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PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to identify the categories, criteria, and performance standards of membership in the North American Consortium for Histiocytosis (NACHO) and to define the membership application process.

POLICY

NACHO is the first multi-institutional consortium for Langerhans cell histiocytosis (LCH) in North America with a solid scientific agenda and the research infrastructure necessary for the development and effective implementation of clinical and translational studies and biological research for LCH. The institution wherein NACHO's Operations Center is located is responsible for developing and executing contracts on behalf of NACHO. The institutions participating in the consortium funding application made to and funded by St. Baldrick's Foundation (SBF) defined NACHO's original members. Other parties interested in opening a NACHO study must apply for Associate membership in NACHO to facilitate the contracts and opening of NACHO studies.

PROCEDURES

I. Membership Categories

A. Full Member Institution

1. NACHO's original Full Member Institutions were identified in the funding application to SBF that outlined the design and members of the consortium. Those Full Member Institutions will remain as such when in compliance with NACHO membership standards and the conditions set forth in the Memorandum of Agreement executed between the Operations Center institution and NACHO site institutions regarding SBF funding.
    a) Additional Full level memberships may be granted at the discretion of and/or via a process established by the NACHO Executive Committee (EC), the governing body of the consortium.
2. Each Full Member Institution must identify one individual from their institution to serve as the Principal Investigator (PI) for NACHO studies and activities.
    a) The PI will serve as a member of the NACHO EC.
    b) An Alternate PI must be identified to serve in the PIs role should the PI be unavailable or unable to perform his/her duties.
    c) All PIs must be proposed to and approved by the other members of the NACHO EC.

B. Associate Member Institution

1. Institutions will be considered for Associate membership when meeting at least one (1) of the criteria below, in addition to the criteria listed in Section II of this SOP.
    a) The institution is interested in opening and enrolling patients on a NACHO study.

b) The chair of a study approved for development by the NACHO EC is at that institution.
c) The institution provides significant scientific input for the development of a NACHO study.
d) The institution provides laboratory resources for correlative studies for a NACHO study.
e) Other special reasons as determined by the NACHO EC.

2. Membership applications must be submitted following the process outlined in Section VIII of this SOP.
3. Associate members are considered temporary memberships and will continue based on the guidelines set forth in the NACHO Master Consortium Agreement and any subsequently engaged Clinical Study Protocol Riders.
4. Each Associate Member Institution must identify one individual from their institution to serve as the PI for NACHO studies and activities; the PI will be responsible for:
   a) Directly supervising the performance and administration of NACHO clinical trials, ensuring compliance with protocol documents and identifying investigators and personnel to ensure timely and efficient work, and
   b) Circulating information about and from NACHO to all pertinent personnel.
5. An Alternate PI must be identified to serve in the PI's role should the PI be unavailable or unable to perform his/her duties.
6. Associate Member Institutions are not eligible to serve on the NACHO EC or to receive consortium infrastructure funding.
7. Associate Member Institutions are relieved from meeting the same performance standards as Full Member Institutions.
8. Associate Member Institutions may be considered for Full Membership Institution status at the discretion of and/or via a process established by the NACHO EC.

II. Membership Criteria

All institutions interested in NACHO membership must meet the criteria listed below.

A. Have an investigator with clinical trials experience who has the availability and desire to act as a PI for that institution.
B. Demonstrate and/or have evidence of the infrastructure necessary to perform clinical studies.
C. Be committed to prioritizing NACHO protocols and to providing complete and timely data, including follow-up information. It is understood that this does not prohibit members from engaging in other research activities.
D. Be willing and able to comply with:
   1. NACHO clinical trials audits at least once every three (3) years.
   2. Federal Drug Administration (FDA) requirements and/or other local, regional, state, and national government regulations, as applicable, for conduct of clinical trials.
   3. NACHO regulatory requirements and SOPs.

III. Membership Requirements

NACHO institutions agree to the stipulations and activity listed below.

