University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures			
Revision #11	**TITLE: Unanticipated/Anticipated Problem/Adverse Event Reporting (UK)**		**Page 1 of 8**
Approved By: ORI Director	Signature	Date	Date First Effective: 05-30-05
Approved By: Nonmedical IRB Chair	Signature	Date	
Approved By: Medical IRB Chair	Signature	Date	Revision Date: 02-12-25

OBJECTIVE

To describe the policies and procedures for prompt investigator reporting of unanticipated problems or adverse events, investigator reporting of problems/adverse events that do not meet the prompt reporting requirements, and the procedures for Institutional Review Board (IRB) review of investigator reports for University of Kentucky (UK) studies

GENERAL DESCRIPTION

Regulatory guidance provided in 45 CFR 46.108(a)(4) and 21 CFR 56.108(b) requires the IRB to have written procedures for ensuring prompt reporting to the IRB, appropriate University officials, and applicable regulatory agencies of any unanticipated problems involving risks to human subjects or others. In response to the regulatory obligation, the UK IRB utilizes a three-category reporting system to facilitate review of reports and determinations about whether the problem/event raises new concerns about 1) risks to subjects or others; 2) the risk/benefit ratio; 3) the approved informed consent document; and the 4) need for re-consent.

The UK reporting categories are as follows:

1. Prompt Reporting to the IRB of an unanticipated problem involving risks to subjects or others or all internal research-related deaths and external unanticipated research-related deaths (including anticipated death occurring more frequently than expected);
2. Non-Prompt Reporting to the IRB of anticipated problems/anticipated serious adverse events or unrelated deaths (required by sponsor but not by UK);
3. Continuation Review Reporting to the IRB includes a written summary of both unanticipated problems and available information regarding adverse events since the last IRB review. The summary must include the PI's assessment of whether the problems/adverse events warrant changes to the protocol, consent process, or risk/benefit ratio. For multisite studies, the

written summary should describe external events determined to be unanticipated problems involving risks to subjects.

The policy on prompt reporting, non-prompt reporting, and continuation review reporting of problems/events is the basis for the SOP. The policy details the IRB requirements for reporting, including adverse events and unanticipated problems involving risks to research subjects and others. In addition to the three categories, there are two broad types of reports, internal and external.

Definitions

An *internal event/problem* is one that occurs with research subjects enrolled in a project approved by the UK IRB and directed by an investigator employed by the University or one whose project is under the purview of the UK IRB.

An *external event/problem* is one that occurs with research subjects enrolled in multi-center research projects that do not fall under the purview of the UK IRB.

See UK IRB Policy on Unanticipated Problem and Safety Reporting for additional definitions.

RESPONSIBILITY

Execution of SOP: IRB Chair, IRB, Office of Research Integrity (ORI) Staff, Principal Investigator (PI)/Study Personnel

PROCEDURES

UK Reporting Requirements for Prompt Reporting of Problems/Adverse Events

1. The PI reports unanticipated problems involving risks to subjects or others and internal research-related deaths using the UK Internal *or* External Prompt Reporting Form. Unanticipated problems involving risks to subjects or others are problems/adverse events which are unexpected AND related to the study procedures AND suggest that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. For multi-site studies, the PI reports external events determined to be unanticipated problems involving risks to subjects or others AND unanticipated research-related deaths using the UK External Prompt Reporting Form.

2. The PI reports unanticipated life-threatening events and unanticipated adverse device effects (UADE) within seven (7) calendar days of his/her receipt of the information and all other unanticipated problems involving risks to subjects or others within 14 calendar days of his/her receipt of the information. Institutional policy requires the investigator to provide follow-up reports on life-threatening events within 14 calendar days of his/her receipt of the information.

3. The PI reports deaths meeting prompt reporting criteria using the appropriate UK Internal/External Prompt Reporting Form immediately upon investigator receipt of the information (i.e., within 48 hours).

4. The IRB may request more stringent requirements for reporting events for individual research studies if the respective committee determines it to be necessary.

