

University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures			
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Approved By: ORI Director	Signature	Date	Date First Effective: 05-17-05
Approved By: Nonmedical IRB Chair	Signature	Date	
Approved By: Medical IRB Chair	Signature	Date	Revision Date: 02-15-19

OBJECTIVE

To describe the policies and procedures for conducting continuation review (CR) and annual administrative review (AAR)

GENERAL DESCRIPTION

The Institutional Review Board (IRB) conducts substantive and meaningful CR for research requiring review by the convened board at intervals appropriate to the degree of risk, but not less than once per year. The research protocol must satisfy the criteria set forth in [45 CFR 46.111](#) and [21 CFR 56.111](#) for the IRB to approve the protocol for continuation.

In accord with federal requirements, the IRB approval period for research requiring convened board review can extend no longer than one (1) year after the start of the approval period. The PI may not continue research activities after expiration of IRB approval; continuation is a violation of federal requirements specified in [45 CFR 46.103\(a\)](#) and [21 CFR 56.103\(a\)](#). If the IRB approval expires, the PI must cease all research activities and may not enroll new subjects in the study. However, if the IRB determines there is an overriding safety concern and/or ethical issue or that it is in the best interests of the individual subjects to continue participating in the research activities, the IRB may permit the subjects to continue in the study for the time required to complete the CR process.

Research originally reviewed and approved by the convened board continues to undergo CR review until:

1. The research is permanently closed to the enrollment of new subjects, all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects; OR
2. Study personnel have enrolled no subjects at UK and no additional risks have been identified either at UK or at any site if the research involves a multi-site study; OR
3. The only remaining research activities are limited to data analysis; OR
4. The research involves the study of drugs and/or medical devices AND does not require an Investigational New Drug (IND) ([21 CFR Part 312](#)) and/or an Investigational Device

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Exemption (IDE) ([21 CFR Part 812](#)) and/or the device is approved for marketing and being used in accordance with the approved labeling. The IRB must also have determined and documented at a convened meeting that the research is not greater than minimal risk and no additional risks have been identified.

Once the research meets one of these requirements, the study will have either a CR or AAR reviewed by a single IRB member, usually a Vice Chair.

Research originally reviewed and approved under expedited review procedures undergoes expedited CR if:

- It was approved under the Old Common Rule (i.e., prior to January 21, 2019);
- It is FDA-regulated, regardless of when it was approved; or
- It was approved under the Revised Common Rule (i.e., on or after January 21, 2019) and the IRB has documented justification for requiring substantive and meaningful CR.

Expedited review studies subject to CR are approved for a period of no longer than one (1) year and may not continue after expiration without undergoing subsequent CR.

Unless there is documented IRB justification for requiring an expedited CR, the following research at UK undergoes an annual administrative review (AAR):

- Research originally reviewed and approved by expedited review procedures under the Revised Common Rule (i.e., on or after January 21, 2019); or
- Non-FDA-regulated research originally reviewed and approved by the convened board under the Revised Common Rule that reaches a point where it no longer requires review by the full board (e.g., becomes closed to enrollment, never enrolled subjects, current activities limited to data analysis).

Studies subject to AAR are approved for a period of no longer than one (1) year and may not continue after expiration without undergoing subsequent AAR.

RESPONSIBILITY

Execution of the SOP: Office of Research Integrity (ORI) Staff, IRB Members, IRB Chair, IRB Vice Chair, ORI Research Privacy Specialist (RPS), Principal Investigator (PI)/Study Personnel

PROCEDURES

CR and AAR Requests, Submissions, and Screening

1. The PI is sent either a CR or AAR request and subsequent reminders before the IRB approval period expires (e.g., approximately 90 days, 60 days, and 30 days prior to expiration). The PI is responsible for responding to the requests in a timely manner.

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2. The PI must submit a CR or an AAR for a study until it is eligible for closure. See the Study Closure SOP for details on circumstances in which a PI may close a study.
3. If the CR is submitted for review by the convened board, ORI staff screen the submission to determine whether the study is eligible for expedited review procedures.
4. ORI staff also screen the application to ensure compliance with select federal requirements, such as prisoner representative review if applicable.
5. ORI staff assign ad hoc and cultural consultants regarding issues related to the addition of subject populations for which the IRB does not have the appropriate expertise, using the procedures outlined in the Initial Full Review SOP.
6. The ORI may request additional information or materials from the PI if the application is not complete. (If the PI does not respond, ORI staff contact the PI and/or research staff for additional information/materials.)

