

Procedure for Requesting CIT Approval for an Ancillary Study

1. Introduction

The purpose of this document is to define an Ancillary Study and to outline a procedure for applying for CIT approval and/or support for such an ancillary study.

2. Definition of Ancillary Studies

For the purposes of this document, an Ancillary Study is a study that requires the use of any CIT study subjects or resources for a purpose external to any of the main seven CIT studies. Resources include CIT clinical site staff effort, financial support, or data coordinating center (DCC) time or resources.

There are two varieties of Ancillary Studies within the CIT:

- a. CIT ancillary studies: Studies *developed within the CIT Consortium or by a CIT committee* proposing to use CIT patients and/or resources for a purpose beyond or external to any of the main objectives of one of the seven CIT official studies. Examples might be studies to clarify mechanisms or document additional outcomes. Such studies need both CIT scientific review, with opportunity for recommendation of modifications to the study purposes and methods, and logistic review to assure that the use of the CIT patients/resources will not compromise the completion of the primary seven CIT studies.
- b. External ancillary studies: Studies developed by individuals external to the CIT, or within a single institution of the CIT where the motivation for the study is external to the CIT objectives, but for which use of some CIT study subjects or resources might be essential or desirable. Such studies need review primarily only to assure that the use of the CIT patients/resources will not compromise the completion of the primary seven CIT studies. The CIT takes no responsibility for the design or execution of these studies. Therefore the CIT will not generally be involved in the scientific review of these studies, other than to determine whether their scientific value warrants the commitment of CIT study subjects or resources.

3. Submitting a proposal for a CIT Ancillary Study

The attached outline describes the information that should be submitted to obtain access to CIT resources for an add-on study. It is important that each of the points in this outline be addressed. The completed proposal should be submitted to the DCC. The DCC will circulate the document to the CIT Steering Committee and schedule a discussion for discussion.

4. Review of add-on study proposal

The chair of the steering committee will conduct the review of the proposal. The chair may assign specific reviewers to critique the proposal and prepare questions for the discussion. The proposal will be discussed in open session. At the end of the discussion, the chair may request that any members of the steering committee who are involved in the proposal leave so that a final confidential discussion can take place. A formal vote will be taken and reported to the study investigators. Commitment of funds and or other resources from clinical sites or the DCC will require the approval of NIH.

5. Other studies that may be in competition with CIT Studies

It is possible that individuals at a CIT Study Clinical Center may propose performance of a study that requires no CIT resources but may negatively affect recruitment of patients to a CIT study or availability of donor organs at one or more of the clinical sites. It is a good general policy that no center should intend to recruit patients simultaneously for two studies with overlapping eligibility requirements, or that would compete with resources (such as donor organs) already committed for a previously approved and ongoing study. In the event that such a study is proposed, it would not be considered an Ancillary Study for CIT purposes, as it does not use CIT resources. But it is highly desirable that the CIT study members of an institution with plans to develop a study competing with the CIT in the above sense consult with the CIT and develop ways to minimize such competition.

**Clinical Islet Transplantation Consortium
Internal Ancillary Study Application
Outline**

- I. Sponsoring Study
 - a. Study (CIT 01 – 07) to which this protocol will be added
 - b. Principal Investigator sponsoring the additional study (Must be a member of the CIT consortium)
 - c. Letter from the CIT Center PI indicating support

- II. Investigative Team
 - a. List of Study non-CIT investigators and description of their contributions to the study, with copies of their CVs

- III. Protocol (Requires the following information. May submit a formal protocol if available.)
 - a. Specific Aims
 - b. Background and Significance
 - c. Preliminary Studies
 - d. Experimental Design
 - i. Inclusion/Exclusion Criteria (Study population) if different from sponsoring study
 - ii. Endpoints and time points
 - iii. Methods for any additional assessments
 - e. Statistical and Data Management Considerations
 - i. Statistical methods
 - ii. Sample size and power or precision justification
 - f. Data Management methods

- IV. Human subjects considerations
 - a. Additional risk to the subjects
 - b. How will the additional risks be recognized and minimized
 - c. Additional burden to the subjects

- V. Effect on Sponsoring Study
 - a. Additional assessments (Will these effect those of the sponsoring study in any way? If so, explain and justify.)
 - b. Additional assessment times
 - c. Additional blood volume
 - d. Other

- VI. Effects on Sponsoring Center (Please describe who will be responsible for supplying these resources and who will be responsible for the costs associated with these additional requirements)
- a. Additional burden on center staff
 - b. Additional burden on investigators
 - c. Additional burden on local laboratories
 - d. Additional burden on others
- VII. Effects on NIH and DCC (Please describe the additional requirements in the following areas and who will be responsible for the real or indirect costs associated with these requirements)
- a. Additional regulatory oversight
 - b. Additional safety (SAE) oversight
 - c. Additional DSMB oversight
 - d. Additional central laboratories requirements
 - e. Additional sample collection kits and supplies
 - f. Additional data acquisition and database requirements
 - g. Additional statistical analysis and reporting requirements
- VIII. References Cited

**Clinical Islet Transplantation Consortium
External Ancillary Study Application
Outline**

- I. Sponsoring Study
 - a. Study (CIT 01 – 07) whose patients will be used in this Ancillary Study
 - b. Principal Investigator sponsoring the additional study.
 - c. Letter from the CIT Center PI indicating support

- II. Investigative Team
 - a. List of Study non-CIT investigators with copies of their CVs

- III. Protocol: Attach a copy of the study protocol

- IV. Financial Support: How will this Ancillary Study be supported?

- V. Human subjects considerations
 - d. Additional risk to the CIT subjects
 - e. How will the additional risks be recognized and minimized
 - f. Additional burden to the CIT subjects

- VI. Effect on Sponsoring Study
 - g. Additional assessments (Will these effect those of the sponsoring study in any way? If so, explain and justify.)
 - h. Additional assessment times
 - i. Additional blood volume
 - j. Other

- VII. Effects on Sponsoring Center (Please describe who will be responsible for supplying these resources and who will be responsible for the costs associated with these additional requirements)
 - k. Additional burden on center staff
 - l. Additional burden on investigators
 - m. Additional burden on local laboratories
 - n. Additional burden on others

- VIII. Effects on NIH and DCC (Please describe the additional requirements in the following areas and who will be responsible for the real or indirect costs associated with these requirements)
- o. Additional regulatory oversight
 - p. Additional safety (SAE) oversight
 - q. Additional DSMB oversight
 - r. Additional central laboratories requirements
 - s. Additional sample collection kits and supplies
 - t. Additional data acquisition and database requirements
 - u. Additional statistical analysis and reporting requirements

IX. References Cited