Clinical Monitoring Plan

Protocol Number <protocol number>

<protocol title>

By signing below, I acknowledge my agreement to this plan.

**Sponsor:**

Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_

**Site Representative:**

Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_

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## LIST OF ABBREVIATIONS

{Add, delete or modify abbreviations as necessary per study protocol. It is recommended that abbreviations be listed alphabetically.}

AE Adverse Event

CFR Code of Federal Regulations

CMP Clinical Monitoring Plan

COV Close-Out Visit

CRA Clinical Research Associate

CRF Case Report Form

DSMB Data Safety Monitoring Board

eCRF Electronic Case Report Form

EDC Electronic Data Capture

ED Essential Documents

FDA Food and Drug Administration

GCP Good Clinical Practice

ICH International Conference on Harmonisation

IMV Interim Monitoring Visit

IRB Institutional Review Board

ISF Investigator Site File

MOP Manual of Procedures

PI Principal Investigator

SAE Serious Adverse Event

SC Study Coordinator

SIV Site Initiation Visit

SOP Standard Operating Procedures

TMF Trial Master File

UP Unanticipated Problem

{Add, delete, or modify headings as needed in order to best reflect your study. Abbreviations may need to be revised throughout the document as text is added or deleted.}

## INTRODUCTION

{Briefly describe the purpose of the CMP. Include additional information as it relates to the CMP (e.g., changes in PI, changes in clinical research management, protocol amendments).}

{The sentence listing “monitoring tasks performed in accordance with” should be modified to reflect a regulated or non-regulated study. Currently language reflects a regulated study.}

The Clinical Monitoring Plan (CMP) establishes the guidelines for conducting monitoring visits and related tasks for monitoring Protocol <protocol number, protocol title>. Assigned Clinical Research Associate(s) (CRA(s)) will perform monitoring tasks in accordance with the protocol specific requirements, Title 45, Part 46 of the Code of Federal Regulations (CFR), the International Conference on Harmonisation (ICH) Good Clinical Practice Guidelines (GCP), The Code of Federal Regulations Part 312, and other applicable requirements.

## MONITORING COMMUNICATION PLAN

{Describe the process for distributing monitoring communication. Ensure that all stakeholders are reflected in the plan (PI, etc.) modify as appropriate}

### Email Distribution

The CRA will send monitoring communication to include: site visit confirmation letters, agendas, follow-up letters, action item trackers and, <insert other relevant documents> to the following:

**Program Contacts**

| **Representative** | **Role** |
| --- | --- |
| **Study Program** | |
|  | Principal Investigator |
|  | Study Contact |
| **Study Sites** *{for multi-center studies, include as appropriate}* | |
| *Site PIs listed in the table below* | Site PI |
| *Primary Site Contacts in the table below* | Primary Site Contact |

**Site Contacts:**

| **Representative** | **Role** |
| --- | --- |
| ***<Insert Site Name>*** | |
|  | Site PI |
|  | Primary Site Contact |
| ***<Insert Site Name>*** | |
|  | Site PI |
|  | Primary Site Contact |
| ***<Insert Site Name>*** | |

## VISIT SCHEDULING

{Describe the process for scheduling monitoring visits and expectations for the site study staff during the visits. Include language detailing the frequency of monitoring and the expectation of the site and monitor with respect to timeline for visit scheduling requests.}

The CRA will work with the Site Principal Investigator (PI) and Site Primary Contact to schedule monitoring visits. The Study PI will be apprised of visit scheduling.

Prior to the visit, the PI will receive a visit confirmation letter, agenda and a list of participants to be monitored. The CRA will ensure that this information is communicated to the site personnel within a mutually agreed upon timeframe to allow sufficient time for record requests. The PI and research staff will be expected to secure workspace for the CRA(s) and to be available during the visits to facilitate monitoring activities. The CRA will be available at the end of each monitoring visit day to discuss findings and answer questions from the study staff. The Site PI and Primary Site Contact are also expected to be available for a wrap-up meeting at the conclusion of the visit, as schedules allow. These expectations will be explained in the visit confirmation letter.

