Notice of Opportunity for Collaboration

MULTI-CENTER CLINICAL TRIALS OF NOVEL THERAPIES FOR PATIENTS WITH WELL CHARACTERIZED GASTROPARESIS

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) seeks collaborations with industry to provide novel agents and devices for randomized, placebo-controlled, multicenter clinical trials of novel therapies for the treatment of patients with well-characterized gastroparesis.

Gastroparesis is a clinical syndrome characterized by multiple symptoms, including nausea, vomiting, bloating, abdominal pain, and early satiety. Physiological studies are characterized by delayed emptying of the stomach. There are multiple etiologies, such as diabetes and surgical injury to the vagus nerve, but the most common etiological category is idiopathic.

INTRODUCTION: The Gastroparesis Clinical Research Consortium (GpCRC) will conduct multicenter clinical research studies of patients with gastroparesis using defined clinical, diagnostic, and therapeutic interventions and will collect samples that may be useful for ancillary studies of etiology and pathogenesis.

A prospective Gastroparesis Registry of patients with diabetic, idiopathic, and post-surgical gastroparesis was created by the newly formulated NIDDK-funded Gastroparesis Clinical Research Consortium (GpCRC) that will allow prospective evaluation and follow-up of approximately 1,000 patients for 3 years on average. In addition to collecting clinical patient data, Registry patients will submit serum and DNA samples. Thus, ancillary studies to evaluate the natural history, pathophysiology, diagnosis, imaging studies, genetic factors, proteomics, metabolomics, and determinants of progression and severity of gastroparesis also pose collaborative opportunities.

STUDY GOALS: The GpCRC principal investigators wish to consider potential new diagnostics and therapeutics for patients with gastroparesis. The overall goal of the GpCRC is to perform clinical, epidemiological and therapeutic research in patients with gastroparesis using a standardized and coordinated approach to the evaluation and therapy of gastroparesis and to provide sufficient numbers of patients for the research. This will be done by using the Gastroparesis Registry which includes clinical information as well as serum and DNA samples.

SUMMARY: The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) is seeking proposals in the form of capability statements from companies that are interested in collaborating with GpCRC by providing novel therapeutic agents or devices for randomized, placebo-controlled, multicenter clinical trials of novel therapies, which could include: (1) prokinetic agents such as dopamine D-2 receptor antagonists, motilin receptor agonists, serotonin 5-hydroxytryptamine ($5\text{-}HT_4$) receptor agonists, or cholecystokinin receptor antagonists versus placebo; (2) tricyclic antidepressant and related agents such as selective serotonin or serotonin and norepinephrine reuptake inhibitors versus placebo; (3) botulinum toxin injection versus placebo; (4) antiemetic agents such as aprepitant or serotonin 5-hydroxytryptamine ($5\text{-}HT_3$) inhibitors such as palonosetron versus placebo; (5) novel analgesic agents such as pregabalin or gabapentin or derivatives of the inhibitory neurotransmitter gammaaminobutyric acid (GABA) versus placebo; (6) gastric electrical stimulation or other devices versus placebo; and (7) complementary therapies such as herbal medicine, acupressure and electrical acustimulation, or acupuncture versus placebo in patients with well characterized gastroparesis.

The NIDDK is also seeking capability statements from companies for ancillary studies to evaluate the natural history, pathophysiology, diagnosis, imaging studies, genetic factors, proteomics, metabolomics, and determinants of progression and severity of gastroparesis. Examples of potential

ancillary studies include: 1) Exploration of serum markers for gastroparesis and serum markers for disease activity to predict gastric histology either by themselves or in combination with other clinical, laboratory, proteomic, and metabolomic variables in the Gastroparesis Registry; 2) Exploration of the utility of these serum markers as surrogate markers of therapeutic response in study subjects participating in gastroparesis treatment trials; 3) Development of serum proteomic, metabolomic, and genomic expression arrays that are diagnostic of gastroparesis and that would provide surrogates for symptom severity as well as insights into the pathophysiology of this disease; and 4) Evaluation of the role of noninvasive imaging methods for assessing disease activity in gastroparesis.

SUPPLEMENTARY INFORMATION: Collaborative arrangements may be either Clinical Trial Agreements or Cooperative Research and Developments Agreements (CRADAs) pursuant to the Federal Technology Transfer Act of 1986 (FTTA, 15 U.S.C. 3710; and Executive Order 12591 of April 10, 1987, as amended by the National Technology Transfer and Advancement Act of 1995), as appropriate. Clinical Trial Agreements and CRADAs are agreements designed to enable certain collaborations between Government laboratories and non-Government laboratories. They are not grants, and not contracts for the procurement of goods/services. The NIDDK is prohibited from transferring funds to a Clinical Trial or CRADA collaborator. Under a CRADA, NIDDK can contribute facilities, staff, materials, and expertise to the effort. The collaborator typically contributes facilities, staff, materials, expertise, and funding to the collaboration. The CRADA collaborator receives an exclusive option to negotiate an exclusive or non-exclusive license to Government intellectual property rights arising under the CRADA in a pre-determined field of use and make contributions that qualify one or more of its employees as a co-inventor(s) of new technology developed under the CRADA. Examples of the Clinical Trial Agreement and the CRADA can be found at http://techdev.niddk.nih.gov/.

CAPABILITY STATEMENTS: The Steering 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 Steering Committee through their capability statements. The Capability Statement should not exceed 10 pages of narrative and should address the following selection criteria:

1. The proposed preparation must have been tested in Phase I trials in humans.
2. The statement should provide specific details of the methods to be utilized in the investigation of therapeutic agents including drugs, biologics, and devices in patients with gastroparesis and clearly describe important issues surrounding the evaluation of disease management in these patients.
3. The statement should include a detailed plan demonstrating the ability to provide sufficient quantities of the laboratory test agents in a timely manner for the duration of the study.
4. A description of laboratory tests that are needed including assays and required amount of specimens, to determine specific biomarker levels along with appropriate methods for performing.
5. A description of other core facilities and interactions with core facilities that are needed.
6. A description of the methods that would be used to assure privacy and maintain confidentiality of data.
7. The statement may include outcome measures of interest to the Collaborator. The specifics of the proposed outcome measures and the proposed support should include but not be limited to treatment and evaluation of gastroparesis, personnel, services, facilities, equipment, or other resources that would contribute to the conduct of the commercial development.
8. If appropriate, specific funding commitment to support the advancement of scientific research.

9. Must agree to have their preparation used in the above-mentioned GpCRC-developed protocols which will be conducted by GpCRC and will have data collection and analysis performed by the GpCRC Data Coordinating Center.
10. Must provide IND sponsor of the GpCRC studies with cross-reference access to a US FDA filing that contains the chemistry, manufacturing and controls information for the drug substance and drug product.
11. Dosing and Pharmacokinetic data from human studies must be provided for novel agents.
11. Adverse event profile from human studies must be provided.
12. Must agree to share (with GpCRC) all safety data from other studies involving their preparation as well as relevant efficacy data from other studies (updated Investigator Brochure, etc).
13. The statement must address willingness to promptly publish research results.

SUBMISSION DATES: Only written capability statements received by the NIDDK on or before December 15, 2006 will be considered. Applicants meeting the criteria as set forth in this announcement will be invited at the Applicants own expense to discuss with the GpCRC Steering Committee their plans, capabilities, and research findings pertinent to the study at a meeting of the GpCRC Steering Committee in January 2007 in Baltimore, MD.

CONTACT INFORMATION: Submit Capability Statements to:

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