TEDDY ANCILLARY STUDIES
DEFINITION AND GUIDELINES

Introduction

TEDDY Study data and the biosample repository are valuable resources for the investigation of type 1 diabetes etiology and pathogenesis. The use of this material for TEDDY investigators is determined by TEDDY leadership through its committees and as a result of manuscript proposals which are reviewed and approved by the TEDDY Publications and Presentations Committee. These, collectively, are called TEDDY studies. Proposals from investigators who do not wish to work within this framework are called ancillary studies.

Ancillary studies will be evaluated with careful consideration of their potential impact on the objectives and performance of the TEDDY Study. Studies that complement the objectives and thereby enhance the value of the TEDDY Study are strongly encouraged. These studies however, must not interfere with the continued interest and participation of the study subjects and investigators. To protect the interests of the TEDDY Study, each ancillary study proposal must be individually reviewed and approved by the TEDDY Ancillary Studies Committee before its initiation. All approved ancillary studies will be reviewed by the Ancillary Studies Committee yearly for progress and impact on the TEDDY Study as a whole.

The TEDDY Study has adopted policies and procedures in support of its commitment to sharing data with the scientific community while also protecting the privacy of participants. In accordance with the TEDDY Data Sharing Policy, data are made publicly available via designated controlled-access data repositories. Investigators are encouraged to determine if the TEDDY study data they are seeking can be directly requested from designated NIH Data Repositories. If the desired data is available through the NIH Data Repositories, then an investigator does not need to submit a TEDDY ancillary study proposal and can move forward with seeking approval and data directly from the appropriate NIH Data Repository.

Ancillary Study Definition

An ancillary study is defined as externally funded (not TEDDY-funded) research involving TEDDY Study subjects' data that is not currently available through the NIH Data Repositories (see section below for more details) and/or samples. The investigator for the conduct of the ancillary study is a partner in the TEDDY Study and is therefore obliged to follow the rules and regulations governing the study as defined in the study protocol and by the Steering Committee.

Before submitting a TEDDY ancillary study proposal, the investigator should first confirm if the desired data is or is not already publicly available via the designated controlled-access data repositories (if the desired data is available through the NIH Data

Repositories, a TEDDY ancillary study proposal is not needed). TEDDY data are submitted to designated public NIH Data Repositories in segments that reflect the study's progress. These data releases are submitted at different time points and to various repositories, depending on funding agency requirements and the nature of the data. Please see links below for more detailed information.

- TEDDY NIH Data Repository Submissions
- Data Request Instructions
  - The database of Genotypes and Phenotypes (dbGAP)
  - The NIDDK Central Repository
  - The Sequence Read Archive (SRA)
  - The Metabolomics Workbench
  - The MassIVE Repository

If the data being requested is not available through the NIH Data Repositories:

Regardless of the funding status of the proposed study, if the proposal requires TEDDY Data Coordinating Center (DCC) input, then it will be considered an ancillary study subject to all TEDDY policies and procedures, including those of the TEDDY Publications and Presentations Committee. The TEDDY DCC will charge $250 per hour plus 50% indirect costs for time spent on preparation of the data.

If biological samples are being requested:

1. If the proposal has already received external funding, the investigator should contact the TEDDY DCC at TEDDY@epi.usf.edu to request the samples. The proposal will not be reviewed by the Ancillary Studies Committee as it has already been reviewed and approved by the funding agency. The TEDDY DCC will charge $250 per hour plus 50% indirect costs for time spent on identification of samples and communication with the Fisher BioServices Sample Repository. The Fisher BioServices Repository will charge $12.88 per sample for pulling and aliquoting (minimum charge per order $522.65) or if the ancillary study does not require aliquoting, $8.86 per sample for pulling (minimum charge per order $489.45). The ancillary study will be responsible for all shipment costs from the Repository to the ancillary study lab.

2. If the proposal has not already received external funding, the investigator should submit the proposal to the TEDDY DCC at TEDDY@epi.usf.edu. The TEDDY Ancillary Studies Committee will examine the proposal and provide feedback if the samples requested are available. The TEDDY DCC will charge $250 per hour plus 50% indirect costs for time spent on identification of samples and communication with the Fisher BioServices Sample Repository. The Fisher BioServices Repository will charge $12.88 per sample for pulling and aliquoting (minimum charge per order $522.65) or if the ancillary study does not require aliquoting, $8.86 per sample for pulling (minimum charge per order $489.45).

The ancillary study will be responsible for all shipment costs from the Repository to the ancillary study lab.

Reasons for Required Approval of Ancillary Studies

Investigators and subjects are entitled to prior assurance that all ancillary studies are of high scientific merit and that no ancillary study will:

1. Cause a deviation from the defined study protocol.
2. Complicate the interpretation of the study results.
3. Potentially adversely affect subject cooperation or interest in the study.
4. Jeopardize the public image of the study.
5. Create a significant diversion of study resources locally or at the coordinating center or any other unit.
6. In any way negatively influence the cooperative spirit of the collaborating investigators.
7. Require use of samples for a study of low priority as deemed by the Steering Committee.
8. Otherwise compromise the scientific integrity of the study.

Review by the Ancillary Studies Committee

All proposed ancillary studies will be submitted to the TEDDY DCC which will coordinate its review by the TEDDY Ancillary Studies Committee. The DCC, in consultation with the Chair of that committee, will identify at least two reviewers with such expertise as may be necessary if not already represented by the membership of the Ancillary Studies Committee. It will arrange for reviews and conference calls of committee members to discuss any proposed study. The Ancillary Studies Committee shall vote on the proposed ancillary study.

