Department: UAMS Institutional Review Board
Policy Number: 10.2
Section: Principal Investigator Responsibilities
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SUBJECT: Events that must be reported to the IRB and IRB Actions

POLICY
Federal regulations require the IRB to ensure that Investigators promptly report all unanticipated problems involving risks to subjects or others (UPIRTSO) or serious or continuing noncompliance to the IRB.

This policy identifies the types of events that Investigators must report to the IRB. The IRB will determine if the reported event is an unanticipated problem involving risk to subjects or others or if it meets the definition of serious or continuing noncompliance. If an event is determined to be UPIRTSO, IRB Policy 2.6 on reporting will apply. If an event is determined to be non-compliance, IRB Policy12.6 will apply.

Reports under this policy should be submitted as Reportable New Information in the IRB e-system.

DEFINITIONS
A. Related: For this policy, an event is "related" if it was caused by participation in the research activity or there is a reasonable possibility that the event may have been caused by the procedures involved in the research.
B. Risk: The probability of harm or injury (physical, psychological, social or economic) occurring as a result of participation in a research study.
C. Unanticipated: A problem is "unanticipated" when it was unforeseeable at the time it occurred.
D. Unanticipated Adverse Device Effect: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
E. Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO): Any problem, event or new information that is:
    1. Unanticipated or unexpected;
    2. Related or possibly related to the research; and
    3. Involves new or increased risks to subjects or others.
F. Unexpected: An event is "unexpected" when the nature, severity or frequency are not consistent with either:
        1. The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the study-related documents, and (b) other relevant sources of information; or
        2. The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.
G. See IRB Policy 12.6 for noncompliance definitions.

PROCEDURE
A. Time frame for reporting:
    1. Events requiring reports under this policy which have resulted in death or are life-threatening should be reported immediately to the IRB office or IRB Chair.
    2. All other events listed below must be reported in IRB e-system within 10 days of the event or notification of event if non-local.
    3. Reporting requirements apply regardless of whether they occur during the study, after study completion or after subject withdrawal or completion.

B. Each report should be submitted through the IRB e-system and contain:
   1. Description of the event including date and location;
   2. Nature of the risk to subjects from the event, noting whether Investigator believes the event increases the risk to the subject or others;
   3. How the event relates to the research;
   4. Whether the Investigator believes the consent or protocol should be changed or if subjects should be notified.

C. Reportable Events:
   1. Local adverse events that the Investigator determines are all of the following:
      a. Unexpected;
      b. Related to the research; and
      c. Involve new or increased risks to subjects or others.

   2. Non-local adverse events that have been determined to be unanticipated problems involving risks to subjects or others. (i.e. IND Safety Report)

   3. Unanticipated adverse device effects.

   4. Any change or deviation made to the research without prior IRB approval in order to eliminate apparent immediate harm.

   5. An accidental or unintentional change to the IRB-approved protocol that placed one or more subjects at increased risk or affects the rights and welfare of subjects or others.

   6. Any new information that indicates an unexpected and related change to the study's risk/benefit ratio. This includes, but is not limited to,

      a. Revised Investigator Brochures, Package Inserts, Device Manuals;
      b. Publications in the literature;
      c. Data and Safety Monitoring Reports;
      d. Interim results or other findings.

      Examples include MedWatch reports indicating that a side effect is more frequent or severe than expected, or a publication showing that an arm of study is of no therapeutic value.
   7. A breach in confidentiality that may involve risk to subjects or others. Examples include the loss of a laptop computer on which subject identifiers are stored or the loss of study records on a thumb drive.
   8. Any complaint of a participant that indicates an unanticipated risk or any complaint that cannot be resolved by the research team.
   9. Incarceration of a subject if study was not previously reviewed with the anticipation of enrolling prisoners and if the subject continued participation while incarcerated without IRB rereview.
   10. Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol, if the rationale for the change relates to new or increased risks that are unexpected and related to the product.
   11. Restrictions, suspension or termination of study by the sponsor, Investigator, funding agency, regulatory body, or institutional administration.
   12. The premature completion of a study, due to interim findings indicating a change in the risk/benefit ratio.
   13. Notifications of pending audits, inquiries, or investigations by federal agencies.
   14. Written reports from study monitor that include information that requires reporting under this policy.
   15. Any other problem that was unexpected, related to the research and places the subject or others at a greater risk than previously known.

D. Other problems which do not meet the UPIRTSO or serious or continuing noncompliance definition should be submitted at the time of continuing review in summary format.

E. IRB Responsibilities
   1. An IRB Chair, or Experienced IRB Reviewer, will review each report and determine if the reported event is potentially a UPIRTSO or an instance of serious or continuing noncompliance under this policy or a report of potential non-compliance using IRB Policy 12.5.
   2. The reviewer may return contingencies seeking additional information.
   3. If the Reviewer determines that the reported event does not meet the definition of a UPIRTSO, is

not potential noncompliance, and is not otherwise reportable, the reviewer will indicate that the event is not reportable at this time and/or acknowledge the report with no further action.

4. If the Reviewer determines the report may represent a UPIRTSO or noncompliance, the report shall be placed on a convened board agenda.
5. The reviewer will determine if any subject or others are at immediate risk of harm. If so, the reviewer shall consult the IRB chair to see if any study activities should be immediately suspended, as described in IRB Policy 7.9.
6. When reviewed by the convened IRB, two Reviewers will be assigned to review the reported event and present the problem to the convened IRB in sufficient detail to allow the IRB to take appropriate actions. All Reviewers will have access to the entire study file.
7. Actions the IRB may take in response to the report include but are not limited to:
    a. Request more information about the event or about any corrective actions
    b. Require modifications to the protocol;
    c. Require modifications to the information disclosed during the consent process;
    d. Require current subjects to be notified of information deemed to relate to subjects' willingness to continue to participate in the research;
    e. Require current subjects to re-consent to participation;
    f. Require additional information be provided to past subjects;
    g. Request the research be audited by the Office of Research Integrity;
    h. Require monitoring of the consent process;
    i. Require more frequent continuing reviews;
    j. Require additional monitoring from an independent monitor;
    k. Refer to other organizational entities as appropriate. Examples include, but are not limited to, working with the HIPAA Office if the problem involves an unauthorized use, loss, or disclosure of Protected Health Information; requiring specific research education training in conjunction with the research education office or involving the Organizational Official
    l. Suspend the study for cause in accordance with IRB policy 7.9;
    m. Terminate the study for cause in accordance with IRB Policy 7.9.

8. The IRB shall make the final determination regarding whether an event is a UPIRTSO as described in this policy, or serious or continuing noncompliance as described in policy 12.6.

9. All events determined to be UPIRTSOs or serious or continuing noncompliance will be reported to federal agencies, research funders/sponsors, the organizational official, and/or human research protection program accrediting bodies in accordance with IRB Policy 2.6.

REFERENCES

OHRP Guidance Unanticipated Problems Involving Risks and Adverse Events Guidance

FDA Guidance - Investigator Responsibilities - Safety Reporting for Investigational Drugs and Devices

AAHRPP Elements II.2.G, II.2.H, II.2.I and III.2.D