University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures			
Revision #9	**TITLE: Quality Assurance/ Improvement Program Review of Research Studies**		**Page 1 of 10**
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: 05-28-24

OBJECTIVE

To describe policies and procedures for the Quality Assurance/Improvement Program (QA/QIP) component of the University of Kentucky (UK) Office of Research Integrity (ORI).

GENERAL DESCRIPTION

The ORI/Institutional Review Board (IRB) QA/QIP serves to improve human research protections at UK. Two of the primary quality assurance/improvement activities are directed (aka "for cause") reviews and routine post-approval monitoring (aka "Wellness Checks").

Directed "For Cause" Reviews
The ORI QA/QIP conducts directed for cause 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 review with the principal investigator (PI)/research staff and reports these findings to the IRB that requested the review. To maintain confidentiality,

the QA/QIP does not record research subjects' protected health information in the report disseminated to the IRB.

In reviewing the results of a directed review, the IRB determines if any 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 a 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, the Reviewing/Relying IRB(s) when applicable, or other internal departmental faculty/staff. (See Mandated Reporting to External Agencies SOP.)

If the QA/QIP conducts a directed review 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.

Routine post-approval monitoring ("Wellness Checks")
The ORI QA/QIP conducts Wellness Checks to assist investigators with the conduct of human subjects research protocols at UK and educate them about human subjects protections in general, as needed. Unlike protocols undergoing Directed Review, Wellness Checks are not selected by the IRB. In addition, Wellness Checks are not protocols that have been "flagged" or "reported" for any reason such as participant complaints. Wellness Checks are selected by the QA/QIP using a combination of a risk-based approach (e.g., risk level designated on the protocol, involvement of vulnerable populations, studies with no additional oversight or support, etc.), specified approval time frames (e.g., approximately 6 months after initial IRB approval), and topics of interest (e.g., device studies, survey/interview topic, investigator initiated and/or student-led research, international studies, etc.). Wellness Checks involve 50% medical protocols and 50% nonmedical protocols and can be conducted on any study that undergoes IRB Review.

RESPONSIBILITY

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

PROCEDURES

Directed Reviews

1. If the IRB, VPR, or ORI Director requests a directed 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 review, he/she notifies the PI of the upcoming directed QA/QI review. After sending initial notification, the QA/QIP 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 IRB-approved study personnel may also attend.

5. Prior to the entrance interview, the QA/QIP review the initial review meeting minutes (if applicable), IRB records, protocol documentation/materials, and other resources to become familiar with the protocol(s) and to identify potential issues to address during the QA/QIR review process.

6. The entrance interview precedes the QA/QIP's review of the PI's research records. The QA/QIP and/or participating 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 participating IRB Chair/member may consist of but are not limited to the following:
   - Protocol Binder/Regulatory Documentation – (in hard copy and/or electronic format) The QA/QIP reviews materials and notes whether the records retained meet applicable federal, International Conference on Harmonization /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 participants to ensure that they received and (if applicable) signed the appropriate form(s) for their respective study and that approved study personnel and the participants properly signed and dated the forms as/when required;
- Participant Binders/Files/Case Report Forms (CRFs) –The QA/QIP reviews all participants' records for the review. In cases where the study has enrolled a large number of participants, the QA/QIP randomly selects a portion of the available binders/files for review. The QA/QIP determines whether the subjects met the inclusion/exclusion criteria for their respective study, whether the PI/study personnel recorded and documented items properly, if all data collection materials are present and properly completed;
- Medical Records –the QA/QIP may review medical records to verify the information in the CRFs;

For assistance/clarification during the record review, the QA/QIP may contact the PI directly or, if applicable, inquire with the PI's study personnel, or wait until the exit interview to obtain clarification.

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

9. The IRB may request observation/monitoring of the consent process as part of the directed review using procedures that include but are not limited to:
   - Surveying research participants enrolled in the study about the informed consent process and their experience as a research participant;
   - Witnessing administration of the informed consent process to potential participants by the QA/QIP and/or participating IRB member. The IRB determines the frequency of consent process monitoring on a case-by-case basis; examples of determining factors include the level of risk of the research, enrollment activity, funding agency/source, and targeted subject population.

10. The QA/QIP and/or participating IRB Chair/member conducts the exit interview after the QA/QIP completes the review of the research records and may request clarification regarding the protocol or research procedures at that time. The QA/QIP and/or participating IRB Chair/member provide(s) the investigator with a verbal summary of the findings and explains the remaining procedures for conclusion of the review.

