University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures			
Revision #13	**TITLE: Initial Full Review**		**Page 1 of 9**
Approved By: ORI Director	Signature	Date	Date First Effective: 05-24-05
Approved By: Nonmedical IRB Chair	Signature	Date	
Approved By: Medical IRB Chair	Signature	Date	Revision Date: 03/27/17

OBJECTIVE

To describe the policy and procedures for initial full review by the Institutional Review Board (IRB)

GENERAL DESCRIPTION

The IRB conducts initial review for non-exempt research at convened meetings unless the research is eligible for expedited initial review. See the procedures for conducting a convened meeting, the definition of *quorum*, and the requirements for conducting a full review meeting in the Conduct of IRB Meeting SOP. Investigators must submit studies that do not meet the federally mandated criteria for exempt or expedited initial review for full review. (See Exempt and Expedited Initial Review SOPs.) The IRB only approves research that meets the federal criteria for approval as specified in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. Also, during initial full review the IRB reviews the informed consent process and documentation as specified in the Informed Consent SOP. The IRB Chairs or designated IRB Members document determinations by signing the applicable Reviewer Checklist/Signature Page. IRB Members sign a signature authority document authorizing ORI staff to issue and/or sign investigator correspondence which concurs with the IRB's determination.

RESPONSIBILITY

Execution of SOP: IRB Chairs, IRB Members, Principal Investigator (PI)/Study Personnel, Office of Research Integrity (ORI) Staff, ORI Research Compliance Officer (RCO), ORI Research Privacy Specialist (RPS).

PROCEDURES

Submission and Screening

1. The PI or designee completes an application for IRB review of a research protocol for initial full review and submits it to the ORI.

2. ORI staff schedule the IRB application on the agenda for the next available meeting. Each IRB usually meets approximately once every three weeks. ORI staff schedule protocols for review on a "first-come, first-serve" basis, limiting number of reviews as appropriate in order to permit adequate time for discussion and deliberation of agenda items. ORI staff send the PI a request for the PI or designee to attend the meeting unless the ORI or IRB waives the requirement to attend.

3. ORI staff screen the application to determine whether it is complete (e.g., includes all pertinent forms and appropriate signatures). If it is not complete, ORI staff return the application to the investigator or, in cases where only a few minor items are missing, the ORI staff call or write the investigator to request the missing items.

4. ORI staff screen the IRB application to ensure coordination with other university committee reviews as outlined in the applicable standard operating procedures or to ensure compliance with pertinent federal requirements. Examples of screening include, but are not limited to, the items listed below.

    - If the investigator checks “cancer” on the General Information Sheet (GIS), (i.e., Form A in the full application) ORI staff forward a copy of the IRB submission to the Markey Cancer Center Protocol Review and Monitoring Committee (PRMC) following the procedures outlined in the Markey Cancer Center/IRB/ORI SOP.

    - If the investigator checks items on the GIS which indicate Institutional Biosafety Committee (IBC) approval is necessary, the investigator must include IBC provisional approval materials. ORI staff check to ensure that the PI has submitted the materials. ORI staff do not schedule the application for review and return the application to the PI if these materials are missing. ORI staff may check with the Institutional Biosafety Officer for advice. The Institutional Biosafety Officer has the authority to make the final decision as to whether the project requires IBC approval.

    - Using the information on the GIS, ORI staff screen to determine whether the PI addressed off-site issues following procedures outlined in the Off-site Research SOP.

    - If the investigator checks items on the GIS which indicate the research involves prisoners, the PI adds “UK/P:” at the beginning of the study title. ORI staff send the protocol to a prisoner representative for review.

    - For full review protocols, ORI staff screen the application to see whether the investigator for the study is a Registered Nurse (RN). If the PI is an RN, ORI staff assign the protocol

to a committee with an IRB member who is an RN and will attend and vote on the protocol at the convened meeting.

- ORI staff determine whether the U.S. Department of Education has funded the research and/or whether the proposed research involves surveying children in the public schools. If so, ORI staff inform the IRB of specific U.S. Department of Education requirements (e.g., "No Child Left Behind").

- ORI staff determine whether the research is supported by other federal agencies which have specific requirements such as the U.S. Department of Defense (DoD) or U.S. Department of Energy (DOE). If so, ORI staff inform the IRB of specific agency requirements for the review and conduct of the research.

- If the investigator indicates in the GIS that the research involves an investigational new drug (IND) or investigational device exemption (IDE), ORI staff confirm the validity of the IND or IDE number by ensuring that the investigator has included a copy (containing the number) of the detailed protocol from the sponsor and/or verification statement from the sponsor or the Food and Drug Administration (FDA).

