

| 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: 06-28-05 |
| Approved By: Nonmedical IRB Chair | Signature | Date | |
| Approved By: Medical IRB Chair | Signature | Date | Revision Date: 08-19-09 |

OBJECTIVE

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

GENERAL DESCRIPTION

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

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

If in reviewing the results of a directed review, the IRB determines that the exposed deficiencies warrant suspension or termination of the research, the IRB develops a plan for follow-up, which

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may require another quality improvement review (QIR) or monitoring of the informed consent process. (See Noncompliance and Termination or Suspension of Research by the IRB SOPs.)

The ORI develops educational programs for investigators, their research staff, ORI staff, and IRB members based on the results of the QIP reviews. When the IRB receives reports of findings from 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 SOP.)

If the QIP Coordinator conducts a directed 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, Markey Cancer Center, Veterans Affairs Medical Center (VAMC), the QIP Coordinator provides the appropriate unit representative with a copy of the resulting review materials. The QIP Coordinator incorporates the Quality Improvement Reporting Coordination Checklist into the review process to ensure reporting of QIR results to applicable institutional units.

RESPONSIBILITY

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

PROCEDURES

1. If the IRB, the VPR, or the ORI Director requests a directed on-site review and does not identify a specific protocol, the QIP Coordinator 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 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 QIP Coordinator runs a report to capture all protocols falling under the targeted area of research.
3. The QIP Coordinator enters a code in the ORI database to reflect initiation of the QIR request and assigns an anticipated IRB meeting date for review of the findings.
4. Once the QIP Coordinator determines which protocol(s) will undergo inspection, he/she notifies the PI by phone and in writing of the upcoming directed on-site QIR. Generally, within five working days after initial notification of the PI, the QIP Coordinator communicates with the PI and/or the study personnel to schedule the date(s) for the review at the earliest time possible.

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5. If the nature of the directed review requires it, the QIP Coordinator conducts entrance and exit interviews with the PI. The IRB Chair/IRB member may participate in these interviews. At the PI's discretion, select study personnel may also attend.
6. Prior to the entrance interview, the QIP Coordinator may review the initial review meeting minutes, IRB records, and ORI database to become familiar with the protocol(s) and to identify issues to address during the QIR process.
7. The entrance interview precedes the QIP Coordinator's on-site review of the PI's research records. The QIP Coordinator and/or IRB Chair/IRB member may use this time to explain the goals of the QIP and the impetus behind the directed review. It also allows the PI/ study personnel an opportunity to explain what the protocol entails, respond to the issues which instigated the directed review, and answer any questions arising from the QIP Coordinator's review of the IRB protocol records.
8. The records reviewed by the QIP Coordinator and/or IRB Chair/IRB member at the PI's site may consist of, but are not limited to, the following:
 - Protocol Binder/Regulatory Documentation – The QIP Coordinator reviews materials and notes whether the records retained meet federal, International Conference on Harmonisation/Good Clinical Practice, and IRB guidelines;
 - IRB Documentation – The QIP Coordinator 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 Forms – The QIP Coordinator examines consent forms used to enroll subjects to ensure that the subjects signed the appropriate consent form for their respective study and that study personnel and subjects properly signed and dated the forms;
 - Case Report Forms (CRF) – When applicable, the QIP Coordinator asks the PI in advance to randomly select three subjects' records for the review. The QIP Coordinator 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 – If applicable, the QIP Coordinator may review medical records for clinical trials to verify the information in the CRFs;
 - Grant Application – If applicable, the QIP Coordinator may compare the grant application to the IRB approved protocol.

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

9. The QIP Coordinator and/or IRB Chair/IRB member may also request a tour of the facilities to verify control, storage, and accountability of investigational new test articles and/or to confirm availability of related research equipment.

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10. The IRB may request monitoring of the consent process as part of the directed review, using procedures which 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 (see below Optional Assessment Tool);
 - Witnessing administration of informed consent to subject candidates by the QIP Coordinator 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.

11. The QIP Coordinator and/or IRB Chair/IRB member conducts the exit interview after the QIP Coordinator completes a review of the PI's records and may request clarification regarding the protocol or research procedures at that time. The QIP Coordinator and/or IRB Chair/IRB member provides the investigator with a verbal summary of the findings and explains the remaining procedures for conclusion of the QI review.

12. After the exit interview, the QIP Coordinator writes a report outlining the findings of the on-site review pertinent to the PI's records. If the IRB Chair/IRB member participates in the on-site review, the QIP Coordinator may give the IRB Chair/IRB member the opportunity to review and edit the report prior to sending it to the PI.

13. Once the QIP review report is complete, the QIP Coordinator 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.

14. Upon receipt of the PI's response, the QIP Coordinator schedules a review with the appropriate IRB at a convened meeting. The QIP Coordinator marks the protocol(s) as "Audited by ORI staff" in the ORI/IRB database.

15. For any QI findings requiring review 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 QIP Coordinator 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 QIR, the QIP Coordinator acts accordingly and processes 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

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request necessitates a response from the PI (see the ORI Customer Service Standards), the QIP Coordinator 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 QIP Coordinator sends the PI a letter describing the outcome of the IRB review.
16. ORI staff file documentation for protocol-specific reviews in the corresponding IRB records and maintain QIR documentation in the IRB records for a minimum of six years after the study closure. (See IRB/ORI Recordkeeping SOP.) The QIP Coordinator maintains a separate QIR notebook containing documentation on all QI activity and reviews the notebook to determine whether to eliminate protocol-specific QI materials from the records based on the retention policy for IRB protocol records. The ORI Director determines whether to discard materials.

Optional Assessment Tool

1. The IRB, ORI Director, or QIP Coordinator may direct the PI to send the subject survey assessment tool to the subjects. The IRB, ORI Director, or QIP Coordinator makes the determination to require the survey based on the nature of the incident that initiated the need for a directed on-site review or the findings of the QIR. The survey gives subjects the opportunity to provide feedback about their experience as a research subject, particularly about the informed consent process.
2. The PI uses the survey responses as a valuable learning tool regarding strengths and weaknesses in the research program (i.e., informed consent process).

REFERENCES

Not applicable