Title: Changes to Adverse Events
SOP # 13
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Subject: Reporting of Unanticipated Problems Involving Risk to Participants or Others

Definitions:

- **Adverse Event:** An adverse event is described as an undesirable and unintended event as a result of therapy or other intervention (e.g., headache following spinal tap or intestinal bleeding associated with aspirin therapy).

- **Definitely Related:** is defined as meeting **all four** of the following conditions:

    - Has a reasonable temporal relationship to intervention.
    - Could not readily have been produced by the research participant's normal state or have been due to environmental or other interventions.
    - Follows a known pattern of response to intervention.
    - Disappears or decreases with reduction in or cessation of intervention and recurs with re-exposure.

- **Possibly Related**: is defined as meeting **any** of the following conditions:

    - Has a reasonable temporal relationship to intervention.
    - Could not readily have been produced by the research participant's normal state.
    - Could not readily have been due to environmental or other interventions.
    - Follows a known pattern of response to intervention.

- **Serious:** Events are classified as serious if they meet any of the following criteria:

    - Any death
    - Any life-threatening event, e.g., an event that places the subject, in the view of the investigator, at immediate risk of death from the event as it occurred (does not include an event that, had it occurred in a more severe form, might have caused death).

- Any event that requires or prolongs hospitalization.

- Any event that results in persistent or significant disability/incapacity.

- Any congenital anomaly/birth defect diagnosed in a child of a subject who participated in this study and received study drug.

- Other medically or psychologically important events that in the opinion of the investigator may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in the definition above.

• **Unanticipated**: Any adverse experience, the frequency or severity of which is not consistent with the current consent form or investigator brochure.

• **Unanticipated Problem Involving Risk to Participants or Others:** Any unanticipated event involving any aspect of a research study involving anyone (participants, research staff, or others not directly involved in the research) that increases a risk to the persons involved. These can occur in biomedical and non-biomedical research.

Examples of Unanticipated Problems Involving Risks to Participants or Others:

- Adverse emotional reactions to study procedures, such as depression or threat of harm to self or others, or that require medical, psychological or legal intervention to prevent such outcomes.

- Unanticipated medical/physical reactions or injuries temporally related to a study.

- A participant unexpectedly becomes pregnant.

- A lab reports blood studies performed the previous week were in error.

- Unanticipated identification of incidences of child abuse, threats of harm, sexual harassment or other reportable events.

- An investigator loses a laptop that contains confidential information about study participants.

- A failure to follow approved protocol procedures that results in increased risks.

Policy:
All unanticipated problems involving risks to participants or others and adverse events shall be reported to the IRB according to the following schedule:

- Adverse Events that are Serious, Unanticipated, and Possibly, Probably, or Definitely Related – must be reported within 10 working days of the Investigator's knowledge of the event.

- Unanticipated Problems Involving Risks to Participants or Others – must be reported within 5 working days of the Investigator's knowledge of the problem.

A summary of all adverse events associated with the study must be reported to the UCM IRB at the time of continuing review.

Procedures:

I. Investigator Responsibilities

The Investigator submits reports of Serious, Unanticipated, and Possibly, or Definitely Related adverse events and Unanticipated Problems Involving Risks to Participants and Others as follows:

A. A "Problem Report" is submitted to the IRB as soon as possible, but no later than **10 working days** after the Investigator first learns of the event or problem. This form contains the Investigator's assessment of causality (related or not related to the study) and a description of the actual event; and

B. In the Report, the Investigator will either justify why no changes to the protocol or consent form are needed or attach proposed modifications to the report.

II. IRB Chair/Designated Committee Member Responsibilities

A. All reports made under the policy are provided to a Chair or a Committee Member who has been designated by the Chair to conduct expedited reviews.

C. The reviewer will review the Report to determine what action, if any, is required. Actions may include, but are not limited to:

1. Providing information concerning the problem or event to subjects, research staff, or whomever else is affected

2. Requiring modifications to the study

3. Shortening the protocol approval period

4. Recommending suspending to terminating approval of the study

D. If modifications are required and all modifications are minor, the chair will review the modifications under an expedited review.

E. If the reviewer:

1. Cannot make a determination as to whether any actions are or are not required; or

2. If modifications are required that are substantive in nature; or

3. If the reviewer determines that the study should be suspended or approval terminated

The Report will be referred to the full IRB committee for review.

F. If participants are at immediate risk of harm and there is insufficient time to wait for review by the convened IRB, the reviewer will request that an IRB Chair or the IRB administration to suspend the study until review can be completed

III. IRB Committee Responsibilities

A. The IRB will review the Report to determine what action, if any, is required. Actions include, but are not limited to:

1. Providing information concerning the problem or event to subjects, research staff, or whomever else is affected

2. Requiring modifications to the study

3. Revising continuing review timetable

4. Suspending to terminating approval of the study

References:

45 CFR 46.103(b)(5)(iii)
21 CFR 56.108(b)(1)
IRB Guidebook (OHRP)