see the Mandated Reporting to External Agencies SOP or OHRP Reporting Requirement Video

**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.

### 1. 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.

*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 Resource Web Links**

***Remember/Consider….***

***The need for an IND or IDE submission to FDA is initially determined by the Sponsor or Sponsor-Investigator.***

***Investigators indicate on the IRB Drug or Device forms if the study meets regulatory criteria to be exempt from IND or IDE requirements. FDA regulations contain limited exemption for some categories (e.g., in vitro diagnostics). Links to FDA guidance is provided for the PI to reference to ensure all exemption criteria are met.***

***INDs or IDEs are NOT limited to clinical investigations conducted in support of a marketing application or labeling change!***

***Investigators may be required to consult the FDA for a determination.***

## FDA Regulated Drug Research:

2. **In addition to IRB review, what regulatory requirements apply to research involving FDA-regulated drugs*?**

   In addition to IRB review, 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. The IRB application includes questions and links to FDA guidance and contact information for determining whether an IND is needed.

   **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.*

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

   Yes, the application 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.

4. **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 drug accountability good clinical practices.

   If using the IDS, have a process for communicating applicable changes in the protocol/intervention, and actions such as protocol suspension.

5. **If you are the Sponsor-Investigator holding the IND application with FDA, how are you informed regarding your sponsor responsibilities?**

   The application includes links to sponsor IND regulatory responsibilities

   IRB policy requires completion of Sponsor-Investigator Good Clinical Practice Training for investigators who hold an IND. Completion of the Sponsor-Investigator Training is required before final IRB approval is granted.

## FDA Regulated Medical Device Research:

**6. In addition to IRB review, what regulatory requirements apply to research involving FDA-regulated medical devices**?**

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 IDE or the research meets one of the exemptions from the requirement for an IDE.

The IRB application includes questions and links to FDA guidance and contact information for determining whether the 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 form IDE issued by FDA].***

***A Medical 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.*

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

Yes, the application 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 sample Device Accountability SOP.*

In addition, the IRB requires periodic quality improvement reviews (QIR) for investigational device accountability. If selected for a device accountability QIR, the Office of Research Integrity (ORI) conducts an on-site evaluation of policies and procedure for storage, control, dispensing, accountability, and monitoring.

**8. Does the IRB ask about qualifications or training needed to use or administer the device the study device?**

Yes, the application asks questions regarding the qualifications or training required to use or administer the device and any plans to obtain or augment applicable qualifications or expertise.

**9. If you are the Investigator for a NSR device study or the Sponsor-Investigator holding the IDE application with FDA, how are you informed regarding your sponsor responsibilities?**

The application includes links to the abbreviated regulatory requirements for NSR device trials and the Sponsor-Investigator requirements for SR device trials.

IRB policy requires completion of Sponsor-Investigator Good Clinical Practice Training for investigators who hold an IDE or abbreviated IDE for a NSR device. Completion of the Sponsor-Investigator Training is required before final IRB approval is granted.

## FDA Emergency Use:

**10. What happens when you need to use a test article in a life-threatening situation (single subject emergency use)?**

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

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.

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.

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

**11. 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 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 Exception from Informed Consent (EFIC) 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 enough 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.

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

Resources to facilitate CER/CBPR.

**1. What resources are available to facilitate the approval and conduct of CER or CBPR?**


Community-based participatory research is a type of community-engaged research which is conducted as an equal partnership between researchers and members of a community.

CBPR is an applied collaborative approach that enables community residents to 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 (ORI), Center for Clinical and Translational Science (CCTS), investigators, and the Institutional Review Board IRB 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' IRB review of CER/CBPR.

The IRB has members with experience with community-engaged research. The IRB application requests 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. For instance, CBPR investigators may propose use of non-traditional, CBPR-focused human subject protection training for community partners.

The CCTS Community Engagement Program provides a network of resources, facilities, consultation, training, and funding for community engaged research.

**Frequently Asked Questions: CER and CBPR**

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

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

1. **Who provides outreach to educate 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, ORI, and research investigators to provide education, outreach, and research opportunities to the public. The CCTS Participant Website provides several mechanisms for the public to learn about research participation including videos, kiosks, and databases.

The ORI Participant Website provides additional participant education links as well as contact information for subject concerns, suggestions or questions.

2. **Who would a prospective subject call with a complaint regarding a perceived invasion of privacy?**

The ORI Director 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.