TITLE: Institutional Review Board Review of Research
RR 404 Adverse Events, Safety Reports and Serious Adverse Events

POLICY STATEMENT: It is the policy of the Mercy Health Regional IRB (Institutional Review Board) to require recording of adverse events and reporting of Serious Adverse Events as defined by OHRP (the Office for Human Research Protections) and FDA (the Food and Drug Administration).

Serious Adverse Events:

It is required that all Serious Adverse Events for active research participants be reported to the Mercy Health Regional IRB within 24 hours of the Mercy Health principal investigator’s knowledge of the problem. This requirement includes serious adverse events, injuries, or deaths occurring at Mercy Health or other locations in which the principal investigator (PI) is responsible for the conduct of the research and the Mercy Health Regional IRB serves as the IRB of Record:

Any serious adverse event that in the principal investigator’s opinion was unanticipated or unexpected, involved risk to participants or others and was possibly related to the research procedures must be reported.

The submission of Serious Adverse Events must include the Mercy Health PI’s assessment of the event. Further, the Serious Adverse Event report should outline any necessary revisions to the Mercy Health Regional IRB approved protocol and associated documents to incorporate the event’s impact on the risk-potential benefit profile of the study.

Safety Reports:

Study related events (such as Safety Reports) that do not occur at Mercy Health or other locations in which the principal investigator is responsible for the conduct of the research and the Mercy Health Regional IRB does not serve as the IRB of Record do not need to be reported to the IRB unless the event is probably related, unanticipated, and places subjects at a greater risk than previously known. In these instances, the PI will submit the event to the Mercy Health Regional IRB via the IRBManager system by completing an electronic submission form entitled, “Safety Report Assurance Form”. Safety reports that fit the criteria for reporting should be reported to the IRB within 10 days of receipt.

The submission of Safety Reports must include the Sponsor and/or DSMB’s assessment of the event and must be reviewed by the Mercy Health PI. The PI should sign and date the original copy of the safety report and the safety report must be uploaded to the IRBManager electronic submission system. Further, the submission of safety reports should outline any necessary revisions to the Mercy Health Regional IRB approved protocol and associated documents to incorporate the event’s impact on the risk-potential benefit profile of the study.

Adverse Events:

All individual participant AEs are to be recorded and maintained by the principal investigator according to the study protocol and sponsor requirements for reporting. Individual AEs are not reported to the IRB unless they are unanticipated, related and places subjects at a greater risk than previously known. If an adverse event meets all of
Institutional Policy & Procedure

These criteria, they are to be reported using the Unanticipated Problem Report Form (RR 405-A) in the IRBManager system. Adverse events that fit the criteria for reporting should be reported within 10 days of the Mercy Health investigator becoming aware of the problem.

DEFINITIONS:

Adverse Event: An AE is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure.

Serious Adverse Event: Any undesirable experience associated with the use of a medical product or device in a patient. The event is serious and should be reported when the patient outcome is:

- **Death**
  Report if you suspect that the death was an outcome of the adverse event, and include the date if known.

- **Life-threatening**
  Report if suspected that the patient was at substantial risk of dying at the time of the adverse event, or use or continued use of the device or other medical product might have resulted in the death of the patient.

- **Hospitalization (initial or prolonged)**
  Report if admission to the hospital or prolongation of hospitalization was a result of the adverse event.
  Emergency room visits that do not result in admission to the hospital should be evaluated for one of the other serious outcomes (e.g., life-threatening; required intervention to prevent permanent impairment or damage; other serious medically important event).

- **Disability or Permanent Damage**
  Report if the adverse event resulted in a substantial disruption of a person's ability to conduct normal life functions, i.e., the adverse event resulted in a significant, persistent or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities and/or quality of life.

- **Congenital Anomaly/Birth Defect**
  Report if you suspect that exposure to a medical product prior to conception or during pregnancy may have resulted in an adverse outcome in the child.

- **Required Intervention to Prevent Permanent Impairment or Damage (Devices)**
  Report if you believe that medical or surgical intervention was necessary to preclude permanent impairment of a body function, or prevent permanent damage to a body structure, either situation suspected to be due to the use of a medical product.

- **Other Serious (Important Medical Events)**
  Report when the event does not fit the other outcomes, but the event may jeopardize the patient and may require medical or surgical intervention (treatment) to prevent one of the other outcomes. Examples include allergic bronchospasm (a serious problem with breathing) requiring treatment in an emergency room, serious blood dyscrasias (blood disorders) or seizures/convulsions that do not result in hospitalization. The development of drug dependence or drug abuse would also be examples of important medical events.