- ORI staff screen the GIS to determine whether the investigator also is serving as the sponsor in accord with FDA regulations. If so, ORI staff verify that the PI has completed the Office of Research Integrity Sponsor-Investigator training.

- ORI staff screen the GIS to determine whether research involves vulnerable subjects and/or sensitive types of research/procedures (e.g., HIV screening). If so, ORI staff add a notation on the agenda for the meeting referring IRB members to the pertinent Protocol Specific Training (PST) materials, which are included in the *IRB Survival Handbook*.

- ORI staff screen the application to determine if the investigator has answered "yes" on the questions in the Research Financial Interest Disclosure Form. If so, ORI staff and the IRB follow procedures outlined in the Investigator Conflict of Interest/OSPA/IRB/ORI Coordination SOP.

5. ORI staff screen the protocol to determine whether additional expertise is necessary to conduct the review. If so, ORI staff may ask an ad hoc or cultural consultant who has appropriate expertise in the discipline or with non-English speaking populations or locations to participate in the review. The ORI maintains a list of potential cultural consultants qualified by cultural and/or linguistic knowledge or training to assist the IRB, as appropriate, and may contact IRB members, UK faculty, or department chairs for advice in identifying consultants.

6. The PI may also recommend cultural consultants provided that they are not directly involved in the study. These consultants may review consent forms, provide verifications of translations, and provide guidance on the impact of the research on subjects and the impact of the culture on the research to be conducted.

7. ORI staff ensure that ad hoc or cultural consultants do not have a conflict of interest in accordance with the IRB Member and Consultant Conflict of Interest SOP.

8. ORI staff send the ad hoc or cultural consultants the same information as voting IRB members and a detailed protocol/grant application, if applicable.

9. ORI staff assign a primary reviewer based on the IRB member's educational background and expertise as necessary. RN IRB members serve as primary reviewers for protocols in which the PI is an RN. When applicable, ORI staff document who served as primary reviewer on the reviewer form (i.e., Criteria for IRB Approval Checklist). If no IRB member has the appropriate expertise, ORI staff ask an ad hoc or cultural consultant to serve as primary reviewer.

10. The ORI Research Privacy Specialist (RPS) screens all initial Medical IRB submissions to determine whether a protocol falls under regulations of the Health Insurance and Portability and Accountability Act (HIPAA) Privacy Rule and/or the Family Educational Rights to Privacy Act (FERPA). The Nonmedical IRB staff conduct the same screening for all initial Nonmedical IRB submissions. The Nonmedical IRB staff forward any protocol regulated by the Privacy Rule and/or by FERPA to the RPS, who writes recommendations for each protocol to ensure compliance with the Privacy Rule and/or with FERPA and forwards them to the appropriate IRB. See the HIPAA in Research SOP for additional information regarding HIPAA review procedures.

Submission of Applications to the IRB and Primary Reviewer Responsibilities

1. Approximately five to 10 days prior to each convened meeting, ORI staff send packets to voting and selected *ex officio* IRB members for review and send PIs requests to attend, unless the requirement is waived by an IRB member or ORI staff. The initial full review applications sent to the IRB members include all applicable sections of the application.
   a. Section 1 - core application with General Information Sheet and research description;
   b. Section 2 - informed consent/assent process and forms including waiver requests, Department of Health and Human Services (DHHS) approved sample informed consent document (e.g., National Institutes of Health [NIH] cooperative group trial), and translated consent document for non-English speaking subjects;
   c. Section 3 - HIPAA forms;
   d. Section 4 - additional materials, including advertisements, proposed data instruments, materials/letters for off-site research, Use of Investigational New Drug Form, Use of Approved Drugs for Unapproved Use Form, Use of Investigational New Device Form; Use of Radioactive Materials Form;
   e. Section 5 - vulnerable populations including forms for research involving individuals with impaired consent capacity, pregnant women, fetuses and/or neonates, prisoners, or children.
2. In addition, the member assigned as the primary reviewer of the study receives the following materials, if applicable:

- Sponsor's grant application;
- DHHS approved protocol (e.g., NIH cooperative group trial);
- Contract or device proposal (if the protocol does not involve the administration of drugs);
- Sponsor's detailed protocol and investigator's brochure (if the protocol involves the administration of drugs);
- Financial disclosure form(s);
- Signature Assurance sheet;
- Other committee review or final approval materials when applicable;
- All other application materials.

