Longitudinal Assessment of Bariatric Surgery (LABS-1)
Protocol
Version 4

Version 4: 02/16/06

Design Synopsis

Primary Objectives

- To assess the **safety** of bariatric surgery by estimating the prevalence of short term adverse outcomes in a multicenter cohort of patients undergoing bariatric surgical procedures
- To determine the associations between short term adverse outcomes after bariatric surgery and both clinical/demographic patient characteristics and features of operative/perioperative care

Type of Study

- Observational

Inclusion Criteria

- Patients at least 18 years of age who undergo bariatric surgery by a LABS certified surgeon

Exclusion Criteria

- Informed consent not obtained

Recruitment/ Sample Size

- Approximately 12,000 patients who undergo bariatric surgery will be recruited over a 4 year period

Duration of Follow-up

- 30 days following bariatric surgery

Outcome Measures

- 30-day mortality
- 30-day complications

Visit Schedule

- The Pre-Operative data collection will occur once a patient provides informed consent for information to be included in the LABS-1 database.
    - A Pre-Operative Evaluation Update will take place within 90 days prior to bariatric surgery. Information regarding smoking status, planned procedure/approach, medication use, blood pressure and co-morbid condition status will be updated at this time. Laboratory values will also be updated. The most recent laboratory values within 180 days prior to bariatric surgery will be recorded.
    - Weight will be obtained within 30 days of bariatric surgery.
- The Operative Form will be completed using information from the surgeon and operative notes.

- Follow-up assessment will occur approximately 30 days following bariatric surgery but is limited to what occurred within 30 days post-surgery.

1 Introduction

1.1 Background

Obesity has become one of the leading health concerns in the United States (US) [1]. Unfortunately, the traditional approach to weight loss consisting of diet, exercise, and medication generally achieves no more than a 5-10% reduction in body weight [2, 3] and regain to or above baseline after such weight loss occurs in more than 90% of people undergoing non-operative therapy within five years [4, 5].

Bariatric surgical procedures, which restrict stomach size or lead to decreased absorption of nutrients, are being increasingly performed to treat extreme obesity. These procedures can have dramatic benefits, such as improved control of blood sugar or even reversal of type 2 diabetes, but also carry substantial risks, including death.

Although an increasing number of people with morbid obesity and obesity-related complications are undergoing bariatric surgical procedures, there has been little systematic research to help determine the risks and benefits of bariatric surgery, or to provide guidance on appropriate patient selection. While there are many different types of bariatric procedures in the US, the Roux-en-Y gastric bypass (RYGB) [6-17] is the most commonly performed procedure. The purely restrictive adjustable gastric band is increasing in use in the US and is the leading procedure performed outside of the US [18]. The biliopancreatic diversion (BPD) with or without the duodenal switch (BPD DS) has also grown in use but is performed by a smaller number of practitioners. Growth in the use of any type of bariatric procedure over the last decade has been truly remarkable with over 120,000 procedures performed in 2003 compared to less than 20,000 performed in 1993[18, 19]. This growth may be related to the reported efficacy of these procedures, the availability of less-invasive laparoscopic procedures, a 10-12% yearly increase in the pool of surgical candidates (as defined by the 1991 National Institutes of Health (NIH) consensus conference criteria), and by increased media exposure of celebrity patients who had successful bariatric procedures [18].

One of the more challenging issues facing payers, health care providers, and patients considering bariatric surgery is a lack of comprehensive and reliable data concerning mechanism of action, risk stratification, effectiveness, cost-effectiveness, and global outcomes.

To facilitate and accelerate research in this area, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), with the support of the NIH Office of Research on Women's Health, established a bariatric surgery clinical research consortium, now known as the Longitudinal Assessment of Bariatric Surgery (LABS). LABS is a consortium of six clinical centers and a Data Coordinating Center (DCC) working in cooperation with NIH scientific staff to plan, develop, and conduct coordinated clinical, epidemiological, and behavioral research in the field of bariatric surgery.

The overarching goal of LABS is to bring together researchers with expertise in bariatric surgery, obesity research, internal medicine, endocrinology, behavioral science, outcomes research, epidemiology, and other relevant fields to plan and conduct studies that will ultimately lead to a better understanding of bariatric surgery and its impact on the health and well-being of patients with obesity and obesity-related diseases.

