STATEMENT OF WORK
FOR
A CENTRAL TESTING LABORATORY
REQUEST FOR PROPOSALS

TITLE OF STUDY: Longitudinal Assessment of Bariatric Surgery Consortium (LABS)

DATE: March 17, 2005

Contact Person:

Deborah Dobransky-Fasiska, PhD
University of Pittsburgh
Epidemiology Data Center
Graduate School of Public Health
127 Parran Hall
130 DeSoto Street
Pittsburgh, PA 15261

Telephone: 412-624-9640
Fax: 412-624-3775
Email: DobranskyD@edc.pitt.edu

Project Coordinator:

Dawne Bolinger
University of Pittsburgh
Epidemiology Data Center
Graduate School of Public Health
127 Parran Hall
130 DeSoto Street
Pittsburgh, PA 15261

Telephone: 412-624-7531
Fax: 412-624-3775
Email: bolingerd@edc.pitt.edu
TABLE OF CONTENTS

I. PROJECT DESCRIPTION
   A. Background and Planning................................................................. 3
   B. Biochemical Measures .................................................................. 3
   C. Estimated Number of Biochemical Samples............................ 4

II. DESCRIPTION OF PROPOSED TASKS TO BE PERFORMED........ 4
   A. General Requirements for the Central Laboratory ................. 4
      1. Central Laboratory to maintain proficiency program .......... 4
      2. Perform biochemical testing .............................................. 4
      3. Provide biochemical testing materials & instructions .......... 4
      4. Location of clinical sites .................................................. 5
      5. Data Management ............................................................ 5
      6. Reports ............................................................................ 5
   B. Specific Tasks for Central Laboratory ........................................ 5
      1. Central laboratory to maintain QA ...................................... 5
      2. Perform testing.................................................................. 6
      3. Provide data to the Data Coordinating Center .................... 6
      4. Submit annual progress report & final report ...................... 6

III. DATA MANAGEMENT .................................................................... 7
   A. Overview.................................................................................... 7
      Biospecimen Tracking System................................................. 7
   B. Central Laboratory.................................................................... 8
      1. Sample tracking................................................................. 8
      2. Assay results..................................................................... 8
      3. Reports ............................................................................ 8

IV. COSTS.......................................................................................... 8
   A. Central Laboratory Costs.......................................................... 8
   B. Personnel Costs ..................................................................... 8

V. QUESTIONS..................................................................................... 8

VI. EVALUATION FACTORS.............................................................. 9
   A. General Evaluation................................................................. 9
   B. Technical Criteria ................................................................... 9
   C. Deadline................................................................................. 10
I. PROJECT DESCRIPTION

A. Background and Planning

It is expected that the Longitudinal Assessment of Bariatric Surgery (LABS) consortium will focus on the role of bariatric surgery in understanding and treating obesity and its complications. The LABS consortium is anticipated to enroll approximately 2,400 obese participants in 3 years, beginning in July, 2005 at six clinical sites and to follow each participant for up to 3 years. Active follow-up is scheduled to be completed by August 2008. Additional information on the study plans and goals can be accessed in the original RFP at:

Clinical Centers and Data Coordinating Center:

The Epidemiology Data Center at the University of Pittsburgh, Graduate School of Public Health has been funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to serve as the LABS Data Coordinating Center (DCC). The DCC will contract with central facilities for services required by the protocol. This statement of work is written on behalf of the LABS Steering Committee to solicit proposals from individuals to serve as the LABS Central Laboratory, under a subcontract to the LABS Data Coordinating Center at the University of Pittsburgh. Final selection and negotiation of a contract or contracts for the Central Laboratory will be conducted by the LABS DCC in consultation with the NIDDK and the LABS Steering Committee. The Request for Proposals does not commit the University of Pittsburgh to award a contract or to pay any costs incurred in the submission of the proposal, nor to procure or contract for any supplies or services. Final protocol decisions on measurements and storage will be based on both scientific and budgetary considerations.

