NOTICE OF OPPORTUNITY FOR CLINICAL TRIAL COLLABORATION

UTILIZATION OF A URINARY ALKALINIZING AGENT IN A NIH SPONSORED MULTI-CENTER CLINICAL TRIAL IN PATIENTS WITH THE PAINFUL BLADDER SYNDROME

The National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health (NIH) of the Public Health Service (PHS) of the Department of Health and Human Services (DHHS) seeks collaboration with industry to provide a urinary alkalinizing agent and matching placebo for use in a National Institutes of Health sponsored multi-center clinical trial in patients with the painful bladder syndrome, including interstitial cystitis.

INTRODUCTION: The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is planning to conduct a randomized controlled clinical trial to evaluate if treatment with a urinary alkalinizing agent will substantially reduce urinary symptoms in patients with the painful bladder syndrome (PBS), including interstitial cystitis. The trial will be conducted by investigators participating in the Interstitial Cystitis Clinical Research Network (ICCRN). The two-arm trial will enroll approximately 260 patients with PBS and randomize them to either a urinary alkalinizing agent or placebo. Treatment will be administered in a double-blind fashion. The target population is patients with PBS who are either newly diagnosed, have had recent onset of symptoms, or have not been previously treated for this condition. Enrollment, expected to take approximately three years, will be performed at the following participating clinical centers: the University of Maryland, Queen's University (Kingston, Ontario, Canada), Stanford University, the University of Rochester, Henry Ford Hospital, William Beaumont Hospital (Royal Oak, MI), Loyola University Medical Center, University of Iowa, and the University of Pennsylvania. Central data collection and analysis will be performed by the NIDDK funded Data Coordinating Center at the University of Pennsylvania.

STUDY GOALS: The aim of this randomized clinical trial is to determine if treatment with a urinary alkalinizing agent for a period of 6 weeks will significantly reduce urinary symptoms associated with PBS compared to placebo. The primary outcome is a change in a Global Response Assessment (GRA). Secondary endpoints include several symptom indices, quality of life, and bladder diaries.

SUPPLEMENTAL INFORMATION: In 2003, the NIDDK established the second 5-year phase of the Interstitial Cystitis Clinical Research Network. The purpose of the ICCRN is to conduct high quality randomized controlled clinical trials in patients with the painful bladder syndrome (including interstitial cystitis). In the first 5-year segment of this program (known previously as the Interstitial Cystitis Clinical Trials Group) investigators conducted two randomized double-blind placebo controlled clinical trials; one trial evaluated the effects of hydroxyzine and pentosan polysulfate sodium and another examined the effects of intravesical administration of Bacillus Calmette Guerin

(BCG). Both trials were double-masked. The outline of a protocol for a clinical trial to evaluate a urinary alkalinizing agent has been recently approved by an independent NIDDK appointed Data and Safety Monitoring Board. It is anticipated that patient recruitment will begin in the summer 2004. However, the Collaborator will have the opportunity to comment on the study protocol prior to implementation. The Collaborator providing the alkalinizing agent will be expected to provide without charge sufficient drug for the 6-week drug treatment period for approximately 260 study participants. The Collaborator will also need to provide sufficient matching placebo without charge.

CAPABILITY STATEMENTS: A Selection Committee will utilize the information provided in the "Collaborator Capability Statements" to help in their deliberations. It is the intention of the NIDDK that qualified applicants will have the opportunity to provide information to the Selection Committee through their Capability Statements. Capability Statements related to use of a urinary alkalinizing agent to significantly reduce urinary symptoms associated with PBS should address the following criteria: time line for ability to provide drug and placebo after selection of Collaborator is determined, approved daily dose of the alkalinizing agent, previous studies of efficacy of the agent in treating patients with lower urinary tract symptoms and known side-effects of the agent. Capability Statements may not exceed 10 pages.

TERMS: The Collaborator will be expected to execute a Clinical Trial Agreement, an example of which can be found at http://techdev.niddk.nih.gov/forms.htm No funding from the Government is available.

SUBMISSION DATES: A written statement of interest is requested to be submitted by May 20, 2004 and all Collaborator Capability Statements must be submitted by June 2, 2004.

CONTACT INFORMATION**:** Submit statements of interest and Capability Statements to:

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