LABS will develop standardized measures and collection instruments for patients undergoing bariatric surgery at the participating clinical centers. Rigorously collected information on patient characteristics, surgical procedures, medical and psychosocial outcomes, and economic factors will ultimately lead to developing rational recommendations for clinical care. LABS is intended to develop evidence-based information regarding the risks and benefits of bariatric surgery.

The LABS consortium will also support studies to answer questions regarding the impact of different bariatric surgical procedures on important clinical outcomes and to use bariatric surgery as a model to better understand the causes of and potential treatments for obesity. A repository of blood and tissue specimens obtained from a subset of the LABS cohort will be stored for future research at the NIDDK tissue repository. These specimens should provide a valuable resource for the study of obesity and its complications.

Investigative centers in LABS include the University of Pittsburgh Medical Center (Pennsylvania), Columbia-Presbyterian Hospital and Cornell University (New York), East Carolina Medical Center (North Carolina), Neuropsychiatric Research Institute (North Dakota), University of California, Davis (California) University of Washington / Virginia Mason (Washington), Oregon Health and Science University and Legacy Good Samaritan Hospital (Oregon). The Data Coordinating Center is at the University of Pittsburgh, Graduate School of Public Health.

The central study design feature of LABS is a prospective, longitudinal cohort with at least three components. LABS-1 will include all patients at least 18 years of age who undergo bariatric surgery by LABS certified surgeons during a 4 year period. Important adverse outcomes (i.e., death, rehospitalization, reintervention) occurring within 30 days of surgery will be recorded to assess the relationship between short-term morbidity and mortality rates among various subgroups of patients. A subset of the LABS-1 cohort will be enrolled in a set of additional LABS studies to be addressed in additional protocols (LABS-2 and LABS-3).

2 Objectives, Specific Aims, and Hypotheses of LABS-1

2.1 Primary Objectives

To assess the safety of bariatric surgery by characterizing short term (within 30 days) postoperative adverse outcomes using standardized measures in a cohort of patients undergoing bariatric surgical procedures at multiple clinical sites.

To determine the associations between these outcomes and:

1. Demographic characteristics
2. Clinical characteristics
3. Features of operative, perioperative and immediate postoperative care

2.2 Study Design of LABS-1

The LABS-1 cohort is designed to provide short-term descriptive and adverse outcome data on approximately 12,000 consenting patients at least 18 years old undergoing bariatric surgical procedures by LABS-certified surgeons at six investigative centers. This cohort will contribute data derived from limited patient assessment(s) including chart review and interviews pre-surgery and at approximately 30 days post-surgery, as well as information about the surgical procedure. Limited information as approved by the Institutional Review Board (IRB) will be collected from chart review for patients who do not provide informed consent.

2.3 Hypotheses

Based on a review of the bariatric surgical literature on factors prognostic of intra-operative and post-operative complications (21-27; 33-40), the following hypotheses will be examined:

- The risk of 30-day mortality after gastric bypass is higher:
  - in men than women
  - in the super obese (BMI $\geq$ 50 kg/m^2) than those with BMI less than 50 kg/m^2
  - in African American compared to Caucasian patients
  - in patients with diabetes compared to those without diabetes
- We also hypothesize that patients undergoing gastric bypass will have lower rates of 30-day mortality than those undergoing BPD DS, but higher rates than those undergoing the laparoscopic adjustable gastric band.
- The risk of 30-day anastomosis–related reintervention is higher in certain subpopulations including men, patients with BMI at least 50 kg/m^2 and in patients with diabetes, and is higher when no tissue sealant is applied.
- The risk of 30-day deep vein thrombosis and pulmonary embolism (DVT/PE) is higher in patients undergoing non-laparoscopic surgery, in men, and in patients with BMI at least 50 kg/m^2.
- The risk of 30-day DVT/PE varies with length of operation, or dosage or type of anticoagulation medications administered.

2.4 Specific Aim 1

To assess **safety** by determining rates of events occurring within 30 days following bariatric procedures (i.e., mortality, operative, rehospitalization, and reintervention) and relate these outcomes to patient demographic/clinical characteristics, operative interventions and perioperative care.

2.5 Specific Aim 2

To develop and validate a scoring system that is predictive of short term adverse outcomes in patients who undergo bariatric surgery.