11. The QA/QIP writes a report outlining the findings of the directed review following the exit interview. If the IRB Chair/member participated in the directed 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 weeks to submit his/her response to the recommendations and/or provide comments on the written report.

13. Upon receipt of the PI's response (if any), the QA/QIP schedules a review with the appropriate IRB at a convened meeting.

14. For any QA/QIP findings related to the protection of human research participants reviewed by the full committee, the IRB members vote for one of the following actions:
    - Acknowledged/Approved – No further action is required. Per the guidelines in the ORI Customer Service Standards, the PI is notified of the outcome of IRB review.
    - Revisions/additional information requested – The IRB withholds acknowledgement/approval of the report 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 subsequent convened meeting. If the IRB request necessitates further QA/QIP review, the QA/QIP 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 request necessitates a response from the PI (see the ORI Customer Service Standards), the QA/QIP or other ORI staff 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 acknowledge/approve the response.
    - 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 or other ORI staff sends the PI a letter describing the outcome of the IRB review.

15. ORI staff save documentation for protocol-specific directed reviews in the corresponding IRB records and maintain QA/QIP 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 restricted-access file containing documentation on all QA/QI activity.

Reliance protocols: Directed Reviews when UK is the Reviewing IRB

1. The QA/QIP notifies the Relying Sites of the pending Directed Review as needed to comply with the signed Reliance Agreement(s) applicable SOPs/Communications Plan as well as to obtain the most recent study documents (i.e., data collection, consent forms, enrollment logs, etc.).

2. In addition to the documentation described under #7 of Directed Reviews section above, the QA/QIP reviews the Reliance Agreement(s), Communications Plan(s), and/or the Local Context Form(s) (when applicable) for all Relying Sites and ensures that the UK PI has distributed the most recent study materials to the Relying Site(s).

3. The QA/QIP informs the Relying Site(s) of the results of the Directed Review if the IRB votes to Suspend or Terminate the research or if the Reliance Agreement/Communications Plan requires this information.

Reliance protocols: Directed Reviews when UK is the Relying IRB

1. If the Reviewing IRB asks for a Directed Review of UK as a Relying Site for a specific protocol, the QA/QIP follows the same procedures as the "*Reliance protocols: Directed Reviews when UK is the Reviewing IRB"* section above.

2. The QA/QIP requests the most recent study documents (i.e., protocol, data collection implements, stamped consent forms, etc.) from the Reviewing IRB.

3. In addition to the documentation described under #7 of the Directed Reviews section above, the QA/QIP reviews the Reliance Agreement and Communications Plan.

4. The QA/QIP informs the Reviewing Site of the results of the Directed Review unless the IRB votes to Suspend or Terminate the research or if the Reliance Agreement/Communications Plan requires this information.

Routine post-approval monitoring ("Wellness Checks")

1. The QA/QIP conducts Wellness Checks to ensure that PIs are meeting their responsibilities, following the research protocol as approved by the IRB, and to assist and educate PIs/study teams in doing so as needed.

2. The QA/QIP identifies studies for Wellness Checks primarily using a risk-based approach and may run reports to identify protocols in targeted areas of interest (e.g., vulnerable populations, research topic, risk level of the research, approved within specified date ranges, non-sponsored protocols, student PI, etc.). The IRB is not involved in selecting protocols for Wellness Checks.

3. Once the QA/QIP determines which protocol(s) will undergo a Wellness Check, each PI is notified of the upcoming QA/QI review and provided with a list of available dates to select from. If the PI is a student, the faculty advisor on the protocol is included in the notification. The QA/QIP and PIs then communicate to schedule the date(s) and location/format for the review at the earliest time possible. At the PI's discretion, select IRB-approved study personnel may also attend. Faculty advisors are expected to participate in Wellness Checks when the PI is a student.

4. The QA/QIP reviews the initial review meeting minutes (if applicable), IRB records, protocol documentation/materials, and other resources prior to the Wellness Check to become familiar with the protocol(s) and identify potential issues to address during the review.

5. The Wellness Check is initiated with an entrance interview. The QA/QIP typically use this time to do introductions and explain the goals of the QA/QIP and the impetus behind Wellness Checks in general. It also provides the PI/study personnel with an opportunity to explain what the protocol entails, provide an update on its status, to answer any questions arising from the QA/QIP's preceding review of the IRB protocol records, and to ask questions of the QA/QIP.