## ESSENTIAL DOCUMENTS/TRIAL MASTER FILE

{Describe required essential documents (ED), process for review, collection and submission of ED as it relates to monitoring.}

### Required Essential Documents

A binder(s), which for purposes of this clinical monitoring plan will be defined as the investigator site file (ISF), will be maintained at the trial site and serves as the central source for essential document (ED) maintenance at the site.

*{If the site is maintaining a combination of paper and/or electronic files, consider the following additional information.}*

EDs for this trial will be maintained by each study site as a combination of paper and electronic documents. The contents of the ISF will include:

* Essential documents maintained in paper form
* Essential documents maintained electronically at the site will have a page referencing the electronically maintained location of the ED. Note: The site may elect to file a paper copy of the electronically maintained document in the ISF.

The following documents represent a complete site essential document packet and are to be maintained in the ISF: *{customize as appropriate}*

* Form <insert appropriate form for study: 1572, 1571, etc.> *{if applicable; if not, remove}*
* Principal Investigator’s (PI) Curriculum Vitae (CV)
* Copy of PI’s current medical license
* PI Human Subject Protection Training documentation
* PI Financial Disclosure Form (FDF) *{if applicable; if not, remove}*
* Sub-Investigator(s) (Sub-I) CV
* Copy of Sub-I Medical License(s)
* Sub-I Human Subject Protection Training documentation
* Sub-I(s) FDF *{if applicable; if not, remove}*
* Protocol/Protocol Amendment(s) Signature Pages
* Site Specific Consent Documents *{if applicable; if not, remove}*
* Institutional Review Board (IRB)-Approved Protocol, Consent Document, Protocol Amendments and approval documentation
* IRB approved Advertisements, Participant Handouts, <insert specific items pertinent to the protocol; dosing diaries, dosing instructions, etc.>
* Laboratory Certifications *{if applicable; if not, remove}*
* Laboratory Reference Ranges *{if applicable; if not, remove}*

### Monitor’s Role in Essential Document Maintenance

During the course of routine monitoring visits, the CRA will review for accuracy and completeness, the ISF and all associated documents as noted in section 5.1.

## MONITORING REPORTS / ACTION ITEMS

{Describe the process and timeframe for providing monitoring reports.}

Monitoring visit findings and resulting action items will be documented in trip reports. The CRA will send finalized monitoring reports within 14 calendar days of the last day of the monitoring visit to identified study team members as noted in section 3.0.These documents should be printed and stored in the ISF.

The CRA will work with designated site staff to resolve any outstanding action items as communicated in the monitoring reports.

## TYPES OF VISITS AND MONITORING ACTIVITIES

{Describe the types of monitoring visits to be conducted during the study and the purpose of each visit.}

The CRA is responsible for conducting <insert number> types of monitoring visits for this study.

* A Site Initiation Visit (SIV) will be conducted prior to site activation to confirm preparedness for protocol execution, satisfactory site facilities, clarify the applicable regulations and requirements of the protocol, carefully review the process of implementing the protocol at the site and conduct any necessary training prior to the assigned Program Official activating the site for enrollment.
* Interim Monitoring Visits (IMVs) will be conducted to confirm participants’ rights are being protected; the study is being conducted according to the protocol and applicable regulations, including GCP; confirm accurate reporting of participant safety data and study endpoints.
* For-cause visits (FCVs) are conducted to address any unanticipated issues that arise which require training, remediation or other situations in which the site requires assistance.
* A Close-Out Visit (COV) will be conducted to ensure that all study data and other study documentation is complete and accurate and that all study records have been reconciled. The types of activities that may be conducted at each onsite visit are described in detail below.

{Describe monitoring activities in detail for each visit. Modify text to accommodate specific visits, EDC, eCRFs, SAE/UP reporting, etc., as appropriate.}

### Site Initiation Visit Activities

The SIV will be conducted prior to participant enrollment. The following activities may be conducted during the SIV:

1. Investigator and Site Responsibilities

* Verify that the PI understands and accepts the responsibility to obtain IRB approval of any amended protocols, consent documents, or advertisements, and to ensure continuing review of this study by the IRB.
* Verify that the PI understands and accepts responsibility for overseeing the conduct of the study in accordance with the protocol, applicable regulations and GCP, as well as ensuring the conduct of all staff performing study procedures.