This is a federally funded study. As such, any subcontractor chosen will be required to abide by federal subcontract clauses. It is anticipated that the services called for herein will be performed under a cost reimbursement type of subcontract, including a firm fixed-price component for unit costs on a per measurement basis. Measurement costs will be determined by including all personnel, overhead, supply, and indirect costs associated with the individual measure. As with most consortia, the study is subject to early termination by a Safety and Data Monitoring Board that will periodically be reviewing the data.

B. Biochemical Measures

Although the protocol decisions are not yet final, the Steering Committee is considering the following biochemical measurements on all participants (serum/plasma unless otherwise noted): fasting insulin, high sensitive C-reactive protein, non-esterified fatty acids, PTH, calcium, 25-OH-vitamin D, vitamin B12, iron, total iron-binding capacity, ferritin, creatinine, cystatin, urine creatinine, and urine albumin.

The frequency of collection for each analyte has not been finalized. The table that follows is an estimate of the number of samples for each analyte that will be collected per year over the course of the study. Adjustments have not been made for additional quality control samples and projected attrition rates.
C. Estimate Number of Biochemical Samples

<table>
<thead>
<tr>
<th>LABS-2 Study Dates</th>
<th>Number of Patients</th>
<th>Number of Biochemical Analyses *</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/01/05 to 6/30/06</td>
<td>1,152 (baseline)</td>
<td>16,128</td>
</tr>
<tr>
<td>7/01/06 to 6/30/07</td>
<td>2,304 (baseline &amp; 12 month)</td>
<td>32,256</td>
</tr>
<tr>
<td>7/01/07 to 6/30/08</td>
<td>2,400 (baseline, 12 month &amp; 24 month)</td>
<td>33,600</td>
</tr>
<tr>
<td>7/01/08 to 8/31/08</td>
<td>480 (12 month, 24 month &amp; 36 month)</td>
<td>6,720</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>88,704</td>
</tr>
</tbody>
</table>

* Includes number of samples analyzed for: fasting insulin, high sensitive C-reactive protein, non-esterified fatty acids, PTH, calcium, 25-OH-vitamin D, vitamin B\textsubscript{12}, serum iron, total iron-binding capacity, ferritin, creatinine, cystatin, urine creatinine, and urine albumin. The numbers have not been adjusted for extra samples or dropouts.

II. DESCRIPTION OF PROPOSED TASKS TO BE PERFORMED

A. General Requirements for the Central Laboratory

The Central Laboratory (CL) shall serve as the primary testing laboratory for LABS. The samples will be sent to the CL monthly in batches from 6 clinical sites. The CL shall provide uniform, efficient, and high quality testing and interpretation in support of the study. The Central Laboratory shall perform the following:

1. Provide documentation of a proficiency program and maintain quality assurance and control systems. Maintain good laboratory practices (GLP).
   a. In all laboratory techniques, the CL will follow the guidelines outlined by the Centers for Disease Control and Preventions (Morbidity and Mortality Weekly Report 36:28 1987) for preventing exposure to blood-borne pathogens.
   b. Include copies of quality control charts, tables and reports for the last year.

2. Perform whichever of fasting insulin, high sensitive C-reactive protein, non-esterified fatty acids, PTH, calcium, 25-OH-vitamin D, vitamin B\textsubscript{12}, iron, total iron-binding capacity, ferritin, creatinine, cystatin, urine creatinine, and urine albumin testing, that the final protocol calls for:
   a. Methodology: Provide detailed description of assays used for each analyte including product information on any reagent that is used, journal references for the methodology (if applicable), and your experience with each of the assays.
   b. Specify the volume of plasma, serum or urine required for each assay.
   c. Specify special requirements or limitations for collecting, handling, and processing specimens at the clinical centers, and for receiving specimens.
   d. Specify facilities and equipment that will be used for the laboratory analyses of LABS samples.