Full CR Procedures

1. The Medical and Nonmedical IRBs conduct continuing review of research at regularly scheduled convened meetings.
2. The Vice Chair or designee serves as the primary reviewer for convened review (full CRs). If the Vice Chair has a conflict of interest (e.g., is study personnel on the protocol), is unavailable, or does not have the appropriate expertise to review the CR, ORI staff send the CR to the Chair, another Vice Chair, a voting member of the IRB, or a consultant with the appropriate expertise.
3. The primary reviewer and the IRB members scheduled to attend the meeting have access to the IRB application approximately 5-10 days prior to the convened meeting.
4. IRB members review information on the agenda in advance of the meeting (including protocols for which the member is not the primary reviewer) to be prepared to discuss the protocol at the meeting and determine whether the research meets the regulatory criteria for approval. Unless otherwise noted, the IRB agrees with ORI screening comments/revisions.
5. IRB members are responsible for evaluating the information communicated to the subject during the consent process as outlined in the Informed Consent SOP. The IRB reviews the informed consent/assent/HIPAA document(s) to ensure accuracy and completeness.
6. The IRB ensures the PI provides any significant new findings that might relate to subjects' willingness to continue participation in accordance with regulations.

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7. When the IRB reviews research that involves categories of individuals vulnerable to coercion or undue influence, ORI staff ensure adequate representation or consultation is present for discussion of research involving vulnerable human subjects. (See Protection of Vulnerable Subjects SOP and Membership of IRB SOP.)
8. ORI staff conduct the convened meeting in accord with the Conduct of IRB Meetings SOP. IRB members who have a conflict of interest follow procedures outlined in both the Conduct of IRB Meetings and IRB Member and Consultant Conflict of Interest SOPs.
9. Primary reviewers provide recommendations to the IRB at the convened meeting on issues they determine do not meet the federal criteria for approval, are controverted, or need additional information.
10. If the primary reviewer is unable to attend the meeting, ORI staff provide the reviewer's comments or recommendations for presentation to the IRB at the convened meeting.
11. The convened IRB assesses the CR materials using the federal criteria for approval (i.e., [45 CFR 46.111](#) and [21 CFR 56.111](#)).
12. At the meeting, the IRB reviews the CR materials and any controverted issues and their resolution prior to voting. During discussion, the IRB members only raise controverted issues they determine do not meet the federal criteria for approval as specified in [45 CFR 46.111](#) and [21 CFR 56.111](#). IRB approval verifies the IRB agrees with the assessment of the protocol and/or specific findings as described by the PI in the CR.
13. The convened IRB makes the final determination on the outcome of the review. The primary reviewer or designated IRB member documents the IRB's determinations on the IRB Continuation Review: Primary Reviewer Checklist.

Expedited CR – Protocols Subject to the Old Common Rule (Approved before January 21, 2019) and FDA-regulated Protocols Subject to the Revised Common Rule (Approved on or after January 21, 2019)

1. The Medical and Nonmedical Vice Chairs or designees serve as the expedited reviewer for expedited CRs. If the expedited reviewer has a conflict of interest (e.g., is study personnel on the protocol), is unavailable, or does not have the appropriate expertise to review the CR, ORI staff send the CR to the Chair, another Vice Chair, or a voting member of the IRB.
2. ORI staff assign the Vice Chair as the primary reviewer, giving the Vice Chair access to all information and materials for the CR submission, including:

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- A completed CR report that includes, when applicable: the number of subjects enrolled (including gender and minority status) and subjects withdrawn from the study;
 - A written summary and assessment of both unanticipated problems and available information regarding adverse events since the last IRB review; recent literature; complaints about the research; and any new significant findings (i.e., new findings and implications for subject participation) described;
 - A copy of the currently approved sponsor protocol for externally funded research (including any prior IRB approved modifications) and/or research description (summary which addresses all elements of criteria for approval); and if applicable:
 - A cover memo if it contains pertinent information to review the protocol;
 - Attachments (e.g., updates/changes, explanations)
 - Summary data and safety monitoring reports;
 - A clean and highlighted copy of the consent/assent form for which the investigator is seeking IRB approval, if requesting changes. If no changes are being made, only a clean copy of the consent/assent necessary;
 - Copies of signed consent forms and HIPAA Authorizations for the two most recently enrolled subjects, if applicable;
 - IRB Continuation Review: Primary Reviewer Checklist;
 - ORI staff recommendations, including HIPAA comments, if applicable.
3. If the expedited reviewer determines full review is necessary, he/she documents this requirement in the *Reviewer's Recommendations* section of the IRB Continuation Review: Primary Reviewer Checklist. The expedited reviewer may also raise controverted issues he/she determines do not meet federal criteria and/or may request additional information. Upon receipt of the reviewer's recommendation, ORI staff follow convened CR procedures.
 4. When informed consent/assent is applicable, the expedited reviewer reviews the informed consent/assent process and document(s) submitted for re-approval to ensure accuracy and completeness.
 5. ORI staff serve as intermediaries between the PI and the IRB expedited reviewer. However, the expedited reviewer may contact the PI directly for clarification. The reviewer documents any issues discussed with the PI in the CR materials.
 6. The expedited reviewer documents in the CR materials any determinations pertaining to specific findings as mandated by federal regulations not previously addressed by the IRB. Expedited reviewer approval of the CR materials documents that the reviewer agrees with the PI's assessment of the specific findings.

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7. The expedited reviewer ensures that the PI provides any significant new findings that might relate to subjects' willingness to continue participation in accordance with the regulations. The reviewer uses the IRB Continuation Review: Primary Reviewer Checklist as a prompt.
8. The expedited reviewer applies the same criteria for approval as outlined above for full review (i.e., applies [45 CFR 46.111](#) and [21 CFR 56.111](#), and informed consent regulatory criteria), and completes the IRB Continuation Review Primary Reviewer Checklist as documentation of his/her determination.
9. Expedited CR protocols are listed on the IRB agenda to advise members of the expedited CR reviews.

Expedited AAR Procedures – Expedited non-FDA-regulated Protocols Subject to the Revised Common Rule (Approved on or after January 21, 2019)

1. All Medical and Nonmedical expedited research protocols not regulated by the FDA, approved on or after January 21, 2019, requires an AAR unless there is documented IRB justification to require a CR. (FDA-regulated research and expedited studies with documented IRB justification to require a CR follow the Expedited Continuation Review procedures (#1-9) listed above.)
2. ORI staff assign the AAR submission to the Vice Chair or designee as the primary reviewer, giving the Vice Chair access to all information and materials including:
 - An update on the status of the research;
 - A written summary and assessment of both unanticipated problems and available information regarding adverse events since the last IRB review;
 - A copy of the consent/assent form for which the investigator is seeking IRB approval, if applicable (highlighted and clean versions if changes are being made);
 - Copies of signed consent forms and HIPAA Authorizations for the two most recently enrolled subjects, if applicable;
 - IRB Continuation Review: Primary Reviewer Checklist;
 - ORI staff recommendations, including HIPAA comments, if applicable.
3. The expedited reviewer determines: if the AAR is approved; if more information is required prior to approval; if the submission needs to undergo an expedited CR; or if the submission should undergo a CR by the convened board. If the reviewer determines that either an expedited or full board CR is necessary, he/she documents the justification for the determination in the Reviewer's Recommendations section of the IRB Continuation Review: Primary Reviewer Checklist. Upon receipt of the expedited reviewer's recommendation, ORI staff implement appropriate CR or AAR procedures (i.e., expedited or full CR).

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4. AARs are listed on the IRB agenda to advise members of the expedited AARs reviews.

Lapse of Approval

1. If a PI fails to submit a CR or AAR or the IRB has not completed review by the end of the approval period, ORI notifies the PI that approval has lapsed. ORI staff inform the PI that research must cease and no new subject enrollment may occur. ORI staff also inform the PI that he/she should, if appropriate, notify subjects that the study approval has lapsed and, if applicable, it is his/her responsibility to notify the funding agency of the expiration of the IRB approval.
2. The PI may ask the IRB for permission to allow subjects currently participating to continue due to an overriding safety concern, ethical issues, or because it is in the best interest of the individual subjects. The IRB makes the determination when appropriate. The ORI or IRB notifies the PI of that determination.
3. If protocol approval has expired and the PI wants to re-activate or re-submit the study, the ORI requests either a document that verifies no research activities have occurred since the lapse (i.e., recruitment or enrollment of new subjects, interaction, intervention, or data collection from currently enrolled subjects, or data analysis) or a written summary of events that occurred from the PI during the lapse.
4. If the PI submits the CR/AAR materials/revisions after the end of approval period, the IRB requires a new initial review application along with the CR/AAR documents.
5. When CR/AAR and approval of a research study does not occur prior to the end of the approval period, the IRB does not report the expiration as a suspension of approval under Food and Drug Administration (FDA) or U.S. Department of Health and Human Services (HHS) regulations.