1. Review of Facilities

* Tour of site facilities where study activities will be conducted, including but not limited to: consent discussions, participant visits, laboratory specimen collection, processing, and storage, records and ISF management, and monitoring workspace.
* Verify presence of study-required equipment, including but not limited to: <insert protocol specific study-required equipment>

1. Protocol Review

* Review study objectives, study design, and study population.
* Review study inclusion/exclusion criteria.
* Review participant randomization. *{remove if not applicable}*
* Review the study schedule of events and sample collection.
* Review protocol required clinical and laboratory assessments.
* Review responsibility to review, sign, and follow-up on laboratory reports.
* Review guidelines for premature discontinuation of study participants.

1. Informed Consent Process

* Discuss the site’s informed consent procedures.
* Verify that the PI understands and accepts the responsibility to obtain informed consent in accordance with all applicable regulations and to document the informed consent process for each participant.

1. Manual of Procedures (MOP) / Standard Operating Procedures (SOP)

* Review to ensure understanding of the necessity of standardization of protocol execution across all relevant study team members.
* In the absence of a MOP, review the applicable site SOPs.

1. Study Documentation

* Review the document retention requirement for all study-related records. Inform the PI that all study records must be retained <insert timeframe (e.g., until disposal is authorized by the Sponsor; See detailed text regarding retention requirements in COV Section 7.4)>
* Verify that the PI understands that he/she is responsible for retaining all study records and making them available for monitoring and audits during the conduct of the study and throughout the retention period.

1. Investigator Site File

* Sign and date the site visit log each day of the visit.
* Verify that all study documents are present in the ISF and make the PI and site personnel aware of their responsibility to keep the file complete and current.
* <Insert appropriate task for review and/or collection of ED based on section 5.0>
* Verify that the Delegation of Responsibilities Log is current and signed by the PI.

1. Electronic Case Report Form (eCRF) Review and Laboratory Tracking Training *{remove if not applicable}*

* Review and provide training on the use of the electronic data capture system and the specimen management and tracking system for the study.

1. Safety Reporting

* Review adverse event (AE), serious adverse event (SAE), and unanticipated problems (UP) definitions, grading, attribution, reporting, and review.
* Review requirements for IRB notification of UPs, AEs, and SAEs.

1. Review Source Documentation Requirements and eCRF Completion.

* Review requirements for maintaining adequate source documentation that supports the data recorded in the eCRFs.
* Review and provide instruction for eCRF completion, as well as completion instructions listed in the MOP.
* Ensure that the PI and site personnel are aware of eCRF correction and data clarification requirements.

1. Review Laboratory Supplies and Procedures

* Verify that the site has adequate supplies available as detailed in <insert where the complete list of study supplies can be found>.
* Review collection, handling, storage, and transport procedures for laboratory samples. Samples collected for this study include: <insert list of samples to be collected, i.e., clinical samples, DNA, future use, etc>.

1. Discussion of General Items

* Obtain documentation of all site personnel present for the SIV on the SIV Training Log.
* Ensure that all required supplies/clinical trial materials (e.g., CRFs, MOP, ISF) have been received by the clinical study site prior to screening or enrolling the first study participant.
* Discuss the expected schedule of monitoring visits with site personnel, including the timing of the first monitoring visit, personnel availability, and monitoring space availability.
* Initiate discussion of site close-out procedures. Study close-out procedures will be discussed in further detail during IMVs.
* Review the findings and action items of the visit with the PI and appropriate site personnel.

### Interim Monitoring Visit Activities

{Modify text as appropriate for each study. Multiple factors should be taken into consideration when determining the amount of source document verification per patient, frequency of monitoring, and timing of first monitoring visit. Considerations include but are not limited to: the complexity of the protocol, target enrollment, number of participant visits, data collected at each visit.}

{Below, find sample text for instances in which the first visit to a site occurs after the site has begun enrollment. In this situation, the first IMV will contain elements of assessment as well as interim monitoring.}

The following activities may take place at the first site visit:

During the first visit at each study site, in addition to performing IMV associated tasks, the CRA will confirm operational and facility related items as discussed in site assessment calls and previous communication with the study staff.