3 Definitions and Target Population

3.1 Criteria for LABS-1

The following are criteria for entry into LABS:

- Age 18 years or older
- Informed consent obtained
- All races and ethnicities
- Both genders
- LABS-certified surgeon performs the bariatric surgery

A LABS-certified surgeon:

- Performs bariatric surgery at one of the LABS clinical centers
- Has undergone training on the LABS protocol and data collection
- Has successfully completed a certification examination
- Agrees to adhere to LABS protocol and provide required data

Data collected about patients who do not undergo bariatric surgery, or whose bariatric surgery is not performed by a LABS-certified surgeon, will be removed from the LABS database.

3.2 Endpoint Definitions

3.2.1 30-day outcomes

30-day outcomes are defined as those occurring from the time of the anesthesia induction until 11:59 pm on the 30th day following surgery.

3.2.2 Adverse perioperative outcomes and interventions

The cohort size chosen for LABS-1 is based on three primary, co-equal outcomes: death, anastomotic complications requiring intervention, and deep vein thrombosis/pulmonary embolism (DVT/PE) requiring intervention within 30 days of bariatric surgery. Collectively, the following additional endpoints will be evaluated in LABS-1:

Abdominal re-operations, tracheal reintubation, tracheostomy, endoscopy, percutaneous drain placement, anticoagulation therapy, rehospitalization, and other surgical interventions.

3.2.3 Outcome endpoints

All deaths and outcome endpoints (see section 3.2.2) whose cause was not confirmed (requirements for confirmation will be in the Manual of Operations) will be reviewed by an adjudication committee. This committee will meet periodically to assign cause(s) to those non-fatal endpoints whose cause was not confirmed. Committee members will not interact directly with LABS investigators concerning the results or classification of causes. Committee members will reveal the results of their work only to the LABS Data Coordinating Center.

3.3 Target Composition of Database Population

Patients at least 18 years old undergoing bariatric surgery performed by LABS-certified surgeons will be entered in the database. Total patient recruitment is estimated to be approximately 12,000 patients in 4 years. Based on information provided by each of the clinical sites, we expect the cohort to have the following characteristics:

- approximately 84% of the patients are expected to be women
- approximately 25% are expected to have a BMI at least 50 kg/m^2
- approximately 18% are expected to be African American
- approximately 15% are expected to be Hispanic or Latino
- approximately 25% are expected to be diabetic
- approximately 2.5% are expected to undergo bariatric surgery with a BPD
- approximately 5% of patients are expected to have a laparoscopic adjustable gastric band placed
- approximately 20% of patients will have an anastomotic sealant used
- approximately 25% of patients will be prescribed low molecular weight heparin
- approximately 25% of patients will be prescribed subcutaneous heparin and
- approximately 25% will have both low molecular weight heparin and subcutaneous heparin
- approximately 22% will be planned open procedures

3.4 Sources of Patients

All patients will be identified during visits to assess eligibility for bariatric surgery.

4 Selection and Enrollment of Subjects

4.1 Inclusion Criteria

All patients age 18 years or older, eligible and undergoing bariatric surgery performed by a LABS-certified surgeon.

4.2 Exclusion Criteria

Patients who do not provide informed consent.

4.3 Enrollment Procedures

Prior to implementing this protocol, the principal investigator must have the protocol and consent form approved by the Institutional Review Board (IRB) for Human Research at his or her institution. Once a candidate for the LABS database has been identified, the study will be discussed in detail with the patient. The patient will be asked to read and sign the IRB-approved informed consent document. After written informed consent is obtained, a copy of

the signed consent form will be placed in the patient's hospital medical record. Where local regulatory requirements differ, clinical sites will abide by local requirements.

A patient is enrolled when the LABS-1 pre-operative evaluation form is completed and entered into the LABS database. If a participant does not undergo bariatric surgery, or has bariatric surgery performed by a surgeon who is not LABS- certified, then any data obtained will be removed from the LABS database.

4.4 Accrual Goal

The goal of LABS-1 is to enroll approximately 12,000 patients over 4 years. This accrual goal was selected to provide a large enough sample to obtain estimates of rare events (e.g., 30-day mortality) with a high degree of precision, and to facilitate statistically valid comparisons between important subgroups. We anticipate the refusal rate to be less than 5% given the observational design of the study.

Precision can be quantified by the variance of the estimate, and is often characterized by a confidence interval. With a sample of 12,000, the 95% confidence interval is about the anticipated mortality proportion of 0.01 is (0.008, 0.012). For an event with an expected probability of occurrence of 0.05 (e.g., anastomotic leak), the 95% confidence interval would be (0.046, 0.054).