3. The primary reviewer is responsible for:

   - Comparing the detailed grant application or industry/DHHS approved protocol with the IRB application;
   - Informing the full IRB of any discrepancies between the detailed protocol and the summary application materials;
   - Determining whether the project involves a DHHS approved protocol (e.g., NIH cooperative group trial) and, if so, comparing the "Risks" and "Alternatives" sections of the DHHS approved sample informed consent document with the UK proposed form to ensure that the DHHS and UK sections of the consent are consistent;
   - Reviewing the financial disclosure form and alerting the IRB if a "yes" disclosure is made; and
   - Conducting an in-depth review.

4. All IRB members review all information in the agenda packet in advance of the meeting (including those protocols for which the IRB member is not the primary reviewer) in enough depth to be familiar with the protocol, to be prepared to discuss the protocol at the meeting, and to be prepared to determine whether the research meets the regulatory criteria for approval.

5. Ad hoc or cultural consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review. IRB staff maintain documentation of written comments or reports in the protocol file. In cases where the consultant participates in the meeting, the minutes of the meeting document the information provided by the consultant. (See Minutes of IRB Meetings SOP.)

IRB Review

1. A majority of the voting IRB members (or their designated alternates), including at least one member whose primary concerns are in nonscientific areas, must be present in order to conduct a convened meeting. For the Medical IRB, a licensed physician must be present. In order for the IRB to approve the proposed research, the protocol must receive the approval of

a simple majority of those members present at the meeting. (See The Conduct of IRB Meetings SOP.)

2. When the IRB reviews research that involves categories of human subjects vulnerable to coercion or undue influence, ORI staff ensure that adequate representation or consultation is present for discussions of research involving vulnerable human subjects. (See Protection of Vulnerable Subjects SOP and Membership of IRB SOP.)

3. All IRB members attending the meeting receive materials listed in the *Submission of Applications* section above, prior to the convened meeting, have the opportunity to discuss each research protocol during the convened meeting, and participate in the determination of whether the research meets the regulatory criteria for approval.

4. The IRB reviews each initial full review application with the PI or co-investigator present during the convened IRB meeting unless the ORI or IRB waives the requirement. After the PI leaves the meeting, the IRB reviews the application and discusses any controverted issues and their resolution prior to voting.

5. During discussion, the IRB members raise only those issues that the committee determines do not meet the federal criteria for approval as specified in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. In addition, the IRB determines whether the risk level assigned by the PI is appropriate. Also, the IRB considers whether the PI's preliminary assessment of federally mandated specific findings requirements (e.g., request for waiver of informed consent) is acceptable with respect to meeting federal requirements.

6. For research involving a drug or device where the PI or the sponsor has not obtained an IND or IDE, the committee determines what action(s) is needed (whether the PI needs to obtain an IND/IDE or whether PI needs to contact the FDA for guidance).

7. In conducting the initial review of the proposed research, the IRB utilizes the Criteria for IRB Approval: Reviewer Checklist.

8. A member or consultant with a conflict of interest must leave the room during the vote and only participate in the review by providing information in accordance with the IRB Member and Consultant Conflict of Interest SOP.

Review Outcome(s)

1. An IRB member makes a motion, another member seconds the motion, and then the convened IRB votes for or against or abstains from one of the following five actions:

   APPROVED (Vote for a #1): IRB approval - A vote for a #1 indicates that the IRB has concluded that the research and consent/assent forms meet the federal criteria for approval. IRB approval verifies that the IRB agrees with the assessment of the protocol

and/or specific findings as described by the PI in the application. ORI staff send the investigator an approval letter, according to the guidelines in the ORI Customer Service Standards, accompanied by an informed consent/assent document (if applicable) with the affixed "IRB Approval" validation stamp, which includes valid dates of IRB approval. If the IRB approves a HIPAA Waiver of Authorization Request, ORI staff send a separate approval letter as well. (See Mandated Reporting to External Agencies SOP.)

REVISIONS and/or ADDITIONAL INFORMATION REQUIRED (Vote for a #2): A vote of #2 indicates that the IRB has approved the protocol pending submission of minor revisions and that the IRB has given the individual chairing the meeting (and/or other IRB member with appropriate expertise or qualifications) the authority to approve the minor revisions. ORI staff send the investigator a letter, according to the guidelines in the ORI Customer Service Standards, describing the revisions requested by the IRB.

The PI responds to the IRB's suggested revisions in writing and sends the response to the ORI, which gives the response to the IRB Chair or member who chaired the meeting for further review. The Chair or designee may forward the responses to the entire IRB for additional review, request additional information, or approve.