Items for confirmation may include:

1. Roles and Responsibilities for site personnel

* Communication between team members
* Appropriate delegation of study tasks to qualified team members

1. Site record keeping

* ISF
* Participant source documentation

1. Protocol submissions, deviations and associated regulatory reporting
2. Safety Reporting

* Process
* Safety Reports to date

1. Data collection methods

* Case Report Forms
* Entry
* Query resolution

1. Facilities appropriate to study execution

* Office set up appropriate to GCP and patient privacy
* Adequate facilities for study supply storage, sample processing, availability to necessary technology for data entry

1. Enrollment: target, current, recruitment strategies

At the conclusion of the visit, or after review of the above, the CRA will meet with the Site PI and Site Study Coordinator (SC) to determine a monitoring strategy for future visits. This strategy will include the type of data to be monitored, an anticipated standard percentage of data to be monitored, as well as any other administrative or study support items for which the site may be delinquent. The first IMV report will include in the overall comment section a bullet point outline of the strategy to be implemented. This strategy may be modified or updated as needed.

Frequency of future IMVs will be based on the developed monitoring strategy taking into consideration: enrollment status, data quality, protocol compliance, and the prescribed amount of data to be monitored according to the monitoring plan. Irrespective of other factors, the site will be monitored twice per year.

At a minimum the following participant data will be included in the monitoring strategy to be monitored at each visit:

{Below, find sample text monitoring oversight began with a site initiation visit.}

The first IMV will be conducted at each site after approximately <insert number of participants> have been <insert qualifier, i.e., screened, enrolled, randomized>, subsequent visits will be conducted after approximately every <insert number of participants and qualifier>. Frequency of future IMVs will be based on enrollment status, data quality, protocol compliance, and the prescribed amount of data to be monitored according to the monitoring plan.

{Below is sample text where 100% source document verification will be conducted for a percentage of participants.}

At a minimum the following participant data will be monitored at each visit:

* 100% review of consent documents for all participants consented or re-consented since the last onsite visit
* 100% of SAEs
* 100% of study files for <insert percentage> of participants enrolled at the site overall.

{Below is sample text where source document verification will be 100% of key variables for 100% of participants}

At a minimum the following participant data will be monitored at each visit:

* 100% review of consent documents for all participants consented or re-consented since the last onsite visit
* 100% of AEs, SAEs and UPs
* 100% of key variable CRF pages noted below for unmonitored participants:
  + <insert bullet points to reflect CRF pages to be source document verified>

{Below is sample text for 100% source document verification for all participants}

All data for all participants will be monitored over the course of the trial, but not necessarily at each visit. The participants selected for monitoring and the extent of record review at each visit will be based on the progress of enrollment, as well as any concerns that may emerge about the safety of human participants or the integrity of study data.

At a minimum the following participant data will be monitored at each visit:

* 100% review of consent documents for all participants consented or re-consented since the last onsite visit
* 100% of SAEs
* 100% of participants dosed since last onsite visit

While follow-up data will be monitored for all participants, the amount and frequency of follow-up data monitored at each visit will vary based on time and resources.

{Below is sample text for all studies. Text includes references for paper as well as EDC studies. Modify as appropriate per protocol and circumstance.}

Findings of the CRA that might indicate lack of understanding of protocol requirements, deviation from GCP (for example: inadequate attention to protection of human participants), unreported or underreported safety information or other non-compliance may result in an increase in the percentage of participant data monitored or monitoring visit frequency. Changes will be implemented after consultation with the Sponsor.

The following activities may be conducted at each IMV:

{Below is sample text to be customized based on study specific need.}

1. Consent Document Review for All Participants

* Verify consent was obtained prior to initiating study procedures.
* Verify appropriate signatures and dates were obtained.
* Verify that the correct version of the consent document was signed and dated.
* Verify that ongoing participants were re-consented with updated consent documents as directed by the IRB.
* Verify that source documentation includes a description of the consent process.

