NATIONAL INSTITUTES OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

TERMS AND CONDITIONS OF AWARD FOR LARGE SCALE RESEARCH PROJECT APPLICATIONS FOR CLINICAL TRIALS, PREVENTION AND CONTROL INTERVENTIONS, AND EPIDEMIOLOGICAL STUDIES

A. Applicability. These special Terms of Award are in addition to and not in lieu of otherwise applicable OMB administrative guidelines, HHS grant administration regulations in 45 CFR part 74 and 92, and other HHS, PHS and NIH grant administration policy statements.

The administrative and funding instrument used to pay research projects involving clinical trials, prevention and control interventions, or epidemiological surveys in excess of $500,000 direct cost per year (at a single institution or in the aggregate for studies proposing multi-institutional collaborative arrangements submitted as either subcontracts to a single application or as separate applications) shall be a cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism) in which substantial NIDDK scientific and/or programmatic involvement with the awardee is anticipated during performance of the activity. For single applications, the dollar limit excludes indirect costs of any subcontracts that are reported as a direct cost on the application budget page summary.

Under the cooperative agreement, the NIDDK purpose is to support and/or stimulate the recipient's activity by involvement in and otherwise working jointly with the award recipient in a partner role, but it is not to assume direction, prime responsibility, or a dominant role in the activity.

Consistent with the above concept, the dominant role and prime responsibility for the activity reside with the awardee(s) for the project as a whole, although specific tasks and activities in carrying out the studies will be shared among the awardees and the NIDDK Project Scientist or designee.

Under the cooperative agreement, a relationship will exist between the recipient of these awards and the NIDDK, in which the performers of the activities are responsible for the requirements and conditions described below, and agree to accept program technical assistance, advice, and/or other coordination above and beyond normal program stewardship from a named NIDDK Project Scientist in achieving the project objectives.

Failure of an awardee to meet the performance requirements, including these special terms and conditions of award, or significant changes in the level of performance, may result in a reduction of budget, withholding of support, suspension and/or termination of the award.

B. Awardee Rights and Responsibilities.

The Awardee is responsible for:

1. Research design and protocol development, including definition of objectives and approaches, planning, implementation, participant recruitment and follow-up, data collection, quality control, interim data and safety monitoring, final data analysis and interpretation, and publication of results.

2. Establishing a Steering Committee to coordinate and manage the project. Awardee(s) will name investigators to serve as members on a Steering Committee and other subcommittees, as appropriate, meeting periodically. Awardees will be required to accept and implement the common protocol(s) and procedures approved by the Steering Committee.

3. Designating Protocol Chairs. The Principal Investigators (for studies involving multiple coordinated awards) shall designate a single Protocol Chairperson (if the Principal Investigator does not assume this role) for each protocol within the described research plan. The Protocol Chairperson shall function as the scientific coordinator for the protocol and shall assume responsibility for obtaining approval to implement the protocol from the Steering Committee and for developing and monitoring the protocol. Any significant modifications to approved protocols must be submitted to the Steering Committee by the Protocol Chairperson.

4. Implementing the core data collection method and strategy collectively decided upon by the Steering Committee. For a study involving multiple institutions, it is the responsibility of each awardee/site to ensure that data will be submitted in a timely way to the central Data Coordinating Center. Additionally, individual investigators/sites must demonstrate the ability to implement the strategy specifically designed for their individual study population.

5. Establishing mechanisms for quality control and monitoring. Awardees are responsible for ensuring accurate and timely assessment of the progress of each study, including development of procedures to ensure that data collection and management are: (1) adequate for quality control and analysis; (2) for clinical trials, as simple as appropriate in order to encourage maximum participation of physicians and patients and to avoid unnecessary expense; and (3) sufficiently staffed across the participating institutions. For research involving multiple awards, strategies for the analyses of pooled data will be developed by the Steering Committee.

6. Submitting interim progress reports, when requested, to the NIDDK Program Director including as a minimum, summary data on protocol performance. For coordinated multiple awards or a multi-site single award, the Steering Committee may require additional information from individual awardees/sites. Such reports are in addition to the annual awardee noncompeting continuation progress report.