3. Provide (serum/plasma unless otherwise noted) fasting insulin, high sensitive C-reactive protein, non-esterified fatty acids, PTH, calcium, 25-OH-vitamin D, vitamin B\textsubscript{12}, serum iron, total iron-binding capacity, ferritin, creatinine, cystatin, urine creatinine, and urine albumin collection testing materials and instructions to the Clinical Centers. Specify equipment needed at Clinical Centers but not provided by CL (e.g. centrifuge):
   a. Specify special equipment or supplies that will be needed at the clinical sites for collection, processing or shipment of samples (e.g. refrigerated centrifuge, -70° freezer, dry ice, etc.).
b. Provide blood collection supplies to each clinical site (e.g. bulk tubes, visit packet blood collection kits).

c. Describe sample labels to be provided to each clinical site (e.g. pre-printed, bar coded, suitable for long-term storage at -70°C).

d. Provide sample shipping materials (e.g. Federal Express pre-printed labels, freezer boxes, shipper cartons).

e. Describe sample shipping procedures and fees per shipment from the clinics to the Central Laboratory.

4. Location of the clinical sites:

<table>
<thead>
<tr>
<th>Location</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>East Carolina University, Greenville, NC 27858</td>
</tr>
<tr>
<td></td>
<td>UC Davis Medical Center, Davis, CA 95817</td>
</tr>
<tr>
<td>Columbia-Presbyterian Hospital and Cornell University</td>
<td>New York, NY 10029-6574</td>
</tr>
<tr>
<td></td>
<td>University of Pittsburgh Medical Center, Shadyside Hospital, Pittsburgh, PA 15232</td>
</tr>
<tr>
<td>University of North Dakota, Neuropsychiatric Research Institute, Fargo, ND 58107</td>
<td>University of Washington, Seattle, WA 98195-6410</td>
</tr>
</tbody>
</table>

5. Data Management

a. Describe laboratory data management equipment and methods.

b. Describe quality control protocols for laboratory data entry and data management.

6. Reports

a. Prepare and submit progress reports annually and prepare a final report.

b. Provide software and formats used for reporting results.

c. Provide data to the Data Coordinating Center.

B. Specific Tasks for the Central Laboratory

1. Central laboratory to maintain a Quality Assurance (QA) and control system

a. The CL is encouraged to be enrolled in a proficiency program.

b. The CL shall perform satisfactorily on proficiency testing panels provided through independent evaluators such as the College of American Pathologists or a comparable program, and report results to the Data Coordinating Center within two weeks of the CL being notified of the results of its testing. If such certifications are current, provide them with your response to this statement of work.

c. Note normal physiological range of distribution for fasting insulin, high sensitive C-reactive protein, non-esterified fatty acids, PTH, calcium, 25-OH-vitamin D, vitamin B12, serum iron, total iron-binding capacity, ferritin, creatinine, cystatin, urine creatinine, and urine albumin data.

d. The CL shall maintain a Quality Assurance and Control System and provide records of Quality assurance to the Data Coordinating Center.

e. Include accuracy checks used and a plot of the checks over time.

f. Provide procedures for evaluating quality control data and criteria used.

g. Note quality control procedures with regard to unexpected results or outliers that include re-running the assay and notifying the Data Coordinating Center if the value is confirmed by the second result.

h. Describe policy and procedure for reporting alert levels for clinically significant
findings requiring notification/referral of participant prior to routine availability of results from the laboratory.

i. Specify the coefficient of variation (CV) for both intra- and inter-assay measurements.

j. Identify the technician(s) performing each analysis in the records.

2. Perform testing

   a. The CL shall perform all basic tests that are in the final protocol which may include: fasting insulin, high sensitive C-reactive protein, non-esterified fatty acids, PTH, calcium, 25-OH-vitamin D, vitamin B_{12}, serum iron, total iron-binding capacity, ferritin, creatinine, cystatin, urine creatinine, and urine albumin testing on samples provided by the clinical institutions’ laboratories. The required turn-around time for testing will be 28 calendar days.

   b. In responding to the Statement of Work, the CL must articulate the methodology they will employ in conducting the assays and monitoring the accuracy of assays.

