**Department: UAMS Institutional Review Board**

**Policy Number: 10.2**

**Section: Principal Investigator Responsibilities**

**Effective Date: July 31, 2002**

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**SUBJECT: Information that must be reported to the IRB and IRB Actions**

**I. Policy**

Federal regulations require the IRB to ensure that Investigators promptly report all “unanticipated problems involving risks to subjects or others” (UPIRTSO).

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. 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 Policy

12.6 will apply.

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

**II. 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:

a) Unanticipated or unexpected;

b) Related to the research; and

c) Involves new or increased risks to subjects or others.

F. Unexpected: An event is “unexpected” when its specificity, nature, severity or incidences are not accurately captured in the approved consent form. Examples include a lower rate of response to treatment or a side effect that is more severe than initially expected.

**III. Investigator Reporting Responsibilities**

1. Time Frame: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.

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.

Reporting requirements apply regardless of whether they occur during the study, after study completion or after subject withdrawal or completion.

B. Content of the Report:Each report should be submitted through 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:

 a. Unexpected;

 b. Related to the research; and

 c. Involve new or increased risks to subjects or others.

An event must meet all three criteria to require reporting under this policy.

2. Non-local adverse events that have been determined to be unanticipated problems involving risks to subjects or others.

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 change to the risks or potential benefits of the research. 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.

10. Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol

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.

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.

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

**IV. IRB Responsibilities**

**A. Initial Review of Reports.** An IRB Chair, or Experienced IRB Reviewer will review each report and determine if the reported event is a UPIRTSO under this policy or a report of potential non-compliance using IRB Policy 12.5.

**1. Event is not a UPIRTSO.** If the Reviewer determines that the reported event does not meet the definition of a UPIRTSO, the Reviewer will acknowledge the report.

**a. Minor Modifications Submitted.** If any Minor Modifications were submitted with the report, the Reviewer will review and approve in accordance with the Expedited Procedure outlined in IRB Policy 7.5.

**b. Minor Revisions Required.** If the reported event requires Minor Revisions, the

Reviewer will outline those requested modifications in a letter to the Investigator.

**c. Major Modifications Submitted.** If the modifications submitted with the report cannot be considered Minor Modifications, the Reviewer should notify the IRB staff that the report and modifications need to be placed in the “Updates to be Reviewed by Two Reviewers” section of an upcoming agenda.

**d. Major Revisions Required.** If the reported event requires what the Reviewer would consider major revisions, the Reviewer should prepare a Major Revisions Required letter and identify the revisions that are required. The response will be placed in the “Updates to be Reviewed by Two Reviewers” section of the agenda.

**e. Event is report of Non-Compliance.** The Reviewer should follow the requirements of IRB Policy 12.6.

2**. Event is potentially a UPIRTSO.** The reported event will be placed on the next available agenda under the “Reportable New Information” section. The Reviewer will determine if any subject or others are at immediate risk of harm. If so, the Reviewer may suspend the study immediately and notify the Investigator in accordance with IRB policy 7.9

**B. UPIRTSO Review by Convened IRB.** Two Reviewers will be assigned to review the UPIRTSO 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. Actions that may be taken by the IRB include but are not limited to:

1. Require modifications to the protocol

2. Require modifications to the information disclosed during the consent process

3. Require current subjects to be notified when information may relate to subjects’ willingness to continue to participate in the research

4. Require current subjects to re-consent participation

5. Require additional information be provided to past subjects

6. Request the research be audited by the Office of Research Compliance

7. Require monitoring of the consent process

8. Require more frequent continuing reviews9. Require additional monitoring from an

 independent monitor

9. 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.

 10. Suspend the study for cause in accordance with IRB policy 7.9

 11. Terminate the study for cause in accordance with IRB Policy 7.9

**C. UPIRTSO Reporting.** All events determined to be UPIRTSOs will be reported in accordance with IRB Policy 2.6