Investigators are responsible for conducting research in accordance with the IRB-approved protocol, IRB Policies and Procedures, and applicable federal and state regulations. Changes to the IRB-approved project (including the protocol, Introductory Questionnaire, Informed Consent form, recruitment materials, questionnaires, and any other information relating to the research study), whether planned or unplanned, are governed by both the Federal Regulations and IRB policy. IRB policy, consistent with Federal Regulations 45 CFR 46.104 (b)(4)(iii) and 21 CFR 56.108 (a)(4), requires that all changes to previously approved research, no matter how minor, be reviewed and approved by the IRB before being implemented. This includes, but is not limited to, approved changes in industry-sponsored research that have been granted by the sponsor, such as exceptions to eligibility criteria and/or protocol specific timelines/procedures, and/or protocol variances such as an unexpected departure from the IRB-approved protocol or procedures. Any planned change to the IRB-approved protocol, i.e., protocol exceptions must be submitted to and approved by the IRB prior to initiation or implementation of the change. Protocol variances (such as a departure from the specific protocol procedures approved by the IRB) and/or protocol exceptions not approved by the IRB prior to initiation are protocol deviations and must be reported to the IRB as outlined below. In some cases, protocol deviations are inadvertent or are unavoidable because specifications of the protocol, as written, are not realistic (a data collection may be specified for a limited time frame.) Planned protocol exception should be submitted to the IRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human subjects [(DHHS 45 CFR § 46.103(b)(4); (FDA 21 CFR § 56.108(a)(4)].

**Major Protocol Deviations** requiring expedited reporting (within 5 business days) potentially affect:

- the rights and welfare of the research subject,
- subject safety (increase risks and/or decrease benefits to study subjects)
- the subject’s willingness to continue to participate in the study, or
- integrity of research data.

**Minor Protocol Deviations** requiring periodic reporting (at continuing review) and do not affect or potentially affect:

- the rights and welfare of the research subject,
- subject safety (increase risks and/or decrease benefits to study subjects)
- the subject’s willingness to continue to participate in the study, or
- integrity of research data.

**Examples of Major Deviations** (potentially affecting (a) study subject safety, rights, welfare, or willingness to continue participating in the study, or (b) research data integrity) include but are not limited to:
• Administering the incorrect dose of study medication.
• Failure to implement all protocol procedures resulting in increased risk or decreased benefit to the subject.
• Enrolling a vulnerable subject population without receiving prior IRB approval.

Examples of Regulatory Noncompliance include but are not limited to:
• Failure to obtain and/or document a subject’s Informed Consent (provided the IRB has not granted a waiver. I.e. Informed Consent is required, but study procedures are initiated prior the consent form being signed, or an informed consent form is never signed.
• Failure to retain copies of signed Informed Consent forms. (e.g. the PI lost one or more consent forms while moving offices, or cannot produce a signed consent form for all subjects enrolled in the study, etc).
• Conducting research (including data collection) without active IRB approval (including after expiration of the protocol).
• Enrolling subjects without active IRB approval for the protocol (either prior to initial approval or during a period of expired approval). Includes research approved with a waiver of consent, such as survey research or medical record research.
• Implementing a project revision without prior IRB approval (unless to protect the subjects against harm).
• Implementing planned protocol variations/exceptions without obtaining prior IRB approval – e.g. enrolling a subject who does not fit the inclusion/exclusion criteria specified in the protocol without prior IRB approval.
• Recruiting/enrolling subjects at a location or in a manner that has not been previously approved.
• Conducting your research at a site or involving outside investigators without prior IRB approval.

Note: serious or on-going failure to comply with regulatory requirements can result in the suspension or termination of your research, loss of data, disqualification of the investigator(s), and/or other actions by the IRB or other institutional administrative offices. In addition serious or continuing regulatory noncompliance must typically be reported to the appropriate federal oversight agencies.

Examples of Unplanned Minor Deviations include but are not limited to:
• Protocol procedures completed at times outside the period specified in the protocol (e.g. protocol indicates that a blood draw should occur on day 7, but the draw is actually completed on day 8 because the subject did not show up to clinic on day 7) without adversely affecting subject safety, rights, willingness to participate in the study, or possible benefits from the study.

Note: report Unplanned Minor Deviations on the Deviation Tracking Log and submit at time of Continuing Review.
IRB approved project
(protocol, introductory questionnaire, informed consent form, advertisements, investigator’s brochure, grant, questionnaires/surveys, etc)

**Revision**: planned change in previously approved research activities resulting in actual change of protocol or other study materials. Submit to and receive prior IRB approval.

**Protocol Exception**: planned change in previously approved research activities but not resulting in actual change of protocol. Submit to and receive prior IRB approval.

**Major Deviation**: unapproved temporary change in previously approved research activities, implemented without IRB approval, and potentially adversely affecting subjects’ rights, welfare, or safety, willingness to continue study participation and/or integrity of research data. Submit to IRB within 5 days of discovery.

**Regulatory Noncompliance**: conducting research without active IRB approval, implementing revisions without IRB approval (unless to protect patient safety, rights, or welfare), including enrolling subjects who do not meet enrollment criteria, failing to obtain Informed Consent when required, and otherwise conducting research activities not approved by the IRB. Submit to IRB within 5 days of discovery.

**Minor Deviation**: unapproved temporary change in previously approved research activities, implemented without IRB approval, which does not adversely affect subjects rights, welfare, or safety, willingness to continue study participation, and/or integrity of research data. Submit to IRB at Continuing Review / Study.