3. Provide data to the Data Coordinating Center

   a. The CL shall provide results of all basic tests that are in the final protocol which may include: fasting insulin, high sensitive C-reactive protein, non-esterified fatty acids, PTH, calcium, 25-OH-vitamin D, vitamin B_{12}, serum iron, total iron-binding capacity, ferritin, creatinine, cystatin, urine creatinine, and urine albumin assays on biospecimens to the Data Coordinating Center within 28 calendar days of receipt of specimen. The CL and the Data Coordinating Center will determine the format of the results file and the procedure used to transfer the data based on an evaluation of current systems at both organizations.

   b. The CL shall keep, and provide a bi-weekly summary of, the laboratory records on the status of all biospecimens to the Data Coordinating Center, with information on numbers of vials, dates of arrival, testing and storage, testing results, deviations from protocol or good standard operating procedures, e.g. proper labeling and packaging, an account of all vials, etc.

   c. Describe mechanisms that will be implemented to assure data are accurately and completely provided to the Data Coordinating Center. This description should include, but not be limited to,

   - Receipt and logging procedures for biospecimens
   - Procedures for addressing protocol deviations (e.g., improper labeling/packaging)
   - Methodology for conducting and monitoring the accuracy of assays
   - Description of how assay results are maintained including entry/update of results data and the software utilized for these purposes.

4. Submit annual progress reports and prepare final report

   a. The CL shall include in each annual Progress Report a description of the number of samples received, the number of determinations of each assay, the overall results of determinations, the major problems encountered and resolved, and the summary quality control data. The report shall be narrative in form and shall include a summary of progress toward completion of each Statement of Work task for the CL, any changes in the procedures used, and problems encountered to date, including the CL’s assessment of specific impact of such problems on
estimated costs and the scheduled date of completion. In addition, the report shall include the following information:

i. Problems and solutions.
ii. Modifications in data collection or preparation procedures.
iii. Laboratory methods and procedures.
iv. Change in personnel.

b. At the end of the study, prepare a final report.

III. DATA MANAGEMENT

A. Overview

A biospecimen inventory database will be maintained at the Data Coordinating Center to track the collection, shipment, receipt, storage, subsequent use of, and test results from the various biospecimens. The database will be used to generate standard reports (e.g., accrual, delinquency, biospecimen availability and usage, laboratory test results) that will be submitted to the clinical centers, the repository, and central laboratory. For example, routine compliance reports will be sent to the clinical centers for which biospecimens are expected on a monthly basis. These reports will also notify clinical centers of any delinquent cases. Similar reports identifying biospecimens expected will be sent to the repository and central laboratory as a cross-check for biospecimens received. Ad hoc reports to the clinical centers, the repository and central laboratory will be generated when requested.

Based on expected recruitment, biospecimen shipments will be made monthly to the central laboratory by the clinical centers. For optimal efficiency to the central laboratory, three centers will make shipments on the first of the month and three will make shipments on the 15th of the month.

**Biospecimen Tracking System.** The figure below describes the data flow for biospecimen data.

---

**Figure: Biospecimen Tracking System**

- **Clinical Center**
  - Specimens
  - Tracking Logs
  - Compliance Reports
- **Repository**
  - Specimens
  - Tracking Logs
  - Confirmation Reports
- **Central Laboratory**
  - Specimens
  - Tracking Logs
  - Confirmation Reports

---

LABS Statement of Work for Central Laboratory
B. Central Laboratory

1. Sample tracking: CL personnel will enter tracking information into the biospecimen inventory database upon receipt of samples. The Data Coordinating Center distributed web-based data entry system will be used to collect and transmit this information.

2. Assay results: CL will provide results for all basic tests that are in the final protocol which may include: fasting insulin, high sensitive C-reactive protein, non-esterified fatty acids, PTH, calcium, 25-OH-vitamin D, vitamin B₁₂, serum iron, total iron-binding capacity, ferritin, creatinine, cystatin, urine creatinine, and urine albumin testing to the Data Coordinating Center within 28 calendar days of receipt of sample in an agreed upon electronic format. When possible, the Data Coordinating Center will accommodate existing laboratory systems.

3. Reports: The CL will provide to the Data Coordinating Center bi-weekly summaries (see Section B3b) as well as annual progress reports (see Section B4). The Data Coordinating Center will provide to the CL reports that identify inconsistencies in sample tracking, processing, or data. Data inconsistencies identified by the Data Coordinating Center will be addressed and resolved within a two-week period.

