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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 jurisdiction of NACHO.

POLICY

It is the policy of the North American Consortium for Histiocytosis (NACHO) to assure compliance with Good Clinical Practice 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 monitoring findings will be subject to escalated compliance procedures, up to and including membership termination, as deemed necessary by the Study Chair, the Study Coordinating Center (SCC), and the NACHO Data Safety Monitoring Committee (DSMC).

PROCEDURES

I. The SCC will notify a site whenever data, source documents, regulatory documents, or other protocol related items are found to be delinquent. The compliance memo will:
   - A. be sent to the site Principal Investigator (PI), and the site Study Coordinator/Clinical Research Associate(s) (CRAs) listed on the Delegation of Responsibility log,
   - B. outline the deficiencies,
   - C. state that the site has ten (10) business days to resolve the deficiencies.

II. If the site does not sufficiently address the issues, the SCC will send a second memo to the site. This second Compliance Memo:
   - A. will be sent to the site PI, site Study Coordinator/CRA(s), and the Study Chair,
   - B. will be copied to the NACHO Operations Center for inclusion in the Institutional Activity Report,
   - C. will state that the site has ten (10) business days to resolve the deficiencies.

III. If the site does not resolve the issues, the Study Chair will send a third memo. This third Compliance Memo:
   - A. will be copied to the NACHO Operations Center and the NACHO DSMC (if applicable),
   - B. will place a hold on patient enrollment for the applicable study,
   - C. will require a Corrective Action / Preventive Action (CAPA) plan be sent within ten (10) business days to the Study Chair and the SCC,
   - D. will require the site PI to notify the IRB of the enrollment hold and CAPA request,
   - E. will require that the site PI forward a copy of the IRB's acknowledgement of the enrollment hold and CAPA to the Study Chair and the SCC,
   - F. will instruct that the CAPA must include the following elements for each deficiency or category of deficiencies:
     1. A description of the deficiency or category of deficiencies,
     2. Documentation of the action taken (or planned) to correct the deficiency, including responsible person and date of completion (or deadline for completion),
     3. A description of the cause of the deficiency (or category of deficiencies),

4. Documentation of the process improvement to address and prevent the root cause, including a responsible person and a deadline for implementation,
5. A signature from the PI and any additional persons responsible for actions outlined.

IV. The Study Chair and SCC will review and respond to the site within five (5) business days of either the approval of the plan, or with required amendments.

A. If the plan is approved, and deficiencies are corrected, the SCC will:
1. Monitor progress of the process improvement plan on a regular basis,
2. Keep regular communication with the site PI and CRAs,
3. Remove the enrollment hold within thirty (30) days pending resolution of items.

V. If a CAPA is not received within the specified time frame, the Study Chair has the option to remove the site from the study. In a final memo, the Study Chair will:
A. state that the site is removed from the study,
B. Study Chair will copy the NACHO OC,
C. The site PI will inform their IRB and send a copy of the acknowledgement to the Study Chair and the SCC,
D. The NACHO OC will inform the NACHO EC of the site study removal.
E. The site will proceed with study termination activities.

VI. The NACHO 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.

VII. The sites must adhere to the timelines described above unless extenuating circumstances are clearly documented by the site and approved by the Study Chair.

MAINTENANCE RESPONSIBILITY

The NACHO SOP Ad Hoc Committee is responsible for the annual 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.