Notice of Opportunity for Collaboration

**TYPE 1 DIABETES TRIALNET MULTI-CENTER CLINICAL TRIAL OF THE EFFECTS OF METABOLIC CONTROL ON PROGRESSION OF TYPE 1 DIABETES**

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health of the Public Health Service (PHS) of the Department of Health and Human Services (DHHS) seeks collaborations with Industry to provide continuous subcutantous insulin infusion (CSII) pumps and continuous glucose sensors (CGSs) for use in a NIH-sponsored multi-center trial to evaluate the effects of intensive metabolic control in newly-diagnosed type 1 diabetes using a glucose sensor-insulin infusion pump closed-loop system at the onset of diabetes followed by continuous real-time glucose monitoring associated with continuous insulin infusion therapy.

**INTRODUCTION:**

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is planning to conduct a multi-center clinical trial to evaluate the safety and efficacy of tight metabolic control from diagnosis of type 1 diabetes on preservation of endogenous insulin production as measured by stimulated C-peptide. The trial will be conducted by investigators participating in the NIDDK sponsored TrialNet consortium. Study aims are to (1) determine if early and sustained restoration of metabolic control preserves C-peptide production in patients with newly diagnosed type 1 diabetes compared to patients receiving routine diabetes management, and (2) to ascertain whether allowing surviving islet cells to be less metabolically active will impact the underlying autoimmune process of type 1 diabetes.

The TrialNet Metabolic Control Study will enroll 108 patients, age 3-20 years, with newly diagnosed type 1 diabetes. Two-thirds of those enrolled will be randomized to the experimental treatment group while the other one-third will be randomized to standard treatment. Patients assigned to the experimental treatment group will have their insulin administered using a glucose sensor-insulin infusion pump closed-loop system within one week of diagnosis. If admitted for ketoacidosis, the closed-loop system will begin when meals are initiated. The closed-loop system will consist of a subcutaneous glucose sensor with insulin pump for intravenous or subcutaneous insulin delivery. On discontinuing the closed-loop system, patients will be started on CGS monitoring in real time in conjunction with a CSII pump. Patients assigned to standard treatment will receive conventional treatment for newly diagnosed type 1 diabetes. Study subjects will be enrolled over a one year period and then followed for two years. Primary outcome is the effect of tight metabolic control on the maintenance of the C-peptide area under the curve in response to a mixed meal at one year following enrollment and secondary outcomes will include the effect of metabolic control on immunologic assays relevant to type 1 diabetes.

**STUDY GOAL:** The goal of this study is to determine whether intensive metabolic control of type 1 diabetes from the time of diagnosis preserves residual $\beta$ cell function and therefore insulin secretion, improving blood glucose control and decreasing the negative short- and long-term consequences of hyperglycemia.

**CAPABILITY STATEMENT**: The “Collaborator Capability Statements” received in response to this announcement will be reviewed by a Selection Committee. The Committee will utilize the information provided in the “Collaborator Capability Statements” received in response to this announcement to help in its deliberations. It is the intention of the NIDDK that all qualified Collaborators have the opportunity to provide information to the Selection Committee through their Capability Statements. The Capability Statement should not exceed ten (10) pages of narrative (not including appendices) and should address all of the following selection criteria:

1. The statement must include all clinical data available on the use of the device(s).
2. The statement must include the most recent Investigator’s Brochure for such devices.
3. The statement should include a detailed plan demonstrating the ability to provide sufficient quantities of device(s) according to a mutually agreed upon schedule for the duration of the Metabolic Control Study to be conducted by TrialNet.

4. The statement should indicate willingness to supply the device(s) for immediate use in the TrialNet Metabolic Control Study.
5. The statement must indicate willingness to provide TrialNet with cross-reference letter for FDA access to the Device Master File and any other documents that may be necessary to file the IDE.
6. The statement must indicate willingness to have data collection and analysis performed by the TrialNet Coordinating Center (TNCC).
7. The statement must indicate willingness to agree to share the complete adverse event profile from human studies of the device(s) with the TrialNet Consortium.
8. The statement must indicate willingness to agree to share all unanticipated adverse device effects safety data from other studies involving their device(s) with the TrialNet Consortium.
9. The statement should indicate willingness to have the device(s) used in conjunction with other device(s) used in the TrialNet Metabolic Control Study.
10. The statement should address willingness to have the device(s) used at all TrialNet study sites involved in the Metabolic Control Study, including those in North America, Europe, Australia, and New Zealand.
11. The statement must address willingness to allow prompt publication of research results.
12. The statement must include a description of the methods that would be used to assure privacy and maintain confidentiality of data.

For the In-Hospital Closed Loop System:

1. The system should have a CGS which communicates with either a computer or hand-held device (PDA). The computer or device must contain an algorithm for determining insulin delivery based on the CGS signal (absolute value and rate of change) and must then communicate the information to a CSII pump.
2. The sensor should have accuracy with a Mean Absolute Relative Difference (MARD) of <15% excluding glucose values used to calibrate the device.
3. The algorithm should have been previously tested in human subjects with at least 500 hours of viable clinical data.

For the Out-Patient (Home) Real Time CGS Augmented CSII Pump System:

1. The real-time CGS should provide data in real time with rate of change information and alarms for hyper- and hypoglycemia.
2. The CSII pump should calculate insulin doses based on carbohydrate to insulin ratios and insulin sensitivity factors.
3. The information from the CGS and CSII pump needs to be downloadable into an integrated database for the subject to review glucose trends and patterns in association with their insulin doses and carbohydrate intake. This data must be able to be viewed by subjects and study staff on a study website.
4. The information from the CGS and CSII pump should be analyzable by a computer program which recognizes patterns and then provides study staff with recommendations for changes in insulin therapy which can then be communicated to the patient.
5. The Collaborator must be willing to work with the TrialNet Biostatistics Coordinating Center (BSC) to assure that the data generated by the CGS and CSII pump is in a format compatible with the BSC database.

Potential Industry Collaborators can provide some or all of the devices to be used during the TrialNet Metabolic Control study. Three to six TrialNet sites will conduct the study, and each site will need sufficient complete closed-loop apparatus for the study of two subjects simultaneously. In addition, the TrialNet sites will need to provide the components of the open-loop system to approximately 108 study subjects.

Potential Collaborators should submit a brief capability statement to the contact person noted below.

**SUPPLEMENTARY INFORMATION**: The Clinical Trial Agreement (CTA) into which the selected Collaborator is expected to enter is an agreement designed to enable a collaboration between Government laboratories and industry. IT IS NOT A GRANT, AND IS NOT A CONTRACT FOR THE PROCUREMENT OF GOODS OR SERVICES. The NIH is prohibited from transferring funds to a CTA collaborator. Under a CTA, NIH can contribute facilities, staff, materials, and expertise to the effort. The Collaborator typically contributes materials and expertise to the collaboration. This will be an in-kind collaborative arrangement.

**SUBMISSION DATES**: Only written capability statements received by the NIDDK on or before July 13, 2007 will be considered.

**CONTACT INFORMATION**:

Capability Statements should be submitted to:
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A formatted version of the Notice of Opportunity will be posted at:
http://techdev.niddk.nih.gov/TrialNetMCS.pdf