

<b>University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures</b>			
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Approved By: ORI Director	Signature	Date	Date First Effective: 06-28-05
Approved By: Nonmedical IRB Chair	Signature	Date	
Approved By: Medical IRB Chair	Signature	Date	Revision Date: 08-09-19

## **OBJECTIVE**

To describe policies and procedures for the directed on-site review component of the University of Kentucky (UK) Quality Assurance/Improvement Program (QA/QIP)

## **GENERAL DESCRIPTION**

The Office of Research Integrity (ORI)/Institutional Review Board (IRB) QA/QIP serves to improve human research protections at UK. One of the primary quality assurance/improvement activities is the directed on-site review.

The ORI QA/QIP conducts directed on-site reviews at the request of the IRB, the Vice President for Research (VPR), or ORI Director due to unusual circumstances, significant risks to subjects, routine failure on the part of an investigator to comply with federal and/or institutional requirements, and/or allegations or concerns about the conduct of the study. The IRB, VPR, or the ORI Director may also request periodic reviews to evaluate whether investigators meet their responsibilities within specific areas of research (e.g., investigators conducting research using an investigational device). If appropriate, directed reviews also encompass elements of informed consent evaluation, as described in the QA/QIP Administrative Assessment Review SOP. The IRB may request measures to monitor the consent process to determine whether procedures for administration of informed consent are proper. If the IRB deems it necessary, the QA/QIP may review IRB records to determine accuracy and consistency with the investigator's research records and to verify that the investigator made no material changes to the protocol.

The QA/QIP shares findings pertaining to the records with the principal investigator (PI)/research staff and reports these findings to the IRB. To maintain confidentiality, the QA/QIP does not record research subjects' protected health information in the directed review findings disseminated to the IRB.

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In reviewing the results of a directed review, the IRB determines if the deficiencies warrant suspension or termination of the research. If the IRB determination is suspension, the IRB develops a plan for follow-up, which may require another quality assurance/improvement review (QA/QIR) or monitoring of the informed consent process. (See Noncompliance SOP and Termination or Suspension of Research by the IRB SOP.)

The ORI develops educational programs for investigators, their research staff, ORI staff, and IRB members based on the results of the QA/QIP reviews. When the IRB receives reports of findings from QA/QIP reviews, the IRB determines whether to report the findings to the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), the study sponsor, the VPR, or other internal departmental faculty/staff. (See Mandated Reporting to External Agencies SOP.)

If the QA/QIP conducts a directed QA/QIR on a protocol that falls under the purview of a unit with which the ORI has written and approved joint standard operating procedures (e.g., the Institutional Biosafety Committee or Markey Cancer Center), the QA/QIP provides the appropriate unit representative with a copy of the resulting final report. The QA/QIP incorporates the Quality Assurance/Improvement Reporting Coordination Checklist into the review process to ensure reporting of QA/QIR results to applicable institutional units.

### **RESPONSIBILITY**

Execution of SOP: ORI QA/QIP, ORI Director, VPR, IRB Chair/Designated IRB Member, IRB, PI/Study Personnel

### **PROCEDURES**

1. If the IRB, VPR, or ORI Director requests a directed on-site review for an investigator and does not identify a specific protocol, the QA/QIP may use the following criteria to identify protocol(s) for inspection: federal, state, or industry-funded projects; currently approved and active for two years; level of risk to subjects; or subjects currently enrolled in the study.
2. For directed reviews that provide post-IRB approval evaluations to determine whether the PI is meeting responsibilities in a specific area of research (e.g., research using an investigational device), the QA/QIP runs a report to identify all protocols in the targeted area of research.
3. Once the QA/QIP determines which protocol(s) will undergo inspection, he/she notifies the PI of the upcoming directed on-site QA/QIR. After sending initial notification, the QA/QIP

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communicates with the PI and/or the study personnel to schedule the date(s) for the review at the earliest time possible.

