NOTICE OF OPPORTUNITY FOR CLINICAL TRIAL COLLABORATION

UTILIZATION OF AN ALPHA-ADRENERGIC BLOCKING DRUG IN A NIH SPONSORED MULTI-CENTER CLINICAL TRIAL IN MEN WITH LOWER URINARY TRACT SYMPTOMS ATTRIBUTABLE TO BENIGN PROSTATIC HYPERPLASIA

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Center for Complementary and Alternative Medicine, and the Office of Dietary Supplements 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 an alpha-adrenergic blocking drug and matching placebo for use in a National Institutes of Health sponsored multi-center clinical trial in men with lower urinary tract symptoms attributable to benign prostatic hyperplasia.

INTRODUCTION: The National Institute of Diabetes and Digestive and Kidney Disease, the National Center for Complementary and Alternative Medicine and the Office of Dietary Supplements is planning to conduct a randomized controlled clinical trial to evaluate if treatment with *Serenoa repens* or *Pygeum africanum* or an alpha-adrenergic blocking agent serving as an active control delays or prevents the progression of benign prostatic hyperplasia compared to placebo. Treatment will be administered in a double-blind fashion. The trial is known as the Complementary and Alternative Medicine for Urological Symptoms (CAMUS). The four-arm trial will enroll approximately 2,800 men over a period of two years. The following centers will be enrolling study participants: Northwestern University, Queen's University (Kingston, Ontario, Canada), Kaiser Permanente of Northern California, Washington University, the University of Texas Southwestern Medical Center, the University of Colorado, Yale University, New York University, Columbia University and the University of Maryland. Central data collection and analysis will be performed by the NIDDK funded Data Coordinating Center at the University of Alabama, Birmingham.

STUDY GOALS: The aim of this randomized clinical trial is to determine if treatment with *Serenoa repens* or *Pygeum africanum* or an alpha-adrenergic blocking agent selected as the active control will delay or prevent the progression of benign prostatic hyperplasia compared to placebo. The treatment period will range from four to six years. The

primary outcome is the time to clinical progression of benign prostatic hyperplasia defined as one of the following: an increase from baseline in the American Urological Association symptom score index of 4 or more points confirmed at the next scheduled study visit, acute urinary retention, recurrent symptomatic urinary tract infections or urosepsis, new incontinence or progression of minor incontinence, and initiation of active, unblinded therapy for benign prostatic hyperplasia, including phytotherapy, alpha-adrenergic blockers, 5-alpha reductase inhibitors, or any invasive therapy for benign prostatic hyperplasia.

SUPPLEMENTAL INFORMATION: The protocol for this trial has been approved by an independent Data and Safety Monitoring Board established by the NIDDK. It is anticipated that recruitment of study participants for this trial will begin in spring 2005. The Collaborator providing the alpha-adrenergic blocking drug will be expected to provide drug without charge for the expected 4-6 year treatment period for approximately 2,800 participants. The Collaborator will also provide sufficient matching placebo without charge. It is also expected that Collaborator will ship drug and placebo to a NIH-supported Drug Distribution Center free of 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 treatment with an alpha-adrenergic blocking drug for lower urinary tract symptoms in men with benign prostatic hyperplasia should address the following criteria: timeline for ability to provide drug and placebo after selection of Collaborator is determined, approved daily dose of drug, previous studies of efficacy of drug in treating men with lower urinary tract symptoms attributed to benign prostatic hyperplasia and known side-effects of drug. 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./forms.htm. No funding from the government is available.

SUBMISSION DATES: A written statement of interest should be submitted by August 4, 2004 and all Collaborator Capability Statements must be submitted by August 19, 2004.

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

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