A. Execute the NACHO Master Consortium Agreement within six (6) months of receipt, if applicable.
B. Comply with all provisions outlined in the written NACHO Master Consortium Agreement for the duration of membership in NACHO, including the confidentiality clause.
C. Execute individual Clinical Study Protocol Riders, as applicable, for each NACHO study within nine (9) months of receipt.
D. Report to the NACHO EC any conflicts of interest for the PI, Alternate PI and all sub-investigators as per the policy established by the NACHO EC.
E. Comply with NACHO clinical trials audits at least once every three (3) years.
F. Comply with FDA requirements and/or other local, regional, state, and national government regulations, as applicable, for conduct of clinical trials.
G. Adhere to NACHO regulatory requirements and SOPs.

H. Participate in NACHO teleconferences and in-person meetings.

IV. Executive Committee Meetings

A. Monthly Executive Committee teleconferences and one in-person meeting (hereafter referred to collectively as "meetings") are held to provide updates on NACHO clinical studies and activities and to address other consortium related business.
   1. Meeting dates, times and location, if applicable, will be communicated at least 14 days in advance of the event.

B. Attendance at meetings is open to NACHO Full Member institution PIs and/or Alternate PIs. Other participants may be invited at the discretion of the NACHO EC.

C. The PI or Alternate PI for all NACHO Full Member institutions is expected to attend and participate in no fewer than 50% of meetings during a six (6) month period of time.

D. The presence of a majority of NACHO EC members constitutes a quorum.
   1. If a PI and Alternate PI from the same institution both participate in a meeting, only the PI will have the right to vote.

E. Unless otherwise stated, the monthly group teleconference will take place at the same time each month.

F. The NACHO Operations Center staff is responsible for organizing meetings that support the business of NACHO.

V. Performance Standards for Full Member Institutions

The guidelines below define participation levels needed from Full Member Institutions to maintain membership in good standing with NACHO. Refer to Section VI of this SOP for Associate Member Institution performance standards.

A. Reporting Period
   1. The annual accrual period will be based on the start date of June 1.
   2. Institution Activity Reports summarizing IRB approvals, Patient Screening Logs, patient accrual, and meeting attendance will be generated by the NACHO Operations Center quarterly on June 1, September 1, December 1 and March 1 of each year.

B. Study Activation
   1. An active study is defined as one that has been open within NACHO for three (3) months.
   2. Full Member Institutions are expected to have 50% or more of all active NACHO studies approved by their local IRB and to do so within nine (9) months of executing Clinical Study Protocol Riders.
      a) Studies on hold for nine (9) months or more, either for drug supply or other reasons as determined by the NACHO EC, will not be considered in this evaluation.

C. Patient Screening Logs
   1. All member institutions will maintain monthly Patient Screening Logs (PSL).
   2. The NACHO Operations Center will provide members with a PSL template following membership approval or at an otherwise designated time.
   3. Institutions will be responsible for completing and submitting PSLs to the NACHO Operations Center on a monthly basis.
      a) The PSL template will include a choice to demonstrate that no patients were screened during a particular month.

D. Patient Accrual
   1. Full Member Institutions are expected to enroll eligible patients on active NACHO studies for which Clinical Study Protocol Riders have been executed and that have received local IRB approval.
   2. The measures below are calculated based on active NACHO studies collectively of those that have received local IRB approval.
      a) A minimum of one (1) patient should be enrolled in the first twelve (12) months following local IRB approval.

b) At least two (2) patients should be enrolled in each subsequent twelve (12) months.