IV. COSTS

A. Central Laboratory Costs
   Include in your proposal, the following information for each measurement - Unit cost per determination including all overhead, direct and indirect costs since reimbursement will be by the unit. Indicate if unit costs will vary based on the number of samples assayed or stored.

B. Personnel Costs
   Include the number of dedicated personnel required to fulfill this subcontract and their level of laboratory expertise. Justify the number of personnel required to fulfill this statement of work.

V. QUESTIONS

Please provide information to the following:

1. Prior experience in serving as a central laboratory for other multi-center studies or research projects.

2. Biosketches for the key personnel who will be involved in this project. Describe the specific responsibilities of the individuals in the performance of the assays on the LABS samples. In the event of laboratory turnover, personnel level to be replaced by staff of comparable level.

3. Experience with providing electronic data to outside organizations which includes the ability to only send the data required by LABS.
4. Current commitments to other studies.

5. Lead time required for your laboratory to be set up and ready to receive specimens from LABS clinical centers for recruitment estimated to begin at July 1, 2005.


7. Willingness to field questions directly from the clinical sites regarding the samples and procedures. Willingness to work with the Data Coordinating Center to resolve any discrepancies with assay results that are identified once the results are transferred to the Data Coordinating Center. This requires a point person at the Central Laboratory.

8. Plans for participating in a centralized training session for clinic personnel. Attend training session held in Pittsburgh, PA and train coordinators in the proper procedure for collecting, preparing, packing and shipping samples (provide documentation).

9. Your interest in serving as a consultant/collaborator with the LABS investigators in the development of publications which include laboratory data/results.

VI. EVALUATION FACTORS

A. General

1. The evaluation will be based on the demonstrated scientific capabilities of the prospective proposal offerors in relation to the needs of the project set forth in this Statement of Work document. Proposals will be evaluated by a peer group of scientists.

2. The evaluation process may require offerors to undergo scientific testing of the preparation, processing, and analysis of selected samples. A site visit may be required.

3. Proposals should be limited to a maximum of 10 pages not including charts, budget information and biosketches.

4. Note: This statement of work reflects our understanding of the goals and objectives and related work to be conducted at this time. The scope of work and its specifications may be altered or refined, to be more consistent with new findings and knowledge. Should such changes occur prior to the deadline (below), they will be communicated to those applicants who send letters of intent.

B. Technical Criteria

Evaluation of proposals by the LABS Steering Committee will include, but is not limited to the following criteria listed in order of relative importance.

1. Technical Expertise
   Methods
   Equipment/Facilities
   Staff

2. Prior Experience
   Large studies
   Stability
   Institutional Support
3. Quality Control
   Maintain quality control procedures by continually monitoring data
   Internal procedures for sample receiving, tracking analysis
   Turn around time for data availability

4. Training and Manual development
   Experience
   Time line
   Participation in external programs
   Procedures for data entry/management
   Timeliness of feedback to centers, where appropriate

5. Capacity
   Commitments to other studies
   Organizational structure and support for the volume and variety of analyses/tasks

C. Deadline

1. For those interested in sending proposals, a non-binding letter of intent should be sent to Deborah Dobransky-Fasiska by March 31, 2005.
2. The deadline to submit proposals is May 2, 2005. Applications will be accepted by mail, fax, or electronically and must be received no later than May 2, 2005. Both the letter of intent and the proposal should be sent to the following address (electronic submissions are encouraged):

   Deborah Dobransky-Fasiska, PhD
   University of Pittsburgh
   Epidemiology Data Center
   Graduate School of Public Health
   127 Parran Hall, 130 DeSoto Street
   Pittsburgh, PA 15261
   412-624-9640
   Fax: 412-624-3775
   Email: DobranskyD@edc.pitt.edu

   Project Coordinator:
   Dawne Bolinger
   University of Pittsburgh
   Telephone: 412-624-7531
   Fax: 412-624-3775
   Email: bolingerd@edc.pitt.edu