TABLED (Vote for a #3): A vote of #3 indicates that the IRB withholds approval pending submission of major revisions/additional information. ORI staff send the investigator a letter, according to the guidelines in the ORI Customer Service Standards. The letter lists the reasons for tabling and includes a description of the revisions or clarifications requested. For some studies, the IRB may appoint one or more members of the IRB to discuss the reasons with the investigator. If the vote is for a #3, ORI staff schedule the PI's response to the requested revisions for review by the full committee; the IRB does not require the PI to attend.

TABLED (Vote for a #4): If the vote is for a #4, the IRB follows the same procedure as for a vote of #3, except the PI needs to attend the future IRB meeting at which the IRB reviews his/her response to discuss or answer IRB concerns or questions. ORI staff notify the PI of the request for him/her to attend that future IRB meeting.

DISAPPROVED (Vote for a #5): If the vote is for a #5, ORI staff send the investigator a letter describing the reasons for disapproving the protocol. Disapproval of a protocol usually occurs when the IRB determines that the risk of the procedures outweighs any benefit to be gained or if the proposed research does not meet the federal criteria for IRB approval.

2. During the convened meeting, the IRB determines the approval period, as appropriate to the degree of risk but not less frequently than once per year. The IRB may set a shorter approval period for high risk protocols or protocols with high risk/low potential benefit ratios.

3. When a protocol receives final approval, the ORI assigns the start of the approval period as the date of the convened IRB meeting. If a protocol has received a vote #2 (the IRB requests minor revisions) and the PI completes the revisions, the approval period starts from the meeting date of the convened IRB on which the IRB initially reviewed the protocol. Should there be serious concerns or a lack of significant information (vote #3 or vote #4) requiring the convened IRB to complete its review and issue approval of the study at a subsequent meeting, the approval period starts with the date of the subsequent convened IRB meeting.

4. Before issuing the IRB approval letter, ORI staff confirm that all of the applicable Institutional Biosafety Committee, Radiation Safety Committee, Radioactive Drug Research Committee, and Research Conflict of Interest Committee, approvals are in place. If applicable approvals are not in place, ORI staff notify the investigator in writing, requesting the appropriate information. When the investigator submits the information, ORI staff may put it on an agenda for review by the IRB, if appropriate. ORI staff only issue the IRB approval letter after obtaining appropriate documentation.

5. Before issuing approval, ORI staff also ensure that all study personnel have completed the required training. If the PI and study personnel have not completed training, ORI staff notify the PI in writing. The investigator must send the appropriate certifications of training before the IRB can issue approval. An investigator may submit a request for an exception to submission of certifications before the IRB issues approval. The ORI Research Compliance Officer, designated ORI staff person, or the ORI Director may approve exceptions.

6. If the PI is serving as the sponsor in accord with FDA regulations, ORI staff ensure that the PI has completed the Office of Research Integrity Sponsor-Investigator web based training, or equivalent training as approved by the ORI Director or the IRB Chair or their designee before issuing approval.

7. Before issuing approval, ORI staff verify that any pending IND or IDE has been approved by the FDA, or has passed the 30 calendar day FDA clearance period. If the IND or IDE submission is pending acknowledgment of receipt by the FDA, or the 30-calendar day clearance period has not passed, ORI stipulate in the IRB approval letter that research must not commence until IND or IDE is in place. The PI provides ORI with FDA correspondence confirming that the IND or IDE is in place or the 30-calendar day period has passed, prior to initiating the research.

8. If the research involves prisoners, ORI staff check to determine whether the PI submitted the protocol for funding to any DHHS agency. If this is the case and the protocol involves prisoners, ORI staff, with input from the PI, prepare and submit a prisoner certification report to the Office for Human Research Protection (OHRP) in accordance with OHRP requirements and the Mandated Reporting to External Agencies SOP.

9. Once the IRB approves a protocol, ORI staff send an approval letter to the PI, which includes the approval period, a reminder to use only the approved consent/assent form, and a reminder that the IRB must approve any changes to the protocol prior to initiation of the changes.

10. Upon request, ORI staff also send the PI a funding agency Certification of Approval form. (See the Mandated Reporting to External Agencies SOP)

11. At IRB approval, it is the PI's responsibility to request an Extent of Compliance Statement if the protocol falls under the International Conference on Harmonisation guidance related to Good Clinical Practice. The ORI maintains a statement of compliance signed by the IRB Chair and provides that statement upon request.

12. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit them to the IRB via a written document that includes a justification for changing the IRB decision. The IRB reviews the request using the standard procedures.

REFERENCES

21 CFR 50.25
21 CFR 56.111
21 CFR 312
21 CFR 812
45 CFR 46.108
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117
45 CFR 46 Subpart B
45 CFR 46 Subpart C
45 CFR 46 Subpart D & 21 CFR 50 Subpart D