Request for Proposals for the Conduct of a Clinical Study: Characterization of the Variability of Insulin Secretory Parameters in the Meal Tolerance and the Maximal Stimulation Tests of Healthy Subjects

Issued by The Biomarkers Consortium of The Foundation for the National Institutes of Health (FNIH) on April 15, 2011

Request for Proposals (RFP) Responses Due by Tuesday, May 31, 2011
Please, keep your responses between 10-15 pages in length (single spaced, font 11).

Eligibility
Any organization from the private and public sector is eligible to apply as long as it can meet the requirements below. Clinical sites have to be located in the continental US in order to be eligible.

Application Process (The protocol will be shared with interested and qualified applicants)
This is a two-step application process. First, indicate your intent to respond to the RFP by e-mailing Dr. Maria Vassileva, Biomarkers Consortium Scientific Program Manager (mvassileva@fnih.org), and copy Cheryl Melencio, Biomarkers Consortium Executive Assistant (cmelencio@fnih.org). Address each of the selection criteria in your letter of intent as described in the RFP below. After the initial screening, the study protocol will be shared with interested applicants. Second, submit your final application containing a statement of work and a detailed budget to the same e-mail address as indicated above. Call 301-594-6596 with any questions regarding the RFP submission and evaluation process.

AWARD Announcement by July 5, 2011
Anticipated Initiation of Screening and Enrollment: Sept. 15, 2011

RFP Executive Summary
The goal of this RFP is to elicit applications from Clinical Research Organizations, Academic Investigators, and private clinical institutes, interested in participating in the Biomarkers Consortium Beta Cell Project as the clinical sites recruiting the necessary subjects and performing the tests for the first protocol of the two methodological studies outlined below. The study protocol has been developed and will be shared with all interested applicants after they have indicated initial interest in responding to the RFP.

I. Overview of The Biomarkers Consortium and The Beta Cell Project
The Biomarkers Consortium (BC), a major public-private biomedical research partnership, was launched in October of 2006 by The Foundation for the National Institutes of Health (FNIH), the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and the Pharmaceutical Research and Manufacturers of America (PhRMA), with a mission to develop new biomarkers and strengthen the evidence for using them to help improve diagnosis, measure disease progression, guide treatment, accelerate drug development and target therapies to individuals. This public private partnership is positioned to leverage the expertise of all its stakeholders from government, industry, patient groups, academia, and other private entities, and to make consortium results broadly available to the public.

The Beta Cell Project is managed by the BC Metabolic Disorder Steering Committee (MDSC). This project describes the first phase of a two-stage strategy to enable the development of biomarkers that predict long-term beta cell function, particularly in response to an intervention or a new therapy for diabetes. The project addresses key methodological issues that are critical to the conduct of the second part of the strategy, which is a longitudinal study to qualify short-term markers as predictors of future beta cell function. This RFP reflects the first of a series of clinical studies to characterize these methodologies.

Background
Although there are many proposed testing regimens that are reported to estimate beta cell function, there is no accepted gold standard. Each investigator has their preferred way of conducting the testing, as well as analyzing data and reporting results. In addition, many of the more accepted testing regimens are technically challenging and complex, making them unsuitable for large, multi-center clinical studies.

This series of fundamental clinical studies will provide a foundation for the effective and confident use of selected methodologies in long-term, multi-center clinical trials. The main hypothesis for the methodology studies is that two specific tests, the Mixed Meal Tolerance Test (MTT) and the Maximal Stimulation Test (MaxStim), will be useful for the conduct of large longitudinal trials.

