NEW YORK UNIVERSITY SCHOOL OF MEDICINE

A prospective, open-label study to evaluate the safety and efficacy of Lap-Band® Adjustable Gastric Band (LAGB®) Operations in the Treatment of Morbidly Obese Adolescents (Ages 14-17)

PROTOCOL DATE:	April 27, 2004
AMENDMENT No 1:	January 05, 2005
AMENDMENT No 2:	February 23, 2005
AMENDMENT No 3:	April 15, 2005
AMENDMENT No 4:	May 25, 2006
AMENDMENT No 5:	July 03, 2008
AMENDMENT No 6:	June 10, 2010
AMENDMENT No 7:	January 28, 2011
AMENDMENT No 8:	December 22, 2011
AMENDMENT No 9:	May 01, 2012
AMENDMENT No 10:	July 17, 2013

NCT00587301
study 11876

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PROTOCOL SUMMARY

TITLE OF STUDY: A prospective, open-label study to evaluate the safety and efficacy of Lap-Band® Adjustable Gastric Band (LAGB®) Operations in the Treatment of Morbidly Obese Adolescents (Ages 14-17)

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PERIOD OF TRIAL: Jan 2005 –Jan 2019

STUDY OBJECTIVES: Is to demonstrate the safety and efficacy of the use of the LAP-BAND® System in the morbidly obese adolescent population in the United States, and therefore provide these individuals with a significantly less morbid and reversible surgical option for weight loss.

STUDY VARIABLES: The primary efficacy variable is weight loss evaluated in terms of % excess weight loss (EWL).

DESIGN: Prospective, open-label, and single center

INCLUSION CRITERIA:

- Be at least 14 and less than 18 years of age at the time of enrollment into the study.
- Have a BMI of at least 40.
- Have a history of obesity for at least 5 years, including failed attempts at diet and medical management of obesity.
- Confirmation by a psychologist or psychiatrist experienced with adolescents that the subject is sufficiently mature emotionally to comply with the study protocol.
- Express willingness to follow protocol requirements.
- Assure investigators that subject, if female of childbearing potential, is using an appropriate form of contraception.

EXCLUSION CRITERIA:

- Intention or need to have another surgical procedure for weight reduction within 12 months of Lap Band placement.
- History of congenital or acquired anomalies of the G.I. tract, such as; congenital or acquired intestinal telangiectasia, Crohn's disease or ulcerative colitis; severe cardiopulmonary disease or severe coagulapathy; hepatic insufficiency or cirrhosis.
- Presence of dysphagia or documented esophageal dysmotility.
- Patients with autoimmune connective tissue disorders.
- Patients with acute abdominal infections.
- Pregnancy or intention of becoming pregnant in the next 12 months.
- Presence of psychiatric problems or immaturity which would compromise cooperation with the study protocol.
- History of previous bariatric surgery, intestinal obstruction or