7. Establishing procedures, where applicable, for all participating institutions in coordinated awards to comply with FDA regulations for studies involving investigational agents or devices and to comply with the requirements of 45 CFR Part 46 for the protection of human subjects, and the NIH policy requirements for the inclusion of women, minorities and children.

8. Cooperating in the reporting of the study findings. The awardee(s) will retain custody of and have primary rights to the data developed under these awards, subject to the Government rights of access consistent with current HHS, PHS and NIH policies. The NIDDK will have access to and may periodically review all data generated under an award. Where warranted by appropriate participation, plans for joint publication with NIDDK of pooled data and conclusions, are to be developed by the Principal Investigator or Steering Committee, as applicable. NIH policies governing possible co-authorship of publications with NIDDK staff will apply in all cases. In general, to warrant co-authorship, NIDDK staff must have contributed to the following areas: (a) design of the concepts or experiments being tested; (b) performance of significant portions of the activity; and (c) preparation and authorship of pertinent manuscripts.

9. Support or other involvement of industry or any other third party in the study -- e.g., participation by the third party; involvement of study resources or citing the name of the study or NIDDK support; or special access to study results, data, findings, or resources -- may be advantageous and appropriate. However, except for licensing of patents or copyrights, support or involvement of any third party will occur only following notification of and concurrence by NIDDK.

10. Study investigators are encouraged to publish and to release publicly and disseminate results and other products of the study, in accordance with study protocols and governances.

11. The NIDDK has established Central Biosample, Genetic, and Data Repositories for the archival and storage of data and biosamples collected in large, multi-site studies funded by NIDDK. The Data Coordinating Center (DCC) will work with the NIDDK Biosample Repository to coordinate procedures for coding, shipping, processing, receipt, and storage of study samples that are to be maintained in the Repository. In addition, the DCC will coordinate with the NIDDK Data Repository to prepare the collected data for eventual archiving and distribution. All samples and data transferred to the Repositories will be under the custodianship of the NIDDK, although the study's Steering Committee will have proprietary control of and exclusive access to the samples and data for an agreed-upon period of time. Subsequently samples and data will be available to the wider scientific community in accordance with the NIH policy on Data Sharing (http://grants.nih.gov/grants/policy/data_sharing/ and, http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm#goals, and http://grants.nih.gov/grants/policy/data_sharing/data_sharing_faqs.htm) through a process that will include prioritized distribution based on review of the scientific merit of the proposed use. Therefore, it is expected that samples and data collected will be available to the broader scientific community, after a proprietary period, at no charge other than the cost of reproduction and distribution.

C. NIDDK Staff Responsibilities

An NIDDK Project Scientist will have substantial involvement in the project above and beyond normal stewardship and monitoring of the award, as described below.

1. Being the contact point for all facets of the scientific interaction with the awardee (s). As required for the coordination of activities and to expedite progress, NIDDK may designate additional NIDDK staff to provide advice to the awardee on specific scientific and/or analytic issues. Such staff may include another Project Scientist or Analyst, who will provide direct technical assistance to the awardees to optimize the conduct and/or analysis of the study; or who may assist in the coordination of activities across multiple sites.

2. For multi-institutional protocols, convening the first meeting of and subsequent participation in the Steering Committee that oversees study conduct. The NIDDK Project Scientist or designee will be a full participant and voting member of the Steering Committee and, if applicable, subcommittees.

3. Serving as a resource with respect to other ongoing NIDDK activities that may be relevant to the protocol to facilitate compatibility and avoid unnecessary duplication of effort.

4. Substantial involvement assisting in the design and coordination of research activities for awardees as elaborated below:

a. Assisting by providing advice in the management and technical performance of the investigations, coordinating clearances for investigational agents held by NIDDK. The NIDDK may reserve the right to cross file or independently file an Investigational New Drug Application form with the FDA.

b. For multi-institutional protocols, through participation in the Steering Committee and with the agreement of the Principal Investigator(s) of any coordinating center and data management centers, the NDDK Project Scientist or designee may coordinate activities among awardees by assisting in the design, development, and coordination of a common research or clinical protocol and statistical evaluations of data; in the preparation of questionnaires and other data recording forms; and in the publication of results.

c. Reviewing and approving advice regarding the establishment of mechanisms for quality control and study monitoring.