Safety Report: Under 21 CFR 312.32(c), the sponsor is required to notify FDA and all participating investigators in an IND safety report (i.e., 7- or 15-day expedited report) of potentially serious risks from clinical trials or any other source as soon as possible. The safety report is the document completed to provide information to the study sponsor and FDA.
Institutional Policy & Procedure

**Probably related:** A harm is at least "probably related" to the human research procedures if in the opinion of the local investigator, the research procedures more likely than not caused the harm (greater than 50% probability)

**Unexpected:** A harm is "unexpected" when its specificity and severity are not accurately reflected in the consent document and/or current investigators brochure.

REFERENCES:
21 CFR 312.66
45 CFR 46.103(b)(5)

ATTACHMENTS:
404-A Serious Adverse Event Report
404-B Safety Report Assurance Form
404-C Serious Adverse Event Review Worksheet
404-D IRB Acknowledgment of Serious Adverse Event Report
404-E Letter to Research Community "Revised IRB Policy on Adverse Events that Require Reporting to the IRB"

PROCEDURE: All Mercy Health Campuses

**Responsibility**

**Principal Investigator**

**Action**

1. Submit the appropriate report to the IRB utilizing the IRBManager system for review according to this policy. 
   *Reports of “Serious Adverse Events” must be submitted to the IRB within 24 hours of principal investigator becoming aware of the information.

2. Describe in detail what the event consisted of, including dates and location.

3. Describe assessment of causality (related or not related to the study) and a description of the actual event (i.e. heart attack, stroke, headache.

4. Describe the evaluation of whether the event meets the following criteria:
   - Does the event suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized?
   - Was the event unanticipated (i.e., the event was not foreseeable); and related (i.e., likely to have been caused by the research procedures).

5. Provide any associated materials such as medical record notations or reports with the name and medical record number of the individual redacted (removed).

6. Describe what action will be taken to prevent the event from occurring in the future or describe the treatment of the participant. Include a statement describing if the protocol, informed consent or other study materials will be updated based on the event.

7. Submit a separate modification request indicating changes associated with the event or problem. (if applicable).

8. Create and store accurate documentation of the investigation and follow-up of all adverse and serious adverse events involving risk to participants or others that occur at the site in which the Principal investigator
is responsible for the conduct of the research.

9. Submit follow-up reports until issue is resolved.

10. Follow-up reports are to be promptly submitted to the IRB until issue is resolved.

IRB Safety Committee

1. Review the submitted report of Adverse Event, Serious Adverse Events or Safety Report (using form RR 404-C) and determine if the event is an adverse event or Serious Adverse Event.
   - If event is a reportable Adverse Event or Serious Adverse event, forward completed review form to the IRB Specialist so it may be added to the next IRB meeting agenda.
   - If the event is not a reportable adverse event, forward the report to the IRB Specialist for IRBManager Database update, notification to investigator and placement in the Office of the IRB study file.

IRB Specialist/IRB Coordinator

1. Upon receipt of a report of Adverse Event, Serious Adverse Event or Safety Report, facilitate review by the Chair and IRB Safety Committee within 2 working days.

2. May consult with the IRB Chairperson for assistance in determining the appropriate level of review.

3. Place reported events on the next IRB meeting agenda.

4. Attach the appropriate documents to the study in IRBManager for the committee members review. Include:
   - The report of Adverse Event, Serious Adverse Event or safety report;
   - Any attached supplemental material submitted with the report;
   - Provide access to pertinent study materials (e.g. consent form, protocol, etc.)

5. Draft committee action letters and final approval letters using the appropriate template and forward to the IRB Chair for signature.

6. Update the IRBManager database with review status throughout the review process.

7. When the report of Adverse Events, Serious Adverse Event or Safety Report is reviewed and acknowledged through an expedited review procedure, include on the next available agenda for IRB Committee notification.

IRB Committee

1. Review the received Report of Adverse Events, Serious Adverse Events or Safety Report.

2. Review the sub-committee findings and recommendations.

3. May consider what changes may need to be made to study materials or study conduct based on the review of the report.

4. May determine if the study should be suspended, terminated or continued as previously approved.

CONCURRENT CONSENTS:

Institutional Official