Review Outcome(s)

1. For Full CR, an IRB member makes a motion, the motion is seconded, and the IRB members then vote for, against, or abstain from one of the following five actions:
 - APPROVED (Vote for a #1): IRB approval - A vote of #1 indicates the IRB concluded that the research and, if applicable, consent/assent forms meet the federal criteria for approval. The IRB's approval vote verifies that the IRB members agree with the information/materials submitted for continuation of the protocol and/or specific findings described in the CR report by the PI.

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- REVISIONS and/or ADDITIONAL INFORMATION REQUIRED (Vote for a #2): A vote of # 2 indicates 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 which do not involve substantive issues.
 - TABLED - Vote for a #3: A vote of #3 indicates the IRB withholds approval pending submission of major revisions/additional information. The requested revisions list the reasons for tabling. 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 the future IRB meeting.
 - TABLED – Vote for a #4: A vote of #4 follows the same procedure as 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 the future IRB meeting.
 - DISAPPROVED (Vote for a #5): A vote of #5 indicates the IRB disapproves the protocol. ORI staff send the investigator a letter describing the reasons for disapproving the protocol. This outcome usually occurs when the IRB determines the risk of the procedures outweighs any benefit or if the research does not meet the federal criteria.
2. The IRB determines during the convened meeting the approval period as appropriate to the degree of risk in the research, but not less frequently than once per year. The IRB may set a shorter approval period (i.e., for CR to occur more often than annually) for high risk protocols or protocols with a high risk/low potential benefit ratio. No approval period extends beyond one (1) year. When a protocol receives final approval, ORI staff document the approval period in the approval letter to the investigator. For Full CR, ORI staff include the approval period in the meeting minutes.
 3. For expedited CRs, the reviewer may make the following determinations: 1) approved; 2) revisions and/or additional information required; 3) review by the full committee required. The reviewer exercises all the authority of the IRB except he/she may not disapprove the CR. Only the convened IRB may disapprove the submission.
 4. For convened review, Full CRs, the date of the start of the approval period is the date of the convened meeting. When the outcome of the IRB vote is for a #2 (approved pending submission of minor revisions), ORI staff issue approval after the IRB Chair or the individual chairing the meeting reviews and approves the PI's response. The approval period begins on the date on which the convened IRB reviewed the protocol and voted for a #2. For Expedited

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CR/AAR, the date of the start of the approval period is the date the expedited reviewer approves the CR/AAR.

5. For convened review, expedited AARs, the reviewer may make the following determinations: 1) approved; 2) revisions and/or additional information required; 3) expedited CR required; 4) CR review by the committee required. The reviewer exercises all the authority of the IRB except he/she may not disapprove the AAR. Only the convened IRB may disapprove the submission.
6. If the approval lapses before approval of the CR/AAR, the reviewer can make a determination to allow subjects currently participating to continue in accord with procedures described in the section on lapses of approval.
7. Upon request, ORI staff also send the PI a funding agency Certification of Approval form. (See the Mandated Reporting to External Agencies SOP.)
8. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she submits a written appeal that includes a justification for changing the IRB decision. The PI sends the appeal to the ORI. The applicable reviewer or convened IRB reviews the appeal. The appeal determination is final.

REFERENCES

[21 CFR 56.108\(a\)\(1\)&\(2\)](#)
[21 CFR 56.109\(f\)](#)
[21 CFR 56.110](#)
[21 CFR 56.111](#)
[21 CFR 56.115\(a\)\(3\)&\(7\)](#)
[45 CFR 46.108](#)
[45 CFR 46.109\(f\)](#)
[45 CFR 46.111](#)
[45 CFR 46.115\(a\)\(3\)&\(7\)](#)
[45 CFR 160](#)
[45 CFR 164](#)