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Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the process for ensuring participant safety and verifying the data for Research Protocols conducting by the North American Consortium for Histiocytosis (NACHO) through its participating sites.

Policy

All research protocols approved by the Clinical Studies Committee of NACHO will be monitored to assure adherence to regulatory requirements for the protection of human subjects; that the reported research protocol data are accurate, complete, and verifiable from source documents; and the conduct of the trial is in compliance with the currently approved protocol, amendment(s), with Good Clinical Practices and applicable regulatory requirements. All NACHO research protocols must include a Monitoring Plan.

Definitions

Site Qualification Visit (SQV): The assessment of proposed sites for suitable participation in NACHO Clinical Trials.
Site Initiation Visit (SIV): A meeting to ensure the site investigator and delegated staff have a thorough understanding of the protocol and regulatory requirements needed to perform a NACHO clinical trial prior to starting enrollment.
Interim Monitoring Visit (IMV): A periodic review of the NACHO clinical trial at a site to ensure protection of human subjects, accurate, complete, and verifiable study data, and compliance with the protocol, SOPs, and other regulatory requirements.
Close Out Visit (COV): A final monitoring visit to ensure that all activities required for trial close-out are completed and copies of essential regulatory documents are held in the appropriate files with the sponsor and at the site.

Procedures

I. Site Qualification Visits (SQV)

A. All sites performing on a NACHO Clinical Trial will have an SQV documented prior to study activation.

i. For low and moderate risk studies, the Membership Qualification Visit (MQV) may satisfy this requirement.

ii. For high-risk studies, those sites who have had an MQV or full SQV as part of another NACHO study, a limited study specific SQV will be performed.

B. The Site Qualification Summary will be utilized to document the site qualification. This summary will highlight the general site facilities, equipment, and staff assessments, as well as study specific items.

C. The SQV will be performed on-site or remotely, as determined by NACHO Operations.

D. The Site Qualification Summary will be finalized by obtaining signatures from the NACHO Monitor, NACHO Study Manager, and Site Principal Investigator.
E. The SQV documentation, including the agenda, site staff participants, and summary information will be stored in the Trial Master Files for each study per site. A copy of the final signed summary will be sent to the site for storage in the site files.
F. In the event of findings of concern on the SQV, the findings would be discussed with the Clinical Studies Committee and the Study Chair. The site will not be allowed to activate until these findings are addressed.

II. Site Initiation Visit (SIV)

A. The SIV will occur after regulatory approval documents (IRB, FDA, etc.) have been obtained. Additionally, regulatory documents required for study start-up will be on file or in the active process of being obtained before the SIV is scheduled.
B. The study monitor will work with the NACHO Ops Study Manager to schedule the SIV.
C. The SIV will be performed remotely with pertinent site staff in attendance.
D. Documentation of the SIV as well as site staff participation will be stored in the Trial Master Files for each study per site.

III. Interim Monitoring Visits (IMV)

A. Monitoring Plan

i. The NACHO Operations Center (NACHO OC) will prepare or oversee the monitoring plan in conjunction with the Study Chair and/or Study Manager. In general, the plan should include:

1. Procedures to review study performance at trial sites (Data collection, protocol adherence, Regulatory Requirements, etc.)
2. Nature and frequency of site monitoring based on risk-level of trial.
3. Selection of participants to be monitored based on risk-level of the trial

ii. Approval for the final monitoring plan will be obtained by signatures from the NACHO Operations staff who authored the document as well as the Study Chair.
iii. The final signed monitoring plan will be kept in the Trial Master Files and made available to the NACHO Clinical Studies Committee.
iv. The monitoring plan may be modified as needed for changes to the protocol or internal processes. Trial amendments (major or minor) that do not change the monitoring process will not require a monitoring plan modification.

B. Scheduling an onsite or remote Monitoring Visit

i. The monitor will contact the Site PI and study coordinator to coordinate dates for the monitoring visit.
ii. A confirmation letter will be sent by the monitor to the PI, Study Coordinator, and NACHO OC reflecting the dates and expectations of the visit.

C. Conducting the Monitoring Visit

i. The NACHO monitor will conduct the monitoring visit in accordance with the approved monitoring plan of the study.
ii. The NACHO monitor will work with the site prior to the visit to obtain any required systems access needed to perform the visit.
iii. The NACHO monitor should meet with the site PI and other staff as applicable during the monitoring visit to communicate monitoring findings as well as ensure resolution plans are in place for these findings.
iv. Additionally, the NACHO monitor will comply with any site-specific SOPs in place at the time of study monitoring.