The sample size required to detect a clinically meaningful difference between subgroups depends on the size of that difference, the distribution of the cohort between (or among) the subgroups and the errors (type I and type II) one is willing to accept. Table 1 below shows the cohort size required to detect the clinically meaningful relative risk of 2.0 between various subgroups for several outcomes. The percentages of the total study group anticipated to be in the various subgroups were obtained from the clinical sites comprising the LABS consortium. Estimated event rates were obtained from an extensive review of the literature [20-27].

For example, to have 90% power to detect a doubling in the relative risk of 30-day mortality, (estimated to be 1% in the lower risk group [20]) between men and women would require 11,588 patients in the cohort. With an anticipated 12,000 eligible patients, LABS-1 would be able to detect this difference even if the dropout rate was as high as 3.5%. Similarly, when comparing those with BMI less than 50 kg/m^2 to those with larger BMI, the cohorts are closer together in size (75% / 25% rather than 84% / 16%) so the sample size needed to detect the same relative risk, given the same base mortality rate, is smaller; n=8,458.

With a more common adverse event (e.g., surgical leak) the required sample size for various subgroup comparisons is even smaller, ranging from 3,311 for diabetics vs. non-diabetics and 4,150 to compare those who had tissue sealant with those who did not have tissue sealant applied.

With the postulated extremely rare event of DVT/PE, the expected cohort of 12,000 will be large enough to provide more than 80% power to detect a difference between some subgroups, including BMI less than 50 versus BMI at least 50 kg/m^2, but not large enough for other subgroups, including use of heparin versus use of low molecular weight heparin.

In summary, based on these accrual targets, LABS-1 will have at least 80% power to identify a two-fold (or greater) increase in the risk of 30-day mortality, reinterventions, or deep vein thrombosis/pulmonary embolism (DVT/PE) in certain patient subgroups.

Table 1. Sample Size Estimates for LABS-1 Assuming Fixed Relative Risk of 2.0

Comparison Groups	Anticipated % of total study cohort*	Event Rates**	Total N Required at 80% Power 2-sided	Total N Required at 90% Power 2-sided
Primary Outcome: 30-Day Mortality				
Women	84%	**1.0%**	8,484	11,588
Men	16%	**2.0%**		
BMI < 50	75%	**1.0%**	6,260	8,458
BMI ≥ 50	25%	**2.0%**		
Non-African American	82%	**1.0%**	7,777	10,596
African American	18%	**2.0%**		
Diabetics	25%	**1.0%**	6,260	8,458
Non-Diabetics	75%	**2.0%**		
BPD	2.5%	**5.0%**	4,760	6,920
Bypass	92.5%	**1.0%**	Comparisons with Bypass	
Band	5.0%	**0.05%**	13,076	14,523
Primary Outcome: Surgical Leak Rate				
Sealant Used	20%	**2.5%**	3,270	4,150
Sealant Not Used	80%	**5.0%**		
BMI < 50	75%	**2.5%**	2,478	3,311
BMI ≥ 50	25%	**5.0%**		
Diabetics	25%	**2.5%**	2,478	3,311
Non-Diabetics	75%	**5.0%**		
Primary outcome: DVT/PE				
Women	84%	**0.7%**	12,171	16,626
Men	16%	**1.4%**		
BMI < 50	75%	**0.7%**	8,980	12,135
BMI ≥ 50	25%	**1.4%**		
Heparin	80%	**1.2%**		
Low Molecular Wt Heparin	20%	**0.6%**	14,028	17,807

*Anticipated percentages of comparison groups shown in the above table were derived from a description of the demographic characteristics of bariatric surgery patients at each clinical site in LABS-1 groups (i.e. males, superobese, diabetics, African Americans, and those who had certain operative techniques).

**Estimated event rates were obtained from an extensive review of the literature [20-27, 33-36].

5 Study Process

At each site, patients who intend to undergo bariatric surgery, meet eligibility criteria (i.e., are at least 18 years of age) and agree to participate in LABS-1 by signing an informed consent will be enrolled. We will attempt to determine why consent is not provided when potential participants refuse. At those sites where IRB permits, age, gender, race, ethnicity, height and weight will be recorded from patients' medical charts for de-identified patients who refuse consent to compare these factors to those who do consent. This will be done to ascertain the generalizability of LABS-1 results. A copy of the signed consent form will be placed in the patient's hospital medical record. Where local regulatory requirements differ, clinical sites will abide by local requirements. Primary and alternative contact information, including the names, addresses and telephone numbers of two contacts and the primary care physician, will be requested, but not entered into the LABS database. Permission will be requested to contact these alternative contacts should the patient be unreachable for the 30-day follow-up.