4. The QA/QIP conducts an entrance and exit interview with the PI as part of the review. The IRB Chair and/or an IRB member may participate in these interviews. At the PI's discretion, select study personnel may also attend.
5. Prior to the entrance interview, the QA/QIP may review the initial review meeting minutes, IRB records, and other resources to become familiar with the protocol(s) and to identify issues to address during the QA/QIP process.
6. The entrance interview precedes the QA/QIP's on-site review of the PI's research records. The QA/QIP and/or IRB Chair/member may use this time to explain the goals of the QA/QIP and the impetus behind the directed review. It also provides the PI/study personnel with an opportunity to explain what the protocol entails, to respond to the issues that instigated the directed review, and to answer any questions arising from the QA/QIP's preceding review of the IRB protocol records.
7. The records reviewed by the QA/QIP and/or IRB Chair/member at the PI's site may consist of but are not limited to the following:
  - Protocol Binder/Regulatory Documentation – The QA/QIP reviews materials and notes whether the records retained meet federal, International Conference on Harmonisation (if applicable)/Good Clinical Practice, and IRB guidelines;
  - IRB Documentation – The QA/QIP compares the PI's records with the IRB's records. Review of IRB documentation affords the opportunity to determine whether the PI made material changes prior to IRB approval;
  - Consent/Assent Forms – The QA/QIP examines consent/assent forms used to enroll subjects to ensure that the subjects signed the appropriate form for their respective study and that study personnel and subjects properly signed and dated the forms;
  - Case Report Forms (CRF) – When applicable, the QA/QIP randomly selects three (3) subjects' records for the review. The QA/QIP determines whether the subjects met the inclusion/exclusion criteria for their respective study and whether the PI/study personnel recorded and documented items properly;
  - Medical Records – the QA/QIP may review medical records for clinical trials to verify the information in the CRFs;

For assistance/clarification during the review, the QA/QIP may contact the PI directly or, if applicable, inquire with the PI's study personnel.

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8. The QA/QIP and/or IRB Chair/member may also request a tour of the facilities to verify control, storage, and accountability of investigational new test articles, to confirm availability of related research equipment, and/or to verify secure storage of research records.
9. The IRB may request monitoring of the consent process as part of the directed review using procedures that include but are not limited to:
  - Surveying research subjects enrolled in the study about the informed consent process and their experience as a research participant;
  - Witnessing administration of informed consent to subject candidates by the QA/QIP and/or IRB member. The IRB determines the frequency of consent process monitoring on a case-by-case basis; examples of determining factors include level of risk, enrollment activity, funding agency, and targeted subject population.
10. The QA/QIP and/or IRB Chair/member conducts the exit interview after the QA/QIP completes a review of the PI's records and may request clarification regarding the protocol or research procedures at that time. The QA/QIP and/or IRB Chair/member provides the investigator with a verbal summary of the findings and explains the remaining procedures for conclusion of the review.
11. After the exit interview, the QA/QIP writes a report outlining the findings of the on-site review pertinent to the PI's records. If the IRB Chair/member participated in the on-site review, the QA/QIP may give the IRB Chair/member the opportunity to review and edit the report prior to sending it to the PI.
12. Once the QA/QIP review report is complete, the QA/QIP sends it to the PI with a requested response date determined on a case-by-case basis. Typically, the PI has two to three weeks to submit his/her response to the recommendations and/or comments on the report.
13. Upon receipt of the PI's response, the QA/QIP schedules a review with the appropriate IRB at a convened meeting.
14. For any QA/QI findings reviewed by the full committee, the IRB members vote for one of the following actions:
  - Approved – No further action is required. Per the guidelines in the ORI Customer Service Standards, the QA/QIP sends the PI a letter describing the outcome of IRB review.
  - Revisions/additional information requested – The IRB withholds approval pending submission of revisions/additional information. The IRB may give the individual chairing the meeting the authority to approve non-substantial revisions/additional information or require review of substantial revisions/additional information at a convened meeting. If the IRB request necessitates further QA/QIR, the QA/QIP acts accordingly and processes

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any additional findings/information for review based on the IRB's determination at the convened meeting (either gives them to the individual who chaired the IRB meeting or assigns them to a convened IRB meeting for review). If the IRB request necessitates a response from the PI (see the ORI Customer Service Standards), the QA/QIP sends the PI a letter describing the IRB's request. When the PI responds to the IRB's request in writing, the ORI processes the response based on the IRB's determination at the convened meeting (either gives it to the individual who chaired the IRB meeting or assigns it to a convened IRB meeting for review). If the individual who chaired the meeting is the IRB's designated reviewer, he/she may decide to forward the response to the entire IRB for additional review, request additional information, or approve.

- Suspension or termination of the research - (See Termination or Suspension of Research by the IRB SOP.) Per the guidelines in the ORI Customer Service Standards, the QA/QIP sends the PI a letter describing the outcome of the IRB review.

15. ORI staff save documentation for protocol-specific reviews in the corresponding IRB records and maintain QA/QIR documentation in the IRB records for a minimum of six years after study closure. (See IRB/ORI Recordkeeping SOP.) The QA/QIP maintains a separate QA/QIR file containing documentation on all QA/QI activity.

## **REFERENCES**

Not applicable