6. The QA/QIP reviews the research records following the entrance interview. The PI and study personnel are not present for this portion of the Wellness Check. The records reviewed during this process consist of (but are not limited to) the following:
   - Protocol Binder/Regulatory Documentation – (in hard copy and/or electronic format) The QA/QIP reviews materials and notes whether the records retained meet applicable federal, International Conference on Harmonization/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 participants to ensure that they received and (if applicable) signed the appropriate form(s) for their respective study and that approved study personnel and the participants properly signed and dated the forms as/when required;

- Participant Binders/Files/Case Report Forms (CRFs) –The QA/QIP typically reviews all participants' records for the Wellness Check. In cases where the study has enrolled a large number of participants, the QA/QIP randomly selects a portion of the available binders/files for review. The QA/QIP determines whether participants met the inclusion/exclusion criteria for their respective study, whether the PI/study personnel recorded and documented items properly, if all data collection materials are present and properly completed, etc.;
- Medical Records –the QA/QIP may review medical records to verify the information in the CRFs;

For assistance/clarification during the record review, the QA/QIP may either contact the PI directly (or, if applicable, inquire with the PI's study personnel) or wait until the exit interview to obtain clarification.

7. The QA/QIP conducts the exit interview following the review of the research records and may request clarification regarding the protocol or research procedures at that time. The QA/QIP provides the investigator with a verbal summary of the findings and any areas of concern. The QA/QIP also explains the next steps following the Wellness Check and any required actions (e.g., submission of a Modification Request, Protocol Violation report, etc.).

8. The QA/QIP may also request a tour of the facilities to verify control, storage, and accountability of investigational new test articles, confirm availability of related research equipment, and/or to verify secure storage of research records.

9. The QA/QIP writes a report outlining the findings of the Wellness Check following the exit interview. 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 weeks to submit a response to the written report.

10. The Wellness Check report is not provided to the IRB unless significant concerns and/or issues related to the protection of human research participants are noted during the review.

11. If significant concerns were noted during the Wellness Check and the report is provided to the IRB, the PI's response (if any) is also provided to the IRB. The QA/QIP then coordinates with ORI staff to have the written report and all associated information scheduled for review by the relevant IRB at a convened meeting. The IRB then reviews the report and findings following the procedures described for Directed Reviews.

    Reliance protocols: Routine post-approval monitoring ("Wellness Checks") when UK is the Reviewing IRB

1. If a protocol is selected for which UK is the Reviewing IRB, the QA/QIP notifies the Relying Site(s) HRPP of the pending Wellness Check to comply with the signed Reliance Agreement(s) and/or Communications Plan, to obtain the most recent study documents (i.e., data collection, consent forms, enrollment logs, etc.). The QA/QIP may also request the Relying Site(s) HRPP to conduct their own post-approval monitoring of their site depending on UK findings.

2. In addition to the documentation described under #6 of the Wellness Checks section above, the QA/QIP reviews the Reliance Agreement(s), Communications Plan(s), and/or the Local Context Form(s) for all Relying Sites and ensures that the UK PI has distributed the most recent study materials to the Relying Site(s).

3. The Relying Site(s) is/are not informed of the results of the Wellness Check unless the Reliance Agreement(s) or Communications Plan specifies the Sites will receive the reports. If the report contains significant concerns (as defined in the Protocol Violation Review SOP as a Major Violation) that were noted during the visit, then both UK's IRB and the Relying Site(s) will receive the report/findings.

Reliance protocols: Routine post-approval monitoring ("Wellness Checks") when UK is the Relying IRB

1. In addition to the criteria for selecting protocols, the QA/QIP consults with the UK ORI Reliance Manager when selecting a protocol for which UK is a Relying Site.

2. The QA/QIP requests the most recent study documents (i.e., protocol, data collection implements, stamped consent forms, etc.) from the Reviewing IRB.

3. In addition to the documentation described under #6 of the Wellness Checks section above, the QA/QIP reviews the Reliance Agreement and Communications Plan.

4. The QA/QIP informs the Reviewing Site of the results of the Wellness Check only if the Reliance Agreement or Communications Plan specifies that requirement. If the report contains significant concerns (as defined in the Protocol Violation Review SOP as a Major Violation) noted during visit, the Reviewing IRB and UK's IRB will receive the report/findings.

REFERENCES

Not applicable

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