Introduction and Background

Introduction

The Clinical Trials Network's (CTN) multi-site clinical trials provide a valuable resource for accessing diverse patient populations, modalities, and clinical treatment sites. The CTN facilitates collaboration with more than 100 community treatment programs in more than 20 states; implementation of research in these settings enhances generalizability and fosters adoption of research-based treatments for alcohol and drug dependence. The CTN encourages use of the CTN for conducting clinical and basic research. *Three* important ways to enhance the use of the CTN are: to conduct ancillary studies in connection with specific CTN protocols; to utilize it as a platform for externally funded investigations; *and for Nodes to serve as home bases for NIH Training Centers and individual researchers who have NIH fellowships or career development awards.* In addition to benefiting the CTN as a whole with greater productivity, the opportunity for newer researchers to utilize the resources of the CTN and conduct ancillary and external investigations within or upon the CTN, *or take up residence while the recipients of training and fellowship grants*, will advance their careers.

The CTN is a collaborative endeavor and protocols conducted using CTN infrastructure are expected to involve participating community treatment programs in study design and the negotiation of the study budget.

Definitions

Ancillary investigations:

Small, unfunded (or locally funded) projects being conducted at one or more sites adjunctive to an ongoing CTN trial with minimal use of additional CTN resources. Generally, this would be a study-related measurement instrument added to the protocol or administered independent of the protocol at participating study sites. Follow-up studies or nested manipulations would also be considered in the category of ancillary studies.

External investigations:

External investigations, using the CTN as a research platform, are funded through non-CTN resources. Examples of potential research initiatives include a) addition of basic research methods and questions to existing CTN protocols, b) recruiting participants from community treatment programs participating in the CTN for clinical and basic research investigations, c) economic analyses including costs and cost-effectiveness of CTN protocols, d) health services research on the organization and delivery and adoption of evidence-based treatment, and e) any other research protocols that are an appropriate use of the treatment centers, data management centers, and the research and training centers participating in the CTN.

National Research Service & Career Development Awards:

F30 Predoctoral MD/Ph.D fellowships
F31 Individual Predoctoral fellowship
F32 Individual Postdoctoral fellowship
T32 Institutional Pre- and Post-doctoral Traineeships
K01 Mentored Research Scientist Development Award
K08 Mentored Clinical Scientist Development Award
K12 Mentored Clinical Scientist Development Program Award
K23 Mentored Patient-Oriented Career Development Award
K02 Independent Scientist Award
K24 Mid-Career Investigators in Patient-Oriented Research Award
K05 Senior Scientist Award
K30 Clinical Research Curriculum Award

Research Liaison Group (RLG):

The RLG is a constituent organization of the External Affairs Coordinating Committee (EACC) that serves as the initial point of contact for external investigation requests and conducts the review of these proposals and concepts on behalf of the Executive Committee (EC) and the Steering Committee of the Clinical Trials Network. The RLG's responsibilities include the following:

Promote communications between the Principal Investigator (PI) and the Steering Committee of the Clinical Trials Network and facilitate linkages, as necessary.

Consider requests from the Principal Investigator for access to non-restricted parts of Livelink (a web-based, enterprise-wide, collaborative knowledge management system within the CTN) and to make a recommendation to the EC as to access.

Encourage external investigations into areas of interest to the CTN.

Consider requests for secondary data analyses.

Scope

This policy applies to all requests for protocols that require CTN infrastructure and access to the infrastructure. Protocols that seek CTN cost sharing will be referred to the Executive Committee for final approval and may be required to go through the normal CTN concept review and protocol approval process. The policy should be followed when submitting applications to funding to NIH or other entities that may support investigations. The policy is also applicable when funds are available for implementation of a study. Protocols that do not request approval through this policy will be denied access to the CTN infrastructure.

Objective and Purpose

This policy outlines the procedures for requesting permission and implementing research protocols within the CTN, either when conducting an "ancillary study" or "external investigation."

Responsibilities

Investigators seeking to use CTN infrastructure including the participating clinical treatment programs, practitioners, research staff, and patients are expected to follow this policy to gain permission for the investigation and to report study progress and findings to the CTN. The principal investigator of any external investigation has

the primary responsibility for the implementation and timing of a specific protocol in collaboration with the participating CTPs and Nodes. The RLG will have no responsibility for coordinating external investigations.

Procedure

A. Ancillary investigations

1. Anyone wanting to receive CTN consideration for an ancillary study must have:
   a. A 3-5 page proposal briefly describing rationale, methodology and CTN resources involved (See Appendix A Ancillary Study Outline.)
   b. Approval by the PI of the originating node
   c. Approval by the parent study Lead PI, including a letter of support (after consultation with relevant members of the Protocol Design Team representing design, statistical, data management, QA, regulatory, and training expertise).
   d. Endorsement by CTPs expected to participate. By agreeing to participate in the study, the listed nodes and clinics must agree to commit the necessary resources to conduct the study described in the proposal.

