Diabetes Prevention Program Outcomes Study (DPPOS) Ancillary Studies Policy

I. Overall Principles

Ancillary studies offer opportunity for maximizing the scientific impact and research benefits that can be derived from the resources developed during the course of the DPP and DPPOS. Investigators within and outside the DPPOS Study Group are encouraged to submit proposals for ancillary studies. Ancillary studies will be evaluated with careful consideration of their potential impact on the objectives and performance of the DPPOS. Ancillary studies that complement the objectives and thereby enhance the value of these studies are to be encouraged. Such studies should augment and promote the continued interest of both participants and investigators. To protect the integrity of the major DPPOS study, a proposal to conduct an ancillary study must be reviewed and approved by the Ancillary Study Committee and the Steering Committee before its initiation. No center will be required to participate in an ancillary study. Ancillary studies must also be approved by the Steering Committee for impact on the study as a whole.

II. Definition of an Ancillary Study

An ancillary study is defined as research or data collection involving study sites, participants, or specimens, using any technique, medication, procedure, questionnaire, or observation other than those set forth in the Protocol. The investigator responsible for the conduct of an ancillary study may or may not be a member of the DPPOS Study Group. If a proposal for an ancillary study is made by an individual who is not a member of the DPPOS Study Group, a member of the Study Group must be a co-investigator. A member of the DPPOS Study Group who serves as a co-investigator must be scientifically involved in the design, execution, and interpretation of the ancillary study. In addition, he/she shall be responsible for ensuring that DPPOS policies and procedures are observed during the conduct of the ancillary study.

III. Criteria

III. A. Reason for Requirement of Approval

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

- Cause a deviation from the protocol
- Confound interpretation of the DPP and/or DPPOS results
- Adversely affect participant cooperation
- Jeopardize the public image of the DPPOS

- Create a significant diversion of the DPPOS resources, at the clinical sites or at the Coordinating Center or any other level
- In any way negatively influence the cooperative spirit of the collaborating investigators
- Otherwise compromise the scientific integrity of the DPP and/or DPPOS

III. B. Approval Required for Ancillary Studies

The Ancillary Studies Committee welcomes preliminary concept proposals (maximum length two pages) before the submission of a full proposal. Ancillary studies will receive a primary, secondary, and statistical review. An outside reviewer may be used if there is no expertise within the study in a specific area. The Ancillary Studies Committee shall meet to consider new proposals and review the progress of approved ancillary studies at quarterly intervals (January, April, June, and December). The Ancillary Studies Committee will submit its recommendation to the Steering Committee.

After approval by the Ancillary Studies Committee, the Steering Committee, and the NIDDK, final approval is contingent upon the Steering Committee receiving a letter signed by the principal and all collaborating investigators in which they agree to abide by the policies for ancillary studies herein described, including that regarding publication or presentation of results. Approved ancillary studies will be reviewed by the Data, Safety, and Monitoring Board (DSMB). Applicants whose proposals are denied by the Ancillary Studies Committee can appeal to the Steering Committee for reconsideration.

III. C. Funding of Ancillary Studies

The DPPOS will not provide funds for ancillary studies. In particular, no funds are provided for Central Biochemistry Laboratory or the Coordinating Center activities or services in support of ancillary studies. If funds are needed, the investigator must explore other avenues such as: 1) submission of a research grant application or 2) use of other sources of funds (i.e., a foundation, drug company, etc.). The anticipated source of funds must always be identified. Ancillary studies that require extensive data retrieval, analysis, or related services by the coordinating center must make adequate provision for defraying the cost of personnel time and effort. The exact FTE shall be determined in consultation with the DPPOS Coordinating Center.

III. D. Publication of Ancillary Study Results

All manuscripts, abstracts, or presentations for scientific meetings based on ancillary study data must follow the policies of the DPPOS Publications and Presentations Committee before publication or presentation.

III. E. Implementation

The request for approval of an ancillary study should be in narrative form. It should contain a brief description of the objectives, methods, significance of the study, plans for analysis and publications, and information regarding funding level and source. If a proposal for funding (e.g., a grant application) is being submitted elsewhere, the source of funding should be identified and the application may be used as the basis for the request. Full details should be given concerning any procedures or tests to be carried out

on a study participant, including any ophthalmologic, renal, cardiovascular, neurologic, psychological or other evaluation to be performed; any substances to be injected or otherwise administered to the participants; any observations to be made or procedures to be conducted on participants outside of the clinic; any extra clinic visits required of the participant or any prolongation of the participant's usual clinic visits; any additional specimens (blood, urine, etc.) to be obtained or additional procedures to be done on specimens collected according to the DPP and DPPOS Protocol. The proposal should discuss the measures to be taken to ensure participant safety and confidentiality and an assessment by the investigator(s) of the potential impact of the ancillary study on DPPOS. Prior approval by the appropriate Human Subjects Review Committee should be demonstrated.