The LABS-1 pre-operative evaluation, including relevant updated data collection, will be completed through patient assessments, including chart review and interview with the patient as necessary. Laboratory values will be updated within 180 days of surgery; medication and co-morbidities information will be updated within 90 days of surgery; and weight obtained again within 30 days of surgery via the pre-operative evaluation update form. The pre-operative evaluation and update (if applicable) forms will be transmitted to the DCC using the data entry system developed by the DCC. After performing the bariatric operation, the LABS-1 operative form will be completed and the data transmitted to the DCC. Patients or, when necessary, an alternative contact (if agreed to by the patient as noted above) will be contacted no less than 30 days after surgery to ask about post-operative events occurring within 30 days of the bariatric surgery. The research coordinator also will review patients' medical records to determine if a reportable outcome event occurred.

Details of the LABS-1 pre-operative, operative and post-operative data collection forms are listed below. The pre-operative evaluation update form includes a subset of the data collected at the initial pre-operative evaluation which has the potential to change with time.

<u>Pre-operative evaluation data elements:</u>

- Participant identifier (alphanumeric code)
- Date of consent to participate in LABS
- Date of birth
- Gender
- Height
- Weight
- Race
- Ethnicity
- Planned procedure
- Planned approach

- Previous obesity surgery
- Whether or not the planned procedure is a revision of prior bariatric procedure
- Whether or not the planned procedure is a reversal of prior bariatric procedure
- Whether patient is a good candidate for LABS-2 (separate protocol)
- Most recent laboratory values (within 180 days)
- Medications (within 90 days)
- Blood pressure (within 90 days)
- Comorbidities (diabetes, ischemic heart disease, hypertension, CHF, sleep apnea, history of DVT/PE, asthma, functional status, pulmonary hypertension)
- Smoking history
- Other conditions possibly affecting outcomes

A screening log will be kept on patients who do not consent to participate in LABS-1. Information collected on these forms will be:

- Reason for refusal
- Age
- Height and weight
- Gender
- Race and ethnicity

<u>Operative elements</u>

- Date of surgery
- Operative times
- Procedure performed
- Whether a resident or trainee was present
- Method of surgical procedure
- Whether concurrent procedures were performed
- Test of anastomosis
- DVT prophylaxis
- Whether any intra-operative fluids were received
- Anesthesia risk-derived classification
- Whether post-operative anticoagulation was ordered
- Adverse intra-operative events
- Lowest reported or known body temperature

<u>30-day post-operative outcome elements</u>

- Source(s) of information
- Length of hospital stay (days)
- Discharge location
- Whether the surgical wound edges opened.
- Whether the wound edges separated and required packaging or bandaging
- Date of death, if applicable
- Rehospitalization(s), if applicable

- 30-day post-operative outcomes, i.e., abdominal re-operation, tracheal reintubation, tracheostomy, endoscopy, placement of percutaneous drain, anticoagulation therapy for presumed/confirmed DVT, anticoagulation therapy for presumed/confirmed PE, other events requiring intervention

6 Follow up

Follow up information will be collected approximately 30 days following surgery by face-to-face or telephone interview. If a patient cannot be contacted, an alternative contact, for whom the patient provided consent for contact, will be reached in an attempt to obtain follow-up information.

6.1 Criteria for Study Withdrawal

- Patient refuses to continue in the study and withdraws his/her consent
- NIDDK ends the study

