1 PURPOSE
This procedure describes the activities when a study is suspended or terminated at the investigative site.

2 GENERAL INSTRUCTIONS AND RESPONSIBILITIES
a) The Sponsor, Investigator, or the IRB is responsible for final review and determination that the Investigator’s obligations have not been met.

b) The Investigator is responsible for keeping the Office of Human Research (OHR) and the Institutional Review Board (IRB) of record informed if the Sponsor plans to suspend or terminate the site from study.

3 SPECIFIC PROCEDURES
3.1 Suspension Due to Inadequate Enrollment
a) A clinical study site may be suspended when subject enrollment has been insufficient and the terms of the contract and clinical study protocol are not met.

b) Periodic assessments of enrollment by the Sponsor form the basis for decisions to suspend a site for inadequate enrollment. The Sponsor or the Investigator/Sponsor should determine whether site enrollment is on schedule in regards to timelines and enrollment projections.

c) If enrollment is lagging behind schedule, the Sponsor and Investigator should ascertain possible remedies to restore the desired rate of enrollment (e.g. additional recruitment efforts, additional staff, resources).

d) If enrollment is not expected to reach optimum levels, the Sponsor must decide if the site should be allowed to continue enrolling subjects at the current rate, or suspend the study at the site.
e) If continuing enrollment is determined to not be in the best interest of the study, the Sponsor will advise the site Investigator that the site will be suspended per terms defined in the contract in writing.

f) The Sponsor will establish a schedule for conducting a closeout visit when all follow-up on existing subjects has been completed (see SOP 505, Study Closeout).

3.2 Study Suspension or Termination

a) A clinical study site may be suspended or terminated before the designated time period if subjects are placed at unreasonable risk, if the terms of the clinical protocol or contract are violated, or by FDA, OHR, or IRB order.

b) The Investigator can suspend enrollment into his/her own study for operational or other reasons not related to safety. This does not require reporting to IRB or FDA.

c) If FDA orders the Sponsor to terminate a study, the Sponsor will immediately contact all participating Investigators to notify them of the termination, who in turn should immediately notify their IRB of record.

d) If the Sponsor becomes aware of any circumstance that puts study subjects at unreasonable risk, they will proceed to terminate the study by informing all the Investigators of the termination, and the Investigators will keep the OHR and IRB apprised of such decisions.

e) During routine monitoring visits, if the Monitor observes or discovers protocol violations, the Monitor should document the findings and present the information to the Investigator and Sponsor immediately.

f) Protocol violations may result in study subjects being put at risk or rendering the study data untrustworthy. Examples of protocol violations include:
   - Enrolling of subjects who do not fulfill the inclusion-exclusion criteria
   - Failure to document using the investigational product in a manner not specified by the protocol
   - The reporting of inaccurate or fraudulent data revealed during routine monitoring of source documents
   - Failure to apply correct randomization procedures when conducting randomized studies
   - Continual failure to conduct and report on required routine follow-up assessments
   - Failure to employ adequate stock control or investigational product accountability procedures
   - Failure to adhere to the protocol requirements for study visits, testing requirements, timeframes, data collection and submission

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f) The Sponsor will ascertain whether the violation(s) is (are) new or represent an ongoing pattern of non-compliance.

g) The Sponsor will also ascertain the severity of the violation(s), such that either a warning or immediate termination is the appropriate follow-up action.

h) If the site is otherwise in compliance with the protocol and without a history of prior non-compliance, the Sponsor should contact the investigator and discuss the violation(s), requesting that no further violations be permitted to occur (warning).

i) If a pattern of non-compliance is ascertained at the site, or if the violations are so severe that subjects are at risk of serious injury, the Sponsor should contact the site investigator and advise him/her that the study has been terminated effective immediately and the reason(s) for the termination.

j) The site Investigator will be advised to cease enrolling subjects immediately and report the study termination to the IRB and any other appropriate internal and external authorities. The Investigator should promptly notify OHR regarding the specific situation.

k) The Sponsor and site Principal Investigator will create a plan of action for managing subjects already enrolled to assure proper transition off study (e.g., may need to taper off study agent or need other medical treatment, appropriate follow-up, etc.)

l) The Sponsor will confirm all verbal discussions with the site investigator by follow-up letter via certified mail return receipt, or any other means of delivery that can be tracked.

m) As with suspension, subject enrollment may be discontinued at the terminated site but the final closeout visit cannot occur until all enrolled subjects have completed their specified follow-up visits and have completed their participation in the study.

n) The Sponsor will schedule an immediate monitoring visit to retrieve all unused investigational product and study documentation.

4 REFERENCES TO OTHER APPLICABLE SOPS

- 301 Clinical Protocol Development, Implementation, and Compliance
- 503 Documentation and Records Retention
- 505 Study Closeout
- 605 Adverse Event Recognition and Reporting

5 ATTACHMENTS

None

6 APPLICABLE REGULATIONS AND GUIDELINES

- Review of Ongoing Investigations (21 CFR 312.56)
- Disposition of Unused Supply of Investigational Drug (21 CFR 312.59)
- General Responsibilities of Investigators (21 CFR 312.60)
- Investigator Recordkeeping and Record Retention (21 CFR 312.62)
Investigator Standard Operating Procedures

- Investigator Reports (21 CFR 312.64)
- Inspection of Investigator's Records and Reports (21 CFR 312.68)
- Monitoring Investigations (21 CFR 812.46)
- Specific Responsibilities of Investigators (21 CFR 812.110)
- Premature Termination or Suspension of a Trial (ICH E6, Section 4.12)
- Final Reports by Investigator (ICH E6, Section 4.13)
- Monitoring (ICH E6, Section 5.18)
- Noncompliance (ICH E6, Section 5.21)
- Premature Termination of a Trial (ICH E6, Section 5.21)
- Clinical Trial/Study Reports (ICH E6, Section 5.22)