

Process for Solicitation and Review of Clinical Trials for NETT

1. Guideline Development

Guidelines describing the characteristics that make trials well suited to be performed in the network will be created and disseminated. Trials generally should:

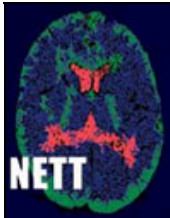
- a. be conducted in the emergency care setting with the primary treatment being delivered in the prehospital or emergency phase of treatment.
- b. have a patient oriented primary outcome.
- c. be “simple” in design with clearly defined endpoints and gather only essential data to answer the scientific question.
- d. have sample sizes amenable to being conducted in a system of hubs and their spokes (if needed).
- e. be phase III interventional treatment or health services trials (not pilot studies).
- f. be designed such that the results are easily translated into clinical practice.

2. Promotion / Solicitation

Appropriate mechanisms for disseminating guidelines and encouraging the development and submission of desirable trials will be pursued including some or all of the following:

- a. Communication with NINDS Program Directors who can refer investigators to the NETT when they are approached with appropriate trials.
- b. A Program Announcement or Notice in the NIH Guide that gets the guidelines in a prominent and searchable location for investigators.
- c. Assist in building new translational partnerships between investigators with promising animal or preliminary clinical data and experienced clinical trials investigators to conduct trials in the network.
- d. Promotion of the NETT in appropriate journals including Neurology, Annals of Neurology, Annals of Emergency Medicine and Academic Emergency Medicine as well as at appropriate scientific meetings such as SFN, AAN, ANA, ISC, SAEM, ACEP, SCCM, etc.
- e. Information about important, unanswered clinical questions and potential clinical trials on the NETT website.
- f. Communication with representatives of industry about guidelines and availability of the NETT.

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3. Purpose and Scope of NETT Concept Consultation and Review

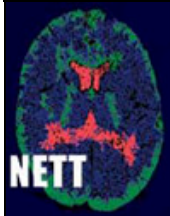
Investigators interested in developing a clinical trial to be conducted in the NETT are encouraged to propose their ideas to the NETT Executive Committee early in the process.

- a. Concept consultation is entirely optional but encouraged, and is a standardized, equitable way for investigators to obtain early feedback on whether a trial is appropriate for the NETT. It provides a standardized process to replace and prevent ad hoc or “curbside” pitches to individual executive committee members. Executive committee members will not provide informal or individual feedback to such pitches.
- b. NETT concept review is NOT intended to be an additional layer of scientific peer review and is NOT a substitute for scientific peer review, which remains the responsibility of the Institute or Center for Scientific Review.
- c. Trials may be proposed to the NETT during the preparation of either R34 clinical trial planning grant applications, or during the preparation of RO1/UO1 applications to perform a phase III clinical trial. Applicants preparing R34s are encouraged to seek NETT approval prior to preparing and submitting their applications, while applicants preparing RO1s are required to do so in order to conduct the trial in the NETT. The NETT review and collaboration process for proposals is illustrated in the attached flow diagram.
- d. The purpose of NETT concept review is:
 - i. to make certain that trials proposed to be performed in the NETT are appropriate for the network and are consistent with our mission and vision;
 - ii. to assist the NETT Steering Committee in managing the “pipeline” of proposed trials, and the allocation of network patients and resources among different trials; and
 - iii. to familiarize investigators with the operations of the NETT such that their applications properly convey the resources needed and the infrastructure available.

4. Protocol Summary Preparation

The concept review process is conducted by evaluating clinical trial protocol summaries. Investigators will be able to obtain this template from the NETT web site

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at <http://www.nett.umich.edu>. Protocol summaries should usually be 10-15 pages in length, and will not be considered if over 20 pages.

5. Phases of NETT Concept Review

Trials to be conducted within the NETT will undergo the review process described below.

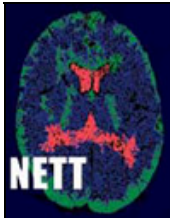
a. Trial Development

- i. This phase of the concept review is optional
- ii. While developing a trial, investigators may submit a draft protocol summary to the NETT executive committee for a “concept consultation” at any time.
- ii. Protocol summaries submitted for “concept consultation” will be circulated to the executive committee and placed on the committee’s agenda.
- iii. After the committee discusses the protocol, the investigator will be provided written comments about the discussion. Comments from the consultation are not binding are not a substitute for the official review and approval process listed below.

b. Clinical Trial Summary Pre-Approval

- i. This phase of the concept review is mandatory
- ii. NETT evaluation does not replace any part of the evaluation and review requirements of the NINDS. Studies proposed for the NETT may require review by the NINDS Clinical Trials Subcommittee. It is advisable to submit projects for NETT evaluation prior to submission to the Clinical Trials Subcommittee.
- ii. Each submitted protocol summary is evaluated by the NETT Steering Committee to determine its appropriateness for the NETT. The NETT CCC PI will assign a member of the Steering Committee to evaluate and present the proposal to the committee.
- iii. The Steering Committee votes a recommendation on the proposal which is forwarded to the NETT Advisory Group (NETT-AG), who makes the final decision on the proposal. The results of the NETT evaluation process will be conveyed to the trial PI in writing along with any comments by the NETT Steering Committee or the NETT-AG.

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c. Grant Application Development

- i. Investigators are permitted to develop grant applications for trials to be conducted in the NETT from protocol summaries approved by the Clinical Trial Subcommittee and the NETT Advisory Group. Trial investigators and members of the NETT Executive Committee (or designees) and administrative staff from the CCC and the SDMC then participate in a mandatory pre-submission consultation. The goals of the consultation are to provide guidance to the trial PI to help craft a final proposal that is optimized for the NETT, and to help the trial PI develop an appropriate budget for the NETT resources to be used in the trial.
- ii. Grant application development can occur at any time.
- iii. Following or in conjunction with this consultation period, the trial PI prepares an RO1/UO1 or R34 or other appropriate grant application. Prior to submission, the NETT CCC PI (or designee) confirms that the application is consistent with what was proposed by the NETT-AG and developed in the consultation process. The NETT CCC PI then provides a letter of support for the grant application.
- iv. Clinical trials approved by the Clinical Trials Subcommittee but deemed not appropriate for the network can continue through the appropriate R01 mechanism, but cannot be performed in the NETT. Trials not approved by the Clinical Trials Subcommittee cannot be conducted in the network regardless of the outcome of the NETT approval process.

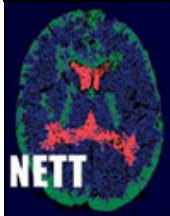
d. Grant Submission and Scientific Review

- i. Grant applications prepared in this manner are submitted to the NIH on the usual application cycle deadlines.
- ii. NINDS will conduct reviews using pre-established guidelines for the review of Phase III clinical trials. The review will be done by a NINDS Clinical Trials Special Emphasis Panel for all NETT proposed trials. The review group will include members with Neurology and Emergency Medicine expertise as well as all other appropriate expertise.

6. Industry Sponsored Studies

NETT will not consider studies composed and designed by industry. Industry may propose potential trials to NETT and NETT will assign a principal investigator to

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design the study protocol and outcomes. The investigator will work with the CCC to develop the budget for the study and the study will undergo review by the NETT Executive and Steering Committees and the NETT AG. If the industry sponsor is willing to help sponsor the study as designed, it will be performed by NETT with the funding supplied by the industrial sponsor.

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