1. Source Documentation and CRF Review

* Verify that accurate, complete, and current source documentation is maintained.
* Verify participant eligibility.
* Verify that all procedures outlined in the protocol were completed.
* Verify that missed visits, clinical procedures, and tests are recorded appropriately and reported to the IRB as protocol deviations, as defined by IRB policy.
* Verify that the PI assessed all abnormal lab values for clinical significance.
* Verify that all withdrawals and dropouts of enrolled participants are recorded in the source documentation and on the CRF.
* Verify that AEs, SAEs, UPs, and concomitant medications are documented and reported according to the protocol.
* Ensure that the PI has reviewed, signed, and dated all required CRF pages <specify for paper based studies, wet ink signature, or electronically signed all necessary electronic Case Report Forms (eCRF) pages (for Electronic Data Capture (EDC) systems)>.
* Verify data entries in the CRF pages with the source documentation, and note any errors, omissions, or discrepancies by issuing manual queries <insert form or system as appropriate (e.g., on Data Correction Forms (DCF); within the EDC system), and revise other bullets/text accordingly.>
* Work with site staff to resolve queries while on-site and request the resolution of any remaining queries that cannot be resolved during the visit.
* Verify that previously outstanding data queries have been resolved, signed, <wet ink signature for paper studies, remove if EDC> and dated by the PI or designee.

1. Unanticipated Problems, Adverse Events, and Serious Adverse Events

* Follow-up on previously reported UPs, AEs, and SAEs.
* Verify all newly reported UPs, AEs, and SAEs against source documentation.
* Confirm that all UPs, AEs, and SAEs have been reported to the IRB and Food Drug Administration (FDA) as required.
* Identify any unreported UPs, AEs, and SAEs in source documentation.
* Review UP, AE, and SAE reporting procedures, as necessary.

1. Investigational Product

* Confirm that investigational product is stored at the correct temperature in a secure storage area.
* Review temperature logs to confirm stability of storage conditions.
* Confirm that investigational product is being dispensed according to protocol.
* Confirm that product accountability records are accurate, current, and reconciled.

1. Laboratory and Specimen Management

* Assess maintenance of research specimen logs and associated documentation.
* Review handling of laboratory specimens.
* Review specimen storage conditions and maintenance of temperature logs.
* Ensure organization and storage of specimens in a secure location.
* Ensure appropriate specimen labeling.

1. Protocol Deviations

* Verify that all protocol deviations are documented appropriately in each participant’s research record and on the appropriate protocol deviation form.
* Ensure that the site has reported all protocol deviations to the IRB, as defined by IRB policy.
* Address any protocol deviations with site personnel during the IMV and identify ways to prevent the recurrence of similar issues.
* Protocol deviations will also be reviewed throughout the study with the PI during routine conference calls, which include monitoring staff and the clinical site. Any trends or serious errors will be discussed, and the group will develop a plan of action to prevent further problems.

1. Quality Management (QM) Documentation

* Review site-generated quality management efforts and documentation.
* Review site-generated quality management reports, if utilized, to confirm the items identified by the study team have been addressed. The CRA may offer suggestions for additional quality control efforts or additional follow-up for the site to consider.

1. Investigator Site File

* Ensure that essential document files are complete and current.

1. Investigator and Site Personnel Responsibilities

* Ensure that the Delegation of Responsibilities Log is complete and signed.
* Ensure that the Authorized Signature Log is complete and signed.
* Verify that the PI and site personnel are adhering to the protocol and conducting the study according to regulatory requirements and good clinical practice guidelines.
* Verify that study activities are being performed by the PI or have been delegated to personnel qualified by appropriate education or training.

Provide and document any necessary training for the PI and site personnel, such as training on good clinical practice guidelines and use of the data management and lab tracking system software.

1. Visit Conclusion

At the conclusion of the visit, the CRA will meet with the PI and site research staff to review visit findings and answer questions. The CRA will discuss the following topics at a minimum:

* Enrollment progress.
* Consent process and documentation.
* Study conduct and documentation of study activities.
* UPs, AEs, and SAEs experienced by study participants.
* Scheduling of the next IMV.

1. Action Plan for Identified Issues

The CRA will meet with the site SC and PI periodically during the visit to explain findings, ask questions, and work with the SC and PI to address issues at the time of the IMV. Issues identified at the IMV will be documented in the IMV report and associated follow-up letter. If the CRA encounters a serious issue, negative performance trend, or general non-compliance, the CRA will contact the Sponsor to determine the appropriate course of action.

