1. PURPOSE
   1.1. Federal regulations (45CFR46.103(a)and(b)(5) & 21CFR56.108(b)) require written procedures for ensuring prompt reporting of any unanticipated problems involving risks to subjects or others; any serious or continuing non-compliance with federal regulations, the requirements or determinations of the IRB; and any suspension or termination of IRB approval to appropriate institutional officials, any supporting department or agency head (or designee), and OHRP.

2. REVISIONS FROM PREVIOUS VERSION
   2.1. None

3. POLICY
   3.1. The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Events which meet the prompt reporting criteria must be reported to the MU IRB within 10 working days. Events which do not meet the prompt reporting criteria may be reported to the MU IRB at the time of annual renewal or during the next status update.

   3.2. **Definitions:**

      3.2.1. **Adverse event (AE):** Any undesirable and unintended (although not necessarily unexpected) event experienced by a subject occurring as a result of interventions, interactions, or collection of identifiable private information in research. An adverse event can be internal or external as it relates to the location of the site.

      3.2.2. **Serious adverse event (SAE):** Adverse events classified as serious include those resulting in death, life-threatening injury, hospitalization or prolongation of hospitalization, persistent or significant disability, or a congenital anomaly or birth defect. Events not meeting the above criteria but requiring intervention to prevent one of these outcomes are also considered serious adverse events.

      3.2.3. **Unanticipated adverse event (UAE):** An adverse event that is not consistent in nature, frequency, or severity with the current IRB protocol, investigator's brochure, device manual/instructions for use, consent form, or other available information.

3.2.4. **Protocol deviation:** Any deviations, whether intentional or unintentional, from the IRB-approved protocol that are implemented without prior to IRB approval. Examples include but are not limited to, accidental over-recruitment for a minimal risk study; a change implemented without prior Marquette IRB approval to eliminate apparent immediate hazards to research subjects; and posting of a recruitment flyer without prior Marquette IRB approval.

3.2.5. **Non-Compliance:** Non-compliance is any departure from the Marquette IRB approved protocol procedures, forms, and other attachments and/or any failure to follow any applicable human research protection regulations and policies (including but not limited to HHS, FDA, and Marquette University IRB). Examples include, but are not limited to, initiating research prior to IRB approval, implementing changes in the IRB-approved protocol without prior IRB approval, using inadequate procedures for informed consent, failing to meet education and training requirements, and lapses in IRB approval.

3.2.6. **Serious Non-Compliance:** Serious non-compliance is an act or omission that resulted in increased physical, psychological, health, safety, or privacy risk that may have compromised the rights and welfare of participants, research staff or others, or substantively compromises the effectiveness of the MU IRB. Examples include, but are not limited to failure to obtain or document informed consent from human subjects (for research that requires that requires consent); adding or modifying a research procedure that increases risk to participants without prior IRB approval; and failure to report unanticipated problems/adverse events to the IRB.

3.2.7. **Continuing Non-Compliance:** Continuing noncompliance is a pattern of repeated acts or omissions that indicate an inability or unwillingness to comply with any applicable human research protection regulations and policies (including but not limited to HHS, FDA, and Marquette IRB). Examples include consistently late submissions of items that require prompt reporting to the IRB; repeated failure to submit required documents to the IRB; repeated refusal to comply with any IRB request.

3.3. **Prompt reporting:** Within 10 working days of when the investigator learns of the event. The Following:

3.3.1. **Unanticipated problems involving risks to subjects or others:** Unanticipated problems involving risks to subjects or others are defined as any incident, experience, or outcome that meets **all** of the following criteria:

i. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
ii. related or possibly related to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been *caused* by the procedures involved in the research); and
iii. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, health, economic, or social harm) than was previously known or recognized.

3.3.2. Any instances of Non-Compliance (e.g., protocol deviation). For instance, failure to use IRB approved consent form, recruiting more than currently approved, etc.