3. Accrual expectations may be adjusted based on the total number of and/or specific, active NACHO clinical studies.

E. Membership Probation and Termination (for Full Member Institutions)

1. A warning notice will be issued to institutions that do not meet the standards below, as demonstrated in quarterly activity reports.
   a) No patients have been accrued in the first twelve (12) months after a NACHO study is approved by a local IRB, and/or
   b) Less than 50% of active NACHO studies have local IRB approval, based on studies that have been active with NACHO for at least six (6) months at the time of the report, and/or
   c) Fewer than ten (10) PSLs have been submitted during a twelve (12) month period.
2. An initial probation period of six (6) months will be applied to institutions that received a warning notice if the subsequent quarterly activity report demonstrates that the standards cited in the warning notice has still not been met. During the initial probation, institutions must meet the standards below or membership will be terminated.
   a) Accrue at least one (1) patient on an active NACHO study, and/or
   b) Obtain local IRB approval for at least 50% of active NACHO studies, and/or
   c) Submit at least ten (10) of the twelve (12) delinquent PSLs, and/or
   d) Attend at least 50% of group meetings (PI or Alternate PI).
3. Institutions meeting the criteria during initial probation may be granted a second six (6) month probation period during which the standards below must be met or membership will be terminated.
   a) Accrue at least one (1) additional patient on a NACHO study, and/or
   b) Obtain local IRB approval for at least 50% of NACHO studies, and/or
   c) Submit at least 80% of delinquent PSLs and maintain monthly submission thereafter, and/or
   d) Attend at least 50% of group meetings (PI or Alternate PI).
4. Institutions meeting the criteria to be placed on probation for a third time, after having resolved probation successfully on two prior occasions, will have membership terminated.
5. Membership in NACHO can also be terminated for:
   a) Failure to execute the NACHO Master Consortium Agreement within six (6) months of receipt.
   b) The NACHO PI or Alternate PI has attended fewer than three (3) group meetings in a six (6) month period.
   c) Failure to comply with the confidentiality clause in the NACHO Master Consortium Agreement.
   d) Failure to comply with federal and/or other local, regional, state, and national government regulations, as applicable, for conduct of clinical trials.
   e) Failure to disclose conflicts of interest that affects NACHO research and/or goals.
   f) An audit that identifies serious problems in clinical trials conduct as determined by the NACHO EC.
6. The NACHO EC will review membership terminations prior to notices being issued.

VI. Performance Standards for Associate Member Institutions

The guidelines below define the participation needed from Associate Member Institutions to maintain membership in good standing with NACHO. Refer to Section V of this SOP for Full Member Institution performance standards.

A. Reporting Period

1. The annual accrual period will be based on the start date of June 1.

2. Institution Activity Reports summarizing IRB approvals, Patient Screening Logs, patient accrual, and meeting attendance will be generated by the NACHO Operations Center quarterly on June 1, September 1, December 1 and March 1 of each year.

B. Study Activation
   1. An active study is defined as one that has been open within NACHO for three (3) months.
   2. Associate Member Institutions are expected to activate all NACHO studies for which they have executed a Clinical Study Protocol Rider within nine (9) months of signing said Rider.
      a) Studies on hold for nine (9) months or more, either for drug supply or other reasons as determined by the NACHO Executive Committee, will not be considered in this evaluation.

C. Patient Screening Logs
   1. All member institutions will maintain monthly Patient Screening Logs (PSL).
   2. The NACHO Operations Center will provide members with a PSL template following membership approval or at an otherwise designated time.
   3. Institutions will be responsible for completing and submitting PSLs to the NACHO Operations Center on a monthly basis.
      a) The PSL template will include a choice to demonstrate that no patients were screened during a particular month.

D. Patient Accrual
   1. Associate Members are expected to enroll eligible patients on active NACHO studies for which Clinical Study Protocol Riders have been executed and that have received local IRB approval.
   2. The measures below are calculated based on active NACHO studies collectively of those that have received local IRB approval.
      a) A minimum of one (1) patient should be enrolled in the first twelve (12) months following local IRB approval.
      b) At least two (2) patients should be enrolled in each subsequent twelve (12) months.
   3. Accrual expectations may be adjusted based on the total number of and/or specific, active NACHO clinical studies.