7 Statistical and Analytic Considerations

For LABS-1, estimating event probabilities and identifying demographic, clinical, operative, peri-operative, and short-term operative care factors associated with outcomes are of prime interest. Event probabilities, variances, and confidence intervals will be calculated per cohort subset for dichotomous outcomes (e.g., mortality, individual co-morbidities, anastomotic leak, anastomosis-related re-intervention) when follow-up is constant (e.g., 30-day mortality, 30-day rehospitalization). Both rates per person-month and cumulative probabilities of event-free time, and their associated confidence intervals will be calculated when there is variable follow-up (e.g., due to loss to follow-up or when actual time to event is of interest). The cumulative incidence rate is preferred when there are competing risks (e.g., death removes patients from risk of other adverse events or hospitalization occurring following death) so this measure will also be calculated. These statistics will be calculated overall and for important subgroups (e.g., BMI > 50 kg/m^2, people with diabetes, women, African Americans, patients undergoing BPD). Hypothesis tests will also be used to determine whether probabilities, rates, or cumulative probabilities differ between (or among) subgroups using Π^2 tests for association, differences in Poisson parameters or log rank statistics, and the proportional hazards model [28], respectively. For all statistical tests, $p<0.05$ (two-sided) will indicate statistical significance.

To account for possible confounding, regression models will be used: logistic regression for event probabilities, Poisson regression for rates per person-month, and proportional hazards models for dichotomous events with variable follow-up and in the face of competing risks (i.e., events that, when they occur, preclude observing the event of interest) respectively [29-31].

For continuous outcomes, descriptive statistics will include distributional characteristics (e.g., percentiles), measures of central tendency (e.g., median), and measures of variability (e.g., standard deviation, inter-quartile range). When follow-up is constant, distributions can be compared between or among, subgroups such as those given as examples above, using appropriate parametric (e.g., t-test, analysis of variance) or non-parametric (e.g., signed rank

test, Kruskal-Wallis one way analysis of variance) tests. If follow-up is variable, adjustments such as dividing weight loss related measures by observation time will be made. Generalized linear, or non-linear, models, as appropriate, will be employed to test whether subgroups differ with respect to continuous outcomes after adjusting for potential confounding variables.

The second specific aim is to develop and validate a scoring system to predict short term adverse outcomes. These may be individual outcomes, or a cluster of related outcomes. Development and validation will utilize separate sub-samples of the total cohort, with sub-sample selection dependent on the number of observations required. Sample size calculations will be performed to determine how large of a sub-sample is required to have pre-determined statistical power (e.g., 80%, 90%) to identify factors significantly associated (two-sided test with $p<0.05$) with the adverse outcome(s) (see Section 3.2.2). Should the cohort be large enough to use split samples, a randomly selected sample of adequate size, as determined by the sample size calculation, will be selected to develop the scoring system and another, randomly selected sub-sample will be used for validation. Random selection will help prevent biases resulting from, for example, changes in surgical techniques or patient selection over time, or at different centers. Analytical methods include modeling (e.g., logistic regression for dichotomous outcomes,) and empirical classification (e.g., classification and regression trees [32]). Alternative approaches for model development and validation include the jackknife and the bootstrap when the sample size is inadequate for split samples.

8 Human Subjects Issues

8.1 Overview

Required documents (study protocol, consent forms, data collection forms and recruitment materials) will be submitted to each clinical center's IRB and to the DCC's IRB. A site may not initiate any patient contact regarding the LABS database until the site has IRB approval for the protocol and consent, and the DCC has certified the site for initiating LABS-1 activities. All study personnel will have completed training in the Protection of Human Subjects per NIH guidelines. The proposed study anticipates recruiting a significant proportion of racial/ethnic minorities (Black or African American, Hispanics or Latino, Asian, American Indian/Alaska Native, Native Hawaiian or other Pacific Islander) as well as non-Hispanic white subjects. We anticipate that the patients will reflect the entire spectrum of bariatric surgery patients.

8.2 Institutional Review Board Approval

It is the investigator's responsibility to ensure that the LABS-1 protocol and informed consent document are reviewed and approved by the appropriate IRB. Each clinical site must obtain a letter of approval from the IRB prior to enrolling patients into this study. Sites must provide the DCC with copies of the initial IRB approval notice prior to enrolling the first patient, and subsequent renewals, as well as copies of the IRB approved consent documents.

The IRB must also review and approve any other written information provided to the patient prior to any registration of patients.

If, during the study, it is necessary to amend either the protocol or informed consent document, the investigator will be responsible for ensuring the IRB reviews and approves the amended

documents. IRB approval of the amended informed consent document must be obtained before new patients consent to participate in the study using the new version of the consent.

The informed consent document will inform patients of their right to refuse any release of their protected health information.

8.3 Informed Consent

8.3.1 Adaptation of Model Informed Consent Document

A template informed consent document has been prepared for the study. Based on local IRB requirements, each Principal Investigator (PI) may modify the informed consent document or make any necessary editorial changes as long as the meaning or intent of the document is not changed.