The investigators should send their ancillary study proposal to the Coordinating Center, which will distribute it to all members of the Ancillary Studies Committee. The proposal should be written in sufficient detail so that the Ancillary Study Committee can assess the study's scientific merit and potential impact on the DPP and DPPOS. This proposal should include a power calculation and should generally follow the template provided with the DPPOS Ancillary Studies Application package.

To ensure a thorough scientific review, the Chair of the Ancillary Studies Committee may elect to seek outside expert opinion in advance of the Committee meeting. In general, the ancillary proposals will be reviewed by two investigators. A statistical review by the Coordinating Center will also be done. Upon completion of the scientific and statistical reviews, the Chair of the Ancillary Studies Committee will convene a meeting of the Ancillary Studies Committee to discuss these reviews and vote on the merits of the proposal under review. Approval or disapproval is based on a simple majority of the Ancillary Study Committee. A copy of the Ancillary Studies consensus statement will be sent to the submitting investigator(s).

The Ancillary Study Consensus statement and approval will then be forwarded to the Steering Committee. Each Steering Committee member should respond to the Chair of the Ancillary Study Committee within one month. A majority of the voting Steering Committee members must approve the proposal. The DPPOS Data, Safety, and Monitoring Board will be informed of all recommendations of the Ancillary Studies Committee and Steering Committee. The investigator may proceed with the ancillary study once it has been approved by the Steering Committee and funding is available.

In the event that the Ancillary Studies Committee disapproves a proposed ancillary project, the investigator(s) can appeal to the Steering Committee, whose decision may override that of the Ancillary Studies Committee. If the Steering Committee also disapproves of the ancillary study, the proposed study will not be undertaken.

The Ancillary Studies Committee will maintain documentation of the final study design and any later modifications that are approved by the Steering Committee, including any DPPOS data or specimens that are approved to be released.

III. F. Protocol Changes
If the Ancillary Study Committee feels that the proposed ancillary study requires a change in protocol, the committee recommendation must be submitted to the Steering Committee for final consideration and approval.

III. G. Time Line
The Ancillary Study Committee will meet at quarterly intervals (January, April, June, and December) to consider applications and will work expeditiously to minimize delay in approving meritorious proposals. However, prospective investigators should understand that the approval process by the Ancillary Study Committee may take 90 days and that the approval by the Steering Committee may take another 30 days. Therefore, early submission is strongly recommended, especially if approval of an ancillary proposal is deemed necessary in order to secure funding for the proposed research.

III. H. Determination of Priority
Proposals for ancillary studies will ordinarily be reviewed and adjudicated on a first-come, first-served basis. Proposals with identical or closely related scientific objectives, submitted contemporaneously or within the same quarterly review period, will be reviewed and adjudicated on their scientific merits. For efficient use of available resources and to maximize their scientific value, investigators with similar interests are encouraged to submit broad collaborative applications.

III. I. Procedures for Requests of DPP/DPPOS Data
A list of specific items such as participant samples, variables, or other data samples required should be submitted with the original Ancillary Study Proposal. Once an Ancillary Study has been approved, a Coordinating Center statistician will contact the principal investigator to confirm and review the materials requested. In order to keep track of data/samples requested and obtained, the Coordinating Center requires that investigators provide and maintain a status database. You will also be required to send an annual report containing an account of data collected by the Ancillary Study and specimens or data requested and obtained from CBL or the Coordinating Center.

III. J. IRB Requirements
The following documents should be submitted to the Coordinating Center for each clinic that is going to be involved in an ancillary study:

(1) Letter of agreement
(2) IRB approval letter
(3) Approved consent (any future consents should also be sent to the CoC)
(4) HIPAA data use agreement

III. K. Initiation and Progress Report
The Principal Investigator of an approved ancillary study shall provide a brief (2-page maximum length) status report on the progress of the study to the Ancillary Studies Committee every 6 months. The progress report should include the following information:

1. Date of initiation of ancillary study
2. Current or pending sources of funding
3. Number of subjects enrolled
4. Summary of results obtained during the project period
5. Future goals and expected completion date of ancillary study

Approval shall lapse, if the study has not been initiated after 1 year from the date of initial approval, in the absence of extenuating circumstances. Significant deviation from the research plan or scientific, ethical, or procedural infringements will be grounds for termination of an ancillary study.