E. Membership Probation and Termination (for Associate Member Institutions)
   1. A warning notice will be issued to institutions that do not meet the standards below, as demonstrated in quarterly activity reports.
      a) No patients have been accrued in the first twelve (12) months after a NACHO study is approved by a local IRB, and/or
      b) Fewer than ten (10) PSLs have been submitted during a twelve (12) month period, and/or
   2. An initial probation period of six (6) months will be applied to institutions that received a warning notice if the subsequent quarterly report demonstrates the criteria noted in the warning notice has still not been met. During the initial probation, institutions must meet the criteria below or membership will be terminated.
      a) Accrue at least one (1) patient on an active NACHO study, and/or
      b) Submit at least ten (10) of the twelve (12) delinquent PSLs, and/or
      c) Attend at least 50% of group meetings (PI or Alternate PI).
   3. Institutions meeting the criteria during initial probation may be granted a second six (6) month probation period during which the criteria below must be met or membership will be terminated.
      a) Accrue at least one (1) additional patient on a NACHO study, and/or
      b) Submit at least 80% of delinquent PSLs and maintain monthly submission thereafter, and/or
      c) Attend at least 50% of group meetings (PI or Alternate PI).
   4. Institutions meeting the criteria to be placed on probation for a third time, after having resolved probation successfully on two prior occasions, will have membership terminated.

5. Membership in NACHO can also be terminated for:
    a) The NACHO PI or Alternate PI has attended fewer than three (3) group meetings in a six (6) month period.
    b) Failure to comply with the confidentiality clause in the NACHO Master Consortium Agreement.
    c) Failure to comply with federal and/or other local, regional, state, and national government regulations, as applicable, for conduct of clinical trials.
    d) Failure to disclose conflicts of interest that affects NACHO research and/or goals.
    e) An audit that identifies serious problems in clinical trials conduct as determined by the NACHO EC.
6. The NACHO EC will review membership terminations prior to notices being issued.

VII. Benefits of Membership

Full and Associate Member Institutions can become involved in NACHO's work in the ways listed below.

A. Open and enroll patients on active NACHO clinical studies.
B. Have restricted user access to the NACHO website.
C. Participate in NACHO teleconferences and meetings.
D. Assist in the development of future NACHO clinical studies.
E. Serve as a member of NACHO committees.
F. Receive guidance, support and training (when applicable) for NACHO sponsored studies.

VIII. Associate Member Institution Application Process

Institutions meeting the requirements of membership outlined in this SOP may apply for Associate membership with NACHO following the process below. Applications will be accepted on an ongoing basis.

A. Interested parties will complete a membership application and submit other requested materials to the NACHO Operations Center.
    1. Application instructions will be available on the NACHO website and/or by contacting the NACHO Operations Center.
    2. Applicants will be sent notification that an application has been successfully received.
B. Applications will be reviewed and considered for approval by the NACHO EC.
    1. A positive majority vote of NACHO EC members is needed to approve membership.
    2. Voting may take place via teleconference, in-person meeting or electronically.
C. Applicants will be notified via email of their acceptance status within six (6) to eight (8) weeks of submitting an application.
D. Provisional membership approval may be granted in order to expedite the process of initiating a NACHO clinical study.

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
06/25/2015	V 1.0	Original documentation/publication; reviewed/approved by Full Member Institution representatives acting as the Executive Committee (EC), as EC not officially formed as of 06/25/2015.
11/11/2015	V 2.0	Reference to location of operating center removed (policy section); vote needed to approve affiliate members adjusted from two-thirds to majority (VIII.B.1).
10/07/2016	V 3.0	Change to using the term "Associate" members, rather than "Affiliate" Members to

		avoid confusion with St. Jude “Affiliate” sites; move meeting metric to appropriate performance standards sections; group meetings changed to Executive Committee meetings; additional membership benefit added.