D. Reporting of the Monitoring Visit

i. The NACHO monitor will provide a follow-up letter detailing the monitoring findings to the site after the end of the site visit. The follow-up letter will be filed in the regulatory files at the site and at the NACHO OC.

ii. The monitor will prepare a final report of the findings of the monitoring visit to include any unresolved findings from the initial report and all major findings whether or not those have been corrected.

iii. The final report will be signed and dated by the monitor, Study Manager, and Study Chair.

iv. The final signed report will be filed in the research protocol monitoring binder at the NACHO OC.

v. The final report will be available to the Clinical Studies Committee for review.

vi. Findings that are not addressed by the site will be referred to the Clinical Studies Committee as per the NACHO Study Conduct and Compliance SOP

IV. Close Out Visit (COV)

A. Once the study is closed to enrollment and all study participants at the site have completed trial participation to the point that further monitoring is not required, the COV may be scheduled and performed. Additional reasons for performing the COV may include: PI leaving the site or site deciding to close the study.

C. The COV may be performed on-site or remotely as determined by NACHO Operations.

D. Once completed, the monitor will prepare and submit a follow-up letter, as with the IMV, which will be kept in the regulatory files at the site.

E. The Final COV report will be prepared and signed, as with the IMV, and filed in the trial master files for the study per site.

MAINTENANCE RESPONSIBILITY

The NACHO SOP Ad Hoc Committee is responsible for the review of this SOP. Suggested changes must be proposed to and approved by the NACHO Executive Committee.

AUTHORIZATION

This SOP was developed by the SOP Ad Hoc Committee and reviewed and approved by the NACHO ExecutiveCommittee.

VERSION/REVISION HISTORY

Approval Date	Version	Version/Revision Summary
12/18/2018	V 1.0	Original documentation/publication.
07/27/2022	V 2.0	Revised and updated the SOP to current monitoring practices. Included language regarding Site Qualification, Site Initiation, Interim Monitoring, and Close-Out Visits

APPENDIX I: Suggested Monitoring Plan by Risk and Phase of Study Table

NACHO Research Monitoring Plan (Frequency, Participants Monitored, and Elements to Monitor are subject to the discretion of the Study Chair and/or NACHO Operations, as well as external sponsor requirements)			
Risk and Phase	Monitoring Frequency	Participants Monitored	Elements to Monitor
High Risk Phase I (IND)	Quarterly (during dose determination phase)	First 2 participants, then one per dose level, per site	Eligibility and Consent (100% of participants) Regulatory Documentation (Semi-annually during patient enrollment, annually if no enrollment) Protocol Compliance and Data Accuracy/Completeness for elements related to Primary and Secondary Objectives AE/SAE reporting Investigational Product Accountability
High Risk Phase II & III (IND)	Semi-Annually	First 2 Participants, then 15% of subsequent enrollees, per site	Eligibility and Consent (100% of participants) Regulatory Documentation (Semi-annually during patient enrollment, annually if no enrollment) Protocol Compliance and Data Accuracy/Completeness for elements related to Primary and Secondary Objectives AE/SAE reporting Investigational Product Accountability
Moderate Risk Phase I (no IND)	Semi-annually	First 2 participants, then one per dose level, per site	Eligibility and Consent (100% of participants) Regulatory Documentation (Semi-annually during patient enrollment, annually if no enrollment) Protocol Compliance and Data Accuracy/Completeness for elements related to Primary Objectives AE/SAE reporting

Moderate Risk Phase II	Annually	First 2 participants, then 10% of subsequent enrollees, per site	Eligibility and Consent (100% of participants) Regulatory Documentation Protocol Compliance and Data Accuracy/Completeness for elements related to Primary Objectives AE/SAE reporting
Moderate Risk Phase III (no IND)	Annually	First 2 participants, then 10% of enrollees, per site	Eligibility and Consent (100% of participants) Regulatory Documentation Protocol Compliance and Data Accuracy/Completeness for elements related to Primary Objectives AE/SAE reporting
Low Risk Non-Therapeutic	Annually	First 2 participants, then 10% of Enrollees, per site	Eligibility and Consent Regulatory Documentation