2. The items required above shall be submitted to the Executive Committee (EC) and considered for approval according to these criteria:
   a. If approved, site protocol(s) would be amended or separate IRB approval sought, as needed.
   b. If approved, must refer to the Design and Analysis Workgroup for input to the investigator.
   c. If approved, data collection and analysis must be coordinated by the initiating investigator.

3. Review Board Composition
   a. The ancillary projects review shall involve all members of the Executive Committee (currently four PIs, four CTPs). The EC will determine the most appropriate review body on a case-by-case basis. The review body should require a minimum level of time and CTN resources.
   b. The specific composition of the review committee could vary from one review to another in order to eliminate any potential conflict of interest from the review process. In addition, the reviewing body (EC) could invite up to two additional CTN Steering Committee members to participate in a given review in order to contribute needed expertise; this is optional.

4. Submission procedures
   Ancillary study proposals shall be submitted at any time by forwarding applications to the Chair of the EC. In order to facilitate timely implementation, there will be no submission deadlines imposed.

5. Review procedure
   All members of the review board shall read ancillary study submissions. Each member would provide a brief written review outlining merits and weaknesses of the proposal on of the following six (6) major review criteria:

   Clearly stated research question or hypothesis
   Scientific merit whereas the study would add valuable information not obtained in parent project
   Sufficient methodology detail to judge feasibility and cost

Feasible to conduct with minimal cost to CTN
Demonstrated CTP interest
No harm to ongoing protocol or to another protocol (e.g. recruitment, data analysis, burden on CTP, etc.)

6. Each member shall give the application an overall numeric score ranging from 1-5 while taking all review criteria into consideration.

   1 = outstanding, recommended to go forward with high priority
   2 = very good, recommend to go forward with attention to review points
   3 = average, issues have been identified that need to be addressed
   4 = low enthusiasm, could potentially be salvaged with re-write
   5 = not recommended for further consideration due to the serious flaws or weaknesses identified

7. The Executive Committee will make an approval/disapproval decision. However, ancillary projects receiving a score of 3 or 4 can be re-submitted after revision.

8. Reporting
   After approval, the EC will assign the ancillary study to the Operations Coordinating Committee who will monitor the ancillary study.

9. Publications
   Investigators should acknowledge the role of the CTN in any papers prepared for publication. Copies of publications should be sent to the chairs of the Publications Subcommittee and the Dissemination Subcommittee.

B. External investigations

1. Investigators must apply through email for permission to access CTN infrastructure.

2. Requests should be sent to Center for the Clinical Trials Network within the National Institute on Drug Abuse.

3. Submission Procedures:

   a. Requests should attach an electronic copy of the study overview including:
      i. specific aims
      ii. a description of the proposed study methods
      iii. an explanation of how CTN facilities or personnel will be involved in the investigation
      iv. application timelines and expectations for study implementation and completion
      v. source(s) and amount of funds required to conduct the investigation.

   b. Requests to conduct studies in conjunction with a CTN protocol must include a letter of support from the Lead Investigator of the protocol.

4. NIDA will screen requests and forward appropriate requests to the Center for Clinical Trials Network

(CCTN), who in turn will send to the CTN Research Liaison Group (RLG) for review and comment

5. The RLG chair will distribute the request electronically to the RLG; members will use email to provide comments and indicate their inclination to support or not to support the request.

   The RLG chair will return the comments and sense of the RLG to NIDA via the CCTN. When necessary, the request may be referred to the Executive Committee of the CTN for approval.

   NIDA will communicate comments to the applicant and, if appropriate, either issue a letter of support that may be included in a grant application or approve initiation of the protocol.

   When funding has been obtained, the investigator must notify CCTN before attempting to recruit participating programs.

   Treatment programs may decline to participate in the protocol.

   The protocol must fully cover costs associated with the investigation.

   The investigator must work with participating nodes to obtain IRB authorization and to initiate the study. Protocols must receive IRB approval prior to implementation in the CTP. Each of the CTN CTPs have their own Federal Wide Assurance (FWA) with the Office for Human Research Protections (OHRP). The CTP must make arrangements for IRB review prior to study implementation. Costs of IRB application and review must be covered by the protocol.

6. Reporting
   Investigators with approved protocols will provide semi-annual reports to the RLG that summarize study implementation, enrollment, expected completion date, and list study publications; reports will continue until the principal investigator sends a formal notice of study completion to the chair of the RLG with a copy to CCTN.

7. Publications
   Investigators should acknowledge the role of the CTN in any papers prepared for publication. Copies of publications should be sent to the chairs of the Publications Subcommittee and the Dissemination Subcommittee.

C. Research Training Scientists

While the NIDA CCTN encourages and supports the affiliation of individually funded scholars or training centers within the CTN Nodes, it remains the sole prerogative of the Node leadership whether or not to incorporate the individuals or centers. Scientists who are applying for an NIH-funded training or center award should contact the program director of the Node for information on local Node-specific review procedures regarding scholars taking up residence and training centers being located at the Node.