An NIDDK Program Director identified in the Notice of Grant Award will be responsible for the normal stewardship and monitoring of the award. The Program Director may also serve as the Project Scientist.

The NIDDK Program Director responsibilities include:

1. Retaining overall programmatic responsibility for the award, and will clearly specify to the awardee the name(s) and role (s) of any additional individuals with substantial involvement in the project and the lines of reporting authority.

2. Interacting with the principal investigator(s) on a regular basis to monitor study progress. Monitoring may include: regular communications with the principal investigator and staff, periodic site visits for discussions with awardee research teams, observation of field data

collection and management techniques, quality control, fiscal review, and other relevant matters; as well as attendance at Steering Committee, data safety and monitoring board, and related meetings. The NIDDK retains, as an option, periodic external review of progress.

3. Reviewing and approving protocols to insure they are within the scope of peer review and for safety considerations, as required by Federal regulations. The NIDDK Program Director will monitor protocol progress, and may request that a protocol study be closed to accrual for reasons including: (a) accrual rate insufficient to complete study in a timely fashion; (b) accrual goals met early; (c) poor protocol performance; (d) patient safety and regulatory concerns; (e) study results that are already conclusive; and (f) emergence of new information that diminishes the scientific importance of the study question. The NIDDK will not permit further expenditures of NIDDK funds for a study after requesting closure (except for patients already on-study).

4. Making recommendations for continued funding based on: a) overall study progress, including sufficient patient and/or data accrual; b) cooperation in carrying out the research (e.g., attendance at Steering Committee meetings, implementation of group decisions, compliance with the terms of award and reporting requirements); and/or c) maintenance of a high quality of research, which will allow pooling of data and comparisons across multiple cooperative agreement awards for common data elements.

D. Joint Responsibilities

In addition to the interactions defined above, NIDDK Staff and Awardees shall share responsibility for the following activities:

1. Steering Committee.

A Steering Committee organized by the Principal Investigator (or P.I. of the Coordinating Center in the case of multiple coordinated awards) will be the main oversight body of the study.

The Steering Committee has primary responsibility to design research activities, establish priorities, develop common protocols and manuals, questionnaires and other data recording forms, establish and maintain quality control among awardees, review progress, monitor patient accrual, coordinate and standardize data management, and cooperate on the publication of results. Major scientific decisions regarding the core data will be determined by the Steering Committee. The Steering Committee will document progress in written reports to the NIDDK Program Director, and will provide periodic supplementary reports upon request.

The Steering Committee will be composed of all Principal Investigator(s), (including those of data coordinating /statistical centers, if any) and co-investigators as deemed necessary, and the NIDDK Project Scientist or designee. An initial meeting of the Steering Committee will be convened early after award by the NIDDK Project Scientist or designee. The final structure of the Steering Committee will be established at the first meeting. The NIDDK Project Scientist or designee will have voting membership on the Steering Committee, and as appropriate, its subcommittees. Such a committee usually will meet at least twice yearly.

A Chairperson, other than the NIDDK representative, will be selected by a vote of the members. The Chairperson is responsible for coordinating the Committee activities, for preparing meeting agendas, and for scheduling and chairing meetings.

2. Data Safety and Monitoring Board.

An independent Data and Safety Monitoring Board will be established by the NIDDK for Phase III clinical trials. The Data and Safety Monitoring Board will review interim results periodically and report to the Steering Committee and NIDDK. In all other studies where warranted, the NIDDK Program Director will facilitate and the awardee shall allow for interim data and safety monitoring through the establishment of an independent (external) Data and Safety Monitoring Board.

E. Arbitration

Any disagreement that may arise on scientific/programmatic matters (within the scope of the award), between award recipients and the NIDDK may be brought to arbitration. An arbitration panel will be composed of three members --one selected by the awardee (or the Steering Committee, with the NIDDK member not voting), a second member selected by NIDDK, and the third member elected by the two prior selected members. These special arbitration procedures in no way affect the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulations at 42 CFR Part 50, Subpart D, and HHS regulations at 45 CFR Part 16.