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PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to describe the process for addressing site non-compliance with protocol related data, source documents, regulatory documents and other protocol related requirements for NACHO research protocols. This policy applies to all on-going and future research under the sponsorship of NACHO.

POLICY

It is the policy of the North American Consortium for Histiocytosis (NACHO) to assure compliance with Good Clinical Practice (GCP) and regulatory requirements by all members who are engaged in NACHO research protocols. The monitoring procedures in place for all NACHO studies are designed to provide this assurance. A member site which fails to address non-compliance issues will be subject to escalated compliance procedures, up to and including membership termination, as deemed necessary by the Study Chair and the Clinical Studies Committee (CSC) per the "Study Conduct and Compliance" SOP.

PROCEDURES

I. Non-compliance Notifications to Site

A. The Study Manager and/or NACHO monitor will notify a site whenever data, source documents, regulatory documents, or other protocol related items are found to be delinquent. The notice will:
   1. be sent to the site study staff listed on the Delegation of Responsibility log,
   2. outline the deficiencies,
   3. state that the site has ten (10) business days to resolve the deficiencies.

B. If the site does not sufficiently address the issues by the deadline, the Study Manager will send a second notification to the site. This second notification will:
   1. be sent to the site Principal Investigator (site PI) and site study staff
   2. state that the site has ten (5) business days to resolve the deficiencies.

C. If the site does not sufficiently address the issues by the deadline of the second notification, the Study Manager will send a final notification to the site via memo.

   The memo will:
   1. be sent to the site PI, and the site study staff, and will CC the Study Chair and NACHO Operations Center (NACHO OC) for inclusion in the CSC Site Performance Report.
   2. state that this is the final notice of non-compliance
   3. state that the site has five (5) business days to resolve the deficiencies

II. Non-compliance Notification to CSC

A. If the site does not resolve the issues, the Study Manager and Study Chair will report the non-compliance to the CSC.

B. The CSC will review the non-compliance issue(s) and send a memo to the Site PI.

   The memo will :
   1. be copied to the NACHO Operations Center and the NACHO DSMC (if applicable),
   2. place a hold on patient enrollment for the applicable study,
   3. require a Corrective Action / Preventive Action (CAPA) plan be sent within ten (10) business days to the CSC and the Study Chair,
   4. require the site PI to notify the site's IRB of the enrollment hold and CAPA request,

5. require that the site PI forward a copy of the IRB's acknowledgement of the enrollment hold and CAPA to the Study Manager and Study Chair,
6. include the NACHO CAPA form (see attachment "NACHO CAPA form")

III. Review of Correction Action / Preventative Action Plan(s) (CAPA)

A. Upon receipt of the CAPA, the CSC and Study Chair will review and respond to the site within five (5) business days.
   1. If the plan is approved, and deficiencies are corrected, the Study Manager and Study Chair will:
      a. Monitor progress of the preventive action plan on a regular basis,
      b. Keep regular communication with the site PI and CRAs,
      c. Remove the enrollment hold within thirty (30) days pending resolution of items.

B. If the plan is not approved, the CSC may request a new plan, or proceed with Section IV.

C. If a CAPA is not received within the specified time frame or if the plan is not acceptable, the CSC in consultation with the Study Chair has the option to remove the site from the study.
   In a memo, the CSC will:
   1. state that the site is removed from the study,
   2. copy the Study Chair, Study Manager, and the NACHO OC,
   3. Instruct the site PI to inform the local IRB and send a copy of the acknowledgement to the Study Chair and the CSC,
   4. The CSC Chair will inform the NACHO Executive Committee (EC) of the site study removal and the site will proceed with study termination activities.

IV. NACHO CSC Chair Responsibilities

A. The NACHO CSC Chair will send a memo to the EC recommending termination of NACHO membership if so decided as per the NACHO Membership Criteria and Standards SOP.

V. Site Responsibility

A. The sites must adhere to the timelines described above unless extenuating circumstances are clearly documented by the site and sent to the Study Manager by the site PI. Any changes to the timelines must be approved by the Study Chair.

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 EC.

AUTHORIZATION

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

VERSION/REVISION HISTORY

Approval Date	Version	Version/Revision Summary
12/18/2018	V 1.0	Original documentation/publication.
5/25/2022	V 2.0	Added more oversight from the CSC, updated the timelines for noncompliance notifications, clarified responsibilities of Study Chair and NACHO Ops, and included updates for reviewing a CAPA

Appendix A: NACHO Corrective Action/Preventive Action Plan Form

Corrective Action and Preventive Action Plan

Date:	
To:	
NACHO Research Protocol Mnemonic:	
Site:	
Site Principal Investigator:	

Violation or Deficiency (as described in memo or monitor report)			
Root Cause (the reason the issue arose)			
Corrective Action Plan (action taken to correct specific violation or deficiency identified. Include implementation activities)			
Preventative Action Plan (Action taken or planned to prevent the reoccurrence of this issue in the future)			
Responsible Personnel: (to include the site PI, site study coordinator and/or the manager)		**Signature and Date:**	

**Multiple violations/deficiencies may require separate CAPA responses.