Submissions/Screening and Review of Internal Problems/Events: Prompt Report

1. The PI makes the preliminary determination if the event meets the criteria for an IRB reportable internal problem/event in accordance with the UK Policy on Unanticipated Problem and Safety Reporting.

2. The PI completes the UK Internal Prompt Reporting Form and submits the form to the ORI in the time period outlined in the IRB Policy on Unanticipated Problem and Safety Reporting.

3. If the PI recognizes the problem/event involves risks to subjects or others and the information is not already in the consent/assent document(s), he/she submits a revised consent/assent form(s) as well as a highlighted version of the document(s) for review and approval by the IRB.

4. ORI staff screen the report to determine whether it is complete and place the report on an IRB agenda.

5. Staff assign the report(s) and related material(s) to the IRB Chair or designee who serves as the primary reviewer.

6. The primary reviewer may review related material(s) including but not limited to: the complete or relevant portions of the IRB application; documents revised as a result of the problem/event; or documents which provide additional assessments or summary information. The individual serving as primary reviewer receives, at a minimum, the completed UK Prompt Reporting Form.

7. After reviewing the materials, the primary reviewer makes comments in the protocol in the electronic system for review by the convened IRB.

8. The IRB reviews internal events and problems at a convened IRB meeting using initial full review procedures.

9. If the study is federally funded (e.g., by the U.S. Department of Health and Human Services), or is regulated by the Food and Drug Administration (FDA), additional IRB reporting requirements may be in effect. (See the Mandated Reporting to External Agencies SOP.)

Review Outcome(s)

1. For all problems/events submitted under the IRB's prompt reporting policy, the IRB determines whether the problem/event meets the UK definition of unanticipated problem involving risks to subjects or others. If the unanticipated problem/event involves risks to subjects or others, the IRB follows the established reporting policy. (See Mandated Reporting to External Agencies SOP.) The IRB actions may include but are not limited to:
   - Acknowledgment/acceptance without further recommendation;
   - A request for further clarification from the investigator;
   - Changes in the protocol (e.g., additional test or visits to detect similar events in a timely fashion);
   - Changes in the consent/assent form(s);
   - A requirement to inform subjects already enrolled or to re-consent (e.g., when the information may relate to the subject's willingness to continue to take part in the research);
   - A change in frequency of continuation review;
   - Further inquiry into other protocols utilizing the particular drug, device, or procedure in question;
   - Suspension or termination of the study; or
   - Request for quality improvement review; or
   - Other actions deemed appropriate by the IRB.

2. If the IRB acknowledges/accepts the internal problem/event without recommendation, ORI staff generate a letter and send it to the PI indicating the review outcome.

3. If the committee requests clarification(s), additional information, or revisions, ORI staff notify the PI of the need for additional information and/or changes.

4. The PI responds to IRB requests for information or revisions and sends the response to the ORI. ORI staff assign investigator responses to the IRB Chair for further review. The IRB Chair may forward the response to the entire IRB for additional review, request additional information, or acknowledge/accept the response without recommendation.

5. If the PI has concerns regarding the IRB's decision/recommendation for changes in the study, he/she may submit an appeal that includes justification for changing the IRB decision. The PI sends the request to the ORI. The IRB Chair or the convened IRB reviews the appeal. The IRB determination of the review of the appeal is final.

Submissions/Screening and Review of External Problems/Events: Prompt Report

1. The PI makes a preliminary determination whether the external event meets the criteria for an unanticipated problem involving risks to subjects or others in accord with the UK Policy on Unanticipated Problem and Safety Reporting.

2. The PI completes the UK External Prompt Reporting Form and submits it to the ORI in the time period outlined in the UK Policy on Unanticipated Problem and Safety Reporting.

3. ORI staff screen the External Prompt Reporting Form for completeness.

4. ORI staff assign the External Prompt Reporting Form(s), any attached external reports of problems/events, and related material(s) to the IRB Chair or designee. The IRB Chair or designee serves as an expedited reviewer using expedited review procedures. The expedited reviewer may receive related material(s) including but not limited to documents revised as a result of the problem/event and/or documents which provide additional assessments or summary information.