Please refer to section 6.0 for further information on action item follow up.

### For-cause Visit Activities

During for-cause visits, the CRA may complete any of the activities listed for the IMV, discuss clinical operations and study management methods with the research staff, and/or provide training to the research staff.

### Close-out Visit Activities

Study closure activities may require more than one visit to ensure the proper closure of the study. These activities may be conducted during a series of on-site visits or by telephone. Close-out visits may be conducted at study completion or earlier in the case of study termination by the IRB, <insert appropriate Safety Oversight Group or other Regulatory Body: Data Safety Monitoring Board (DSMB), FDA, etc.>. The outcome of the visit and other close-out activities will be documented in a report and follow-up letter.

CRAs will perform the activities below during the study close-out process:

1. Consent Documents

* Confirm that consent was obtained for each participant prior to initiating study activities.
* Confirm that consents contain appropriate signatures and dates.
* Confirm that the correct version of the consent document was signed and dated.
* Confirm that additional consent was obtained for protocol amendments as required by the site’s IRB.

1. Investigator Site File

* Ensure that essential document files are complete and current.
* Identify any missing study documents.
* Ensure that the Authorized Signature and Delegation Logs are complete and signed by the PI.

1. Source Documentation and CRF Review

* Reconcile the final status of all participants listed on the screening log.
* Confirm that all required data fields have been verified against source.
* Confirm that all data queries have been resolved.
* Confirm that the PI has reviewed, signed, and dated all required CRF pages *{revise bullet to reflect use of an EDC system as applicable}*.
* Verify that the site has legible copies of all CRFs *{remove if using EDC}*.
* Confirm that protocol deviations are noted in the source documents.

1. Unanticipated Problems, Adverse Events, and Serious Adverse Events

* Confirm that all UPs, AEs, and SAEs have been reported to the appropriate regulatory agencies as required.
* Confirm that the site has and will continue to meet safety reporting requirements.
* Ensure that copies of SAE reports are filed with the corresponding site files.

1. Investigational Product

* Confirm that all investigational product accountability records have been maintained appropriately and are consistent with the amount of remaining product.
* Ensure that remaining IP will be destroyed per institutional requirements. Document proper destruction of any remaining product.

1. Laboratory Samples

* Confirm that all lab samples have either been analyzed or stored for future analyses.
* Confirm future use specimen disposition and labeling/de-identification, as appropriate.
* Confirm site process for identification and disposition of future use samples connected to participants who withdraw consent.

1. Regulatory Obligations

* Confirm that the PI has met and will continue to meet regulatory obligations.
* Confirm that the PI has provided written notification of study closure to the IRB and verify acknowledgement by the IRB of study closure.
* If the study was terminated prematurely, the CRA will confirm that enrolled participants were informed and that appropriate therapy and follow-up was initiated by the PI.
* Inform the PI of the possibility of future audits by regulatory authorities.

1. Records Retention

* For IND/IDE studies, review the document retention requirement for all study-related records: 21 CFR 312.57 (c), 45 CFR 46.115 (b), 45 CFR Part 74, as well as institutional and local IRB requirements; emphasizing that the more stringent retention policy should be followed.
* For IND/IDE studies, inform the PI that all study records and reports must be retained for 2 years after a market application approval for the drug, or until 2 years after shipment and delivery of drug for investigational use is discontinued and Food and Drug Administration (FDA) has been notified (21 CFR 312.57).]
* HHS protection of human subjects’ regulations (45 CFR 46.115) require institutions to retain records of IRB activities and certain other records for at least 3 years after completion of the research.
* Discuss PI’s responsibility for retaining all study records and making them available for monitoring and audits during the conduct of the study and throughout the retention period.
* Instruct the PI to notify the Sponsor if the study files are to be relocated or responsibility for site files is transferred to another individual.

1. Visit Conclusion

At the conclusion of the COV, the CRA will meet with the PI and site SC to discuss:

* Any findings noted during the visit.
* Retention timeframes for study-related documents.
* Safety reporting requirements.
* Notification of the IRB that the study has concluded.
* Outstanding issues at study closure and a plan for their resolution.