Funding for Ancillary Studies

The TEDDY Study does not provide funds for ancillary studies. If funds are needed, the investigator must explore other avenues such as submission of a research grant application, or use other sources of funds, i.e., foundations. The source and amount of anticipated funds must always be identified in an application to the Ancillary Studies Committee.

The ancillary study applicant should be aware that both the aliquoting and shipping of biological samples and the provision of data cannot be provided free of charge. The cost rates of these services must be taken into account in the application for external funding. The Fisher BioServices Repository will charge $12.88 per sample for pulling and aliquoting (minimum charge per order $522.65) or if the ancillary study does not require aliquoting, $8.86 per sample for pulling (minimum charge per order $489.45). The ancillary study applicant will be responsible for all shipment costs from the Repository to the ancillary study lab. The TEDDY DCC will charge $250 per hour plus 50% indirect

costs for time spent on identification of samples and/or preparation of data for the ancillary study.

Preparation of Proposals for Ancillary Studies Committee Review

The proposal submitted to the Ancillary Studies Committee should follow the National Institutes for Health (NIH) research grant (R01) format.

1. It should include a description of the objectives, methods, significance and plans for analysis.
2. If TEDDY samples are being requested, the type of sample, required volume and timepoints should be specified in the proposal.
3. The proposal should discuss the measures to be taken to ensure subject safety and confidentiality, and a statement by the investigator on the potential impact of the ancillary study on the TEDDY Study trial.
4. If applicable, prior approval by the appropriate Human Subjects Committee should be demonstrated.
5. Information regarding the source of funding should be provided in the proposal. It should clearly indicate the resources available for this study. If resources are being sought from granting agencies this must be indicated in the application.

To facilitate the review of the proposal the investigator should specifically address each of the following points, which will be examined in detail. Responses must be clearly delineated in a document that is separate from the formal grant proposal:

1. The scientific merit of the proposal and the potential contributions that the proposal will make to the TEDDY Study.
2. That the ancillary study does not cause a deviation from the defined study protocol.
3. That the proposed study does not complicate the interpretation of the results of the TEDDY Study.
4. That it does not adversely affect subject cooperation and participation.
5. That the volume of whole blood or sera taken from subjects does not exceed safe or prudent limits.
6. That the proposed study does not create a significant diversion from the TEDDY Study.
7. That the study does not divert or expend resources from the TEDDY Study either locally or at the DCC.
8. That the study does not adversely influence the cooperative spirit of the collaborating investigators.
9. That the study does not compromise the scientific integrity of the TEDDY Study.
10. That adequate resources are available to complete the proposed study or are requested from granting agencies.
11. That techniques and assays essential to the study are well established in the laboratory.

12. Results of ancillary studies will not be revealed to either TEDDY Study participants or their clinical team unless as called for in the description of the proposal.

Finally, a yearly report summarizing study progress, results, and the impact of the ancillary study on the TEDDY Study will be submitted to the TEDDY Ancillary Studies Committee and the TEDDY Steering Committee and reviewed every 12 months for continued approval by TEDDY.

Procedures for Obtaining Approval

The investigator should submit their ancillary study proposal to the DCC at the University of South Florida (TEDDY@epi.usf.edu) which will then distribute it to the Ancillary Studies Committee. To ensure a thorough scientific review the Chairman of the Ancillary Studies Committee may elect to seek outside expert opinion in advance to the committee meeting, as described above. A simple majority vote constitutes an approval by the Ancillary Studies Committee when a quorum of at least 4 members is present. The investigator will be notified within one week of the meeting of the approval status of his/her proposal.

Publication of Approved TEDDY Ancillary Studies

In accordance with TEDDY's Publications and Presentations Policies, all manuscripts written by ancillary study investigators should be submitted to the DCC to be reviewed for appropriate study attribution and acknowledgment prior to journal submission. Any ancillary study manuscript, abstract, presentation, or press release must acknowledge that the TEDDY Study Group is funded by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health (NIDDK-NIH) using the following statement:

"The TEDDY Study is a collaborative clinical study funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Institute of Environmental Health Sciences (NIEHS), Centers for Disease Control and Prevention (CDC), and Breakthrough T1D (formerly JDRF) . This manuscript was not prepared in collaboration with the investigators of the TEDDY Study Group and does not necessarily represent the official views of the TEDDY Study or the National Institutes of Health."

Non-ancillary Studies

Studies that can obtain needed data from the NIH Data Repositories are not considered ancillary studies, unless the investigator chooses to submit the proposal for TEDDY review. Any study requiring TEDDY Data Coordinating Center assistance in the design, analysis, planning, or requests data from the DCC, is regarded as an ancillary study, subject to TEDDY policies and procedures. Studies needing samples must work with the

DCC, since the samples are available only through the DCC. If the request is more than sample identification and availability, then the proposal will also be considered an ancillary study, subject to the aforementioned policies.

Return of samples to the Fisher BioServices Sample Repository

Once analyses are completed, the ancillary study should return any leftover biological samples to the Fisher BioServices Sample Repository. The ancillary study should budget for the payment of the return of the TEDDY samples. The ancillary study should contact the DCC (TEDDY@epi.usf.edu) for information on returning the samples.