There are several objectives of this first study to qualify these tests of beta cell function. These include:
1. Determine within- and between-subject variability (CV) of MTT responses in healthy subjects
2. Compare insulin sensitivity as estimated by the insulin-modified, frequently sampled intravenous glucose tolerance test (FSIVGT) to MTT
3. Compare beta cell function (insulin secretory parameters) as estimated by MTT and FSIVGT
4. Determine within- and between-subject variability (CV) of glucagon and/or arginine stimulation tests (MaxStim) responses in healthy subjects; subjects with impaired fasting glucose and/or impaired glucose tolerance (IFG/IGT); and subjects with type 2 diabetes mellitus; choose between glucagon or arginine as the preferred test to develop further...
II. Project Specifications

Protocol Title: Characterization of the variability of insulin secretory parameters in the meal tolerance and the maximal stimulation tests of healthy subjects

Type of Study: Prospective Observational Clinical Trial

Number of Clinical Sites: One-to-three sites anticipated. All US-based.

Planned Contract Finalization Date: August 1, 2011

Estimated Screening Start Date: September 15, 2011


Enrollment Period Duration: 2 months

Last Patient last visit: Dec. 31, 2011

Total Number of Subjects: 20 to complete, 26 to enroll

Brief Overview of the Protocol: 26 healthy, obese (BMI 27-40) subjects (age range 30-65 y.o., equal number of men and women). Inclusion criteria - subjects who are generally healthy, take no medications, and have no history of diabetes or prediabetes. In addition to general health screening, subjects will have a fasting glucose measurement as well as undergo an oral glucose tolerance test which must be within normal limits. The study design is separated into three Visits. Each Visit will require one or more overnight stays in a clinical research facility. In Visits 1 and 2, subjects will undergo the MTT, an arginine MaxStim test, and a glucagon MaxStim test in random order. An insulin-modified FSIGT will be undertaken during Visit 3. All tests will be conducted on separate days. Visit 2 will occur approximately two to four weeks after Visit 1, simulating use in a clinical trial. The FSIGT will be conducted only once. Blood volume requirements will be less than a donation over the course of four weeks.

Additional details about the subsequent protocols: Following evaluation of healthy subjects, several additional studies will be undertaken, including those with prediabetes and diabetes mellitus. It is intended that these subsequent studies would also be conducted at the same site(s). Responding research organizations, therefore, need to provide evidence that they will be able to recruit subjects from these populations. Prediabetic subjects are defined as those with either impaired fasting glucose (a fasting glucose measurement between 100 and 125 mg/dL on two separate occasions) or impaired glucose tolerance (a two-hour post oral glucose tolerance test response between 140 and 200). Subjects with diabetes will be medication naïve, managed by diet and exercise, and with HbA1c< 7.5%.

III. Requesting the protocol

First, please review the criteria below. If your organization fits these criteria, then we encourage you to respond to this RFP and request the clinical study protocol. The characteristics of a potentially successful respondent include:

1. Prior experience with executing clinical studies of similar scope and size in GCP-compliant fashion.
2. Established reputation for excellence of clinical services.
3. Ability to record and manage data electronically, including CRF generation, monitoring, validation, and transfer, as well as identity protection.
5. Access to the appropriate patient populations to ensure timely recruitment.
6. Experience with performing the Meal Tolerance Test, Frequently Sampled Intravenous Glucose Test and Maximum Stimulation Arginine and Glucagon Tests is preferred.
7. Demonstrated ability to do the project within the indicated timeline and with a justified budget.
8. Prior experience with working on collaborative teams with representatives from all sectors will be considered valuable.
9. Ability to store plasma samples is a plus but not required.

To request the protocol, please send an e-mail to Dr. Maria Vassileva at mvassileva@fnih.org. You will receive a response within two weeks of receipt of your initial e-mail.

**IV. Budget assessment**
In consideration of this proposal, for applicable organizations such as academic institutions, the FNIH has a fixed indirect cost rate of 15%.

**V. Requested Information**
Please note the timelines above to be sure that they are achievable. FNIH will share the study protocol as soon as a confidentiality agreement is in place between the interested applicant and FNIH.

Also, indicate whether your organization could provide biorepository services for the remaining samples from these methodological studies. This is not a requirement for this RFP, but could be considered an asset for the project.