1 PURPOSE
1.1 The purpose of this policy is to define the AMITA Health Institutional Review Board (IRB) requirements for investigators reporting Unanticipated Problems with the research study. This policy only applies to Unanticipated Problems and a certain subset of Serious Adverse Events as defined below. Adverse events not meeting the definition of an unanticipated problem should not be reported to this IRB.

2 REVISIONS FROM PREVIOUS VERSION
2.1 None

3 POLICY
3.1 Unanticipated Problems Involving Risk to Subjects or Others (UPIRSOs) include any incident, experience or outcome that meets all of the following criteria:
   3.1.1 Unexpected (in terms of nature, severity, or frequency);
   3.1.2 Related or probably related to participation in the research (probably related means the event was more likely than not caused by the research procedures);
   3.1.3 Suggests that the research places subjects or others at a different or greater risk of harm than was previously known or recognized

Examples of unanticipated problems include, but are not limited to:
- Breaches of confidentiality, including inappropriate disclosure, lost or stolen confidential information.
- Untimely destruction of study records.
- Unaccounted for study drug.
- An unanticipated adverse device effect.
- An adverse drug experience.

AMITA Health investigators are required to promptly report to the IRB all unanticipated problems during the course of the research that involve risks to subjects or to others. These events are to be reported on the Unanticipated Problems Reporting Form (HRPP-221).

Sponsors are responsible for reporting these events to investigators at other institutions who are conducting research under the relevant IND or IDE of these events. However, these events only need to be reported to the IRB when they constitute an unanticipated problem involving risk to subjects or others (UPIRSO). While non-UPIRSO adverse events may still need to be reported to the Sponsor, they do not need to be reported to the AMITA Health IRB and the AMITA Health IRB will not review them.

3.2 FDA regulations and clinical trial agreements require the prompt reporting of Serious Adverse Events to the Sponsor and to FDA. Sponsors are responsible for reporting these events to investigators at other institutions who are conducting research under the relevant IND or IDE of these events. However, these events only need to be reported to the IRB when they constitute an unanticipated problem involving risk to subjects or others (UPIRSO). While non-UPIRSO adverse events may still need to be reported to the Sponsor, they do not need to be reported to the AMITA Health IRB and the AMITA Health IRB will not review them.
3.2.1 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 protocol, instructions for use, or consent form, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

3.2.2 Adverse Drug Experience: Any serious adverse effect that is “unanticipated” and represents a “problem” for the study (i.e., meets all three (3) criteria in section 3.1 above).

3.3 Unanticipated deaths of research subjects need to be reported to the IRB. Unanticipated deaths that are related or probably related to the research should be reported on the “Unanticipated Problems Report” (HRPP-221) form. Investigators are required to report the unanticipated death of an AMITA Health subject that is related to the research within 24 hours of learning about the death. The unanticipated death of non-AMITA Health subjects do not require to be reported. Anticipated or unrelated deaths of subjects should be reported at the time of continuing review.

3.4 All reports of unanticipated problems will be initially reviewed by the AMITA Health IRB Chairperson or his/her designee to confirm that the problem involves risks to participants or others. If the IRB Chairperson or designee determines that the problem is not a UPIRSO, the matter will be dismissed. A summary of the inquiry and associated findings will be retained in the applicable IRB study file. If the IRB Chairperson or designee determines that the problem is an unanticipated problem involving risks to participants or others, the problem will be reviewed by the full board at the next scheduled meeting.

3.5 The IRB Chairperson or designee will collect and assess all information related to the reported event, including discussing the matter with the investigator and providing the investigator an opportunity to provide further information. During this time, the IRB Chairperson may take emergency corrective action (including an order to temporarily stop research activities) if, in the IRB Chairperson’s assessment, it appears that research subjects may be at risk of harm due to the reported event. If a study is suspended under this emergency procedure, the IRB Chairperson and/or designee will make every effort to conclude their inquiry in as expeditious a manner as possible, including calling for an emergency meeting of the full IRB to review its preliminary conclusions.

3.6 The IRB will take action on reported events. The range of actions includes items listed below, but the IRB may take additional actions as determined on a case-by-case basis:

- Administrative hold on the study pending IRB receipt of further information.
- Suspension of the study until corrective action is taken (Note: If this action is taken, AMITA Health’s Signatory Official (depending on the severity) will be notified and any reporting actions that may be required will be initiated.
- Modification of the protocol, informed consent document, or information disclosed during the consent process.
- Requiring that additional information be provided to past participants.
- Alteration of the frequency for continuing review.
- Requiring additional training of the investigator.
- Additional oversight or reassignment of some or all of the investigator’s duties to another qualified person.
3.7 A summary of unanticipated problems involving risks to subjects or others must also be submitted to the IRB at the time of continuing review, even though UPIRSOs occurring during the approval period will have been reviewed and handled by the IRB Chairperson and/or IRB.

4 RESPONSIBILITIES
4.1 Investigator, IRB Chairperson, IRB members

5 PROCEDURE
5.1 Principal Investigators must report UPIRSOs on the IRB “Unanticipated Problems Reporting (HRPP-221)” form within the timeframes specified above. Reports may be accepted by other means such as e-mail or phone provided all of the required information is relayed to the IRB and followed up with a written report.

5.2 The IRB Chairperson may conduct an initial inquiry on his/her own or convene a committee or call for an emergency meeting of the IRB for the purposes of conducting an initial inquiry. The principal investigator will be provided with written notice and a meaningful opportunity to be heard and/or provide additional information prior to a preliminary determination by the IRB Chair and/or designated committee.

5.3 Prompt written notice of temporary suspension or early termination of IRB approval will be provided to the investigator, Compliance Officer, Signatory Official (if applicable) and applicable affiliate institutions. If required, external reports will be provided.

5.4 Written summaries of preliminary conclusions and emergency actions taken, if any, will be compiled by the IRB Chairperson and IRB Coordinator. Such summaries will be reported to and reviewed by the IRB at its next scheduled meeting, unless an emergency meeting is called by the IRB Chairperson.

5.5 Deliberations and actions taken by the IRB will be recorded in the meeting minutes.

6 MATERIALS
6.1 Unanticipated Problem Report - FORM (HRPP-221)

7 OTHER RELATED POLICY/PROCEDURES
7.1 None

8 REFERENCES
8.1 21 CFR 56.108(b)(2)
8.2 45 CFR 46.103(b)(5)
8.3 Food and Drug Administration Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting to IRBs – Improving Human Subject Protection (dated January 2009)
8.4 Office for Human Research Protections Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (dated January 15, 2007)