5. If the expedited reviewer determines the unanticipated event is an unanticipated problem involving risks to subjects or others, he/she completes the External Prompt Reporting Form. ORI staff schedule review of the unanticipated event(s) by the convened IRB.

6. If the expedited reviewer determines the event is not an unanticipated problem involving risks to subjects or others, he/she documents his/her review by signing the original report and list any concerns/recommendations.

7. ORI staff includes the external problem/event on the IRB agenda for a convened meeting. Any IRB member may request to review the entire IRB file (paper) or access in the electronic system and the expedited reviewer's recommendations.

Review Outcomes

1. The IRB actions may include but are not limited to:
   - Acknowledgment/acceptance without further recommendation;
   - A request for further clarification from the investigator;
   - Changes in the protocol (e.g., additional tests or visits to detect similar events in a timely fashion);
   - Changes in the consent/assent form(s);
   - A requirement to inform subjects already enrolled or to re-consent (e.g., when the information may relate to the subject's willingness to continue to take part in the research);
   - A change in frequency of continuation review;
   - Further inquiry into other protocols utilizing the particular drug, device, or procedure in question;
   - Recommendation for full review;
   - Request for quality improvement program review; or
   - Other actions deemed appropriate by the IRB.

2. If the IRB acknowledges/accepts the external unanticipated problem/event without recommendation, ORI staff send a letter to the PI indicating the review outcome.

3. If the reviewer requests clarification(s), additional information, or revisions, ORI staff notify the PI of the need for additional information and/or changes.

4. The PI responds to requests for information or revisions and submits the response to the ORI. ORI staff assign responses to the IRB Chair or designee for further review. The IRB Chair or designee may request additional information, recommend full review, or acknowledge/accept the response without recommendation.

5. The IRB Chair or designee reviews any replies from the investigators on behalf of the committee unless the IRB Chair or designee determines the reply needs further review by the

convened IRB. The IRB Chair or designee documents acknowledgment/acceptance of the report, and ORI staff notify the PI in writing in a timely manner.

6. If the PI has concerns regarding the IRB decision/recommendation for changes in the study, he/she may submit an appeal that includes justification for changing the IRB decision. The PI sends the request to the ORI. The IRB Chair, designee, or the convened IRB reviews the appeal. The IRB determination of the review of the appeal is final.

Reporting of Problems/Events that Do Not Meet Prompt Reporting Requirements (Non-Prompt Reporting) to the IRB (required by Sponsors, not required by the UK IRB)

1. If the sponsor requires IRB documentation of submission of reports of events, which do not meet the UK IRB's prompt reporting requirements to the IRB, the PI may submit these events to the IRB using the *IRB Cover Form for Non-Prompt Reporting of Problems/Adverse Events*.

2. ORI staff assign the Non-Prompt Report and its attachments to the IRB Chair or designee.

3. If the IRB Chair or designee determines the PI should report the problem(s)/event(s) per the prompt reporting requirements, he/she documents this on the Non-Prompt Report materials. ORI staff notify the PI of the requirement to submit the Internal/External Prompt Reporting Form.

4. ORI staff sends a letter from the IRB acknowledging the materials received although the problem(s)/event(s) does not meet the UK IRB's prompt reporting requirements.

Continuation/Annual Administrative Review Reporting of Problems and/or Adverse Events

1. The PI submits a written summary of both unanticipated problems and available information regarding adverse events since initial or the latest continuing IRB review at Continuation/Annual Administrative Review. For multisite studies, the written summary should describe external events determined to be unanticipated problems involving risks to subjects or others. The summary must include the PI's assessment of whether the problems/adverse events warrant changes to the protocol, consent process/documents, or risk/benefit ratio. (For policies and procedures for conducting continuation review, see the Continuation and Annual Administrative Review SOP.)

REFERENCES

21 CFR 56.108(b)
45 CFR 46.108(a)(4)