8.3.2 Informed Consent Process

The investigator or his/her designee (e.g., research coordinator or study nurse) will inform the patient or the patient's legally authorized representative, of all aspects of the patient's participation in the study.

The process for obtaining informed consent will be in accordance with all applicable regulatory requirements. The informed consent document must be signed and dated by either the investigator or a designee and by the patient BEFORE the patient can participate in the study. The original signed document will be retained in the patient's study file. One copy of the signed consent will be given to the patient and one copy will be placed in the patient's medical record. Where local regulatory requirements differ, clinical sites will abide by local requirements.

8.4 Confidentiality of Patient Data

The clinical site is responsible for the confidentiality of the data associated with patients enrolled in this study in the same manner it is responsible for the confidentiality of any patient information within its sphere of responsibility. All forms used for the study data will be identified by coded number only to maintain subject confidentiality. All records will be kept in locked file cabinets at the clinical centers with access limited to LABS study staff. All study staff will identify patients by a patient identification number generated at the clinical center. Clinical information will not be released without written permission of the participant, except as necessary for monitoring by the IRB or Data and Safety Monitoring Board (DSMB). Clinical information may be reviewed during site visits by the DCC and the NIDDK Project Officer. The patient grants permission to share research data with these entities in the consent document. Federal regulations govern the protection of patient's rights relative to data confidentiality and use of research data.

Consent procedures and forms, and the communication, transmission and stoppage of patient data will comply with individual site IRB and NIH requirements for compliance with The Health Insurance Portability and Accountability Act (HIPAA). The DCC will ensure that the clinical centers associated with the project are in compliance with HIPAA regulations by requiring documentation from the site IRBs with the appropriate authorization or consent form.

9 Risk/Benefit Ratio

There are no risks of physical harm associated with participating in the LABS-1 study. Of minimal risk to patients is the possible inconvenience of reporting medical status to the research coordinator. Another possible risk is a breach of confidentiality, although steps have been taken to minimize such an occurrence. All information collected for this research study will be kept confidential. Patients' names will be used only for the informed consent form and medical chart reviews. Patients will be given unique study identifiers, which will be written on all data collection forms. In addition, data collection forms will be kept in secured, locked files. To help us protect patients' privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. Known breaches of confidentiality will be reported to NIDDK.

Participation may benefit other patients who undergo weight-control surgery.

10 Other Regulatory Considerations

10.1 Clinical Site Eligibility

The clinical site must be formally part of, or affiliated with, a LABS institution (see appendix).

10.2 Inclusion of Women and Minorities

Based on current referral rates of patients undergoing bariatric surgery, LABS-1 expects a ratio of female to male patients of approximately 5 to 1.

Based on the current referral rates of patients undergoing bariatric surgery at LABS clinical centers, LABS-1 also expects the majority of patients to be Caucasian. Some clinical sites anticipate a higher proportion of patients of racial/ethnic minority (Black or African American, Hispanic or Latino, Asian, American Indian/Alaska Native, Native Hawaiian or other Pacific Islander) than other clinical sites.

10.3 Clinical Site Audits

All clinical sites at which patients are enrolled are subject to an on-site audit by the DCC and representatives from the NIDDK.

10.4 Performance Monitoring

The DCC, will perform statistical analyses and prepare materials for monitoring study progress (e.g., recruitment, retention, data processing timeliness and accuracy) and protocol adherence (e.g., proportion of follow-up visits completed on time).

11 References

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12 Appendix

12.1 Participating centers

Clinical Centers

- East Carolina University
- Neuropsychiatric Research Institute
- New York Columbia-Presbyterian / Cornell University Medical Center
- University of California, Davis
- University of Pittsburgh Medical Center
- University of Washington / Virginia Mason
- Oregon Health & Sciences University / Legacy Good Samaritan Hospital

Data Coordinating Center

- University of Pittsburgh Graduate School of Public Health

National Institutes of Health

- National Institute of Diabetes and Digestive and Kidney Diseases

12.2 Committees

Executive Committee
Steering Committee
Adjudication Committee
Ancillary Studies Subcommittee
Coordinator Subcommittee
Committee to Review Outside Participation
Publications and Presentations Subcommittee
Protocol Subcommittee
Recruitment and Retention Subcommittee
Website Subcommittee