3.3.3. New Information that indicates a change to the risks or potential benefits of the research in terms of severity or frequency or impacts the subject's willingness to participate (e.g., DSMB/DSMC Report, other safety information or publication, suspension or premature termination by the sponsor or investigator).

3.3.4. Any Data Safety Monitoring Board (DSMB) or similar report which describes new information regarding risks or unanticipated problems involving risks.

3.3.5. Any complaints from research subjects.

3.4. **Procedures:**

3.4.1. The PI must report any event identified in 3.3 to the IRB using the Reportable Event Form.

3.4.2. The Reportable Event Form will be reviewed by the ORC. The ORC may request clarification or further information from the PI or consult with the IRB Chair, Vice Chair, or IRB member with appropriate expertise to properly evaluate the occurrence.

a. If the ORC determines that the occurrence does not meet the reporting requirements as outlined in this policy, the PI's report is acknowledged as submitted and the PI is notified that the occurrence does not meet the criteria for reporting and no further action is needed.

b. If the ORC determines that the occurrence may be an unanticipated problem, serious non-compliance, or continuing non-compliance, the occurrence is referred to the convened IRB for review, with an evaluation and recommendation from the ORC. The IRB Chair or Vice Chair will serve as the primary reviewer.

    i. The convened IRB evaluates the occurrence by considering whether it is an unanticipated problem, serious non-compliance, or continuing non-compliance and makes a final determination via vote.

        1. If the IRB determines that the occurrence is not an unanticipated problem, serious non-compliance, or continuing non-compliance, the PI's report is acknowledged as submitted and the PI is notified of the IRB's determination.

        2. If the IRB determines that the occurrence is an unanticipated problem, the actions that may be taken include, but are not limited to the following:

            a. The PI is required to submit a protocol amendment.

            b. The PI and/or the PI's staff are required to participate in additional training/education for the protection of human subjects in research.

            c. The PI is required to develop and submit for IRB approval a Data and Safety Monitoring Plan.

            d. The PI is required to submit periodic status reports.

            e. The protocol requires IRB review more frequently than once per year.

            f. The PI is required to provide current subjects with additional information if it might affect their decision to continue participation in the research, or provide additional information to previously enrolled subjects.

            g. The PI is required to re-consent currently enrolled subjects.

            h. The PI is required to notify investigators at other research sites.

            i. Some or all of the research protocol may be suspended or terminated.

3. Research determined by the convened IRB to be (a) an unanticipated problem involving risks to subjects or others; (b) serious or continuing noncompliance; or (c) suspended or terminated by IRB shall be reported to the Institutional Official. For federally funded or supported research, this determination will be reported to appropriate federal agencies (e.g., OHRP, FDA, etc.). All cases of serious or continuing non-compliance may also be reported to appropriate groups within the university (e.g., Office of General Counsel, Board of Trustees, etc.).

c. If the ORC determines that the occurrence may be non-compliance, and is not serious or continuing non-compliance, the occurrence is referred to the IRB Chair or Vice Chair for review.

   i. If the Chair or Vice Chair determines that the non-compliance is serious or continuous, the protocol will be referred to the convened IRB for determination.

   ii. If the Chair or Vice Chair determines that the non-compliance is neither serious or continuous, the actions that may be taken include, but are not limited to the following:

      a. The PI is required to submit a protocol amendment.

      b. The PI and/or the PI's staff are required to participate in additional training/education for the protection of human subjects in research.

      c. The PI is required to develop and submit for IRB approval a Data and Safety Monitoring Plan.

      d. The PI is required to submit periodic status reports.

      e. The protocol requires IRB review more frequently than once per year.

      f. The PI is required to provide current subjects with additional information if it might affect their decision to continue participation in the research, or provide additional information to previously enrolled subjects.

      g. The PI is required to re-consent currently enrolled subjects.

      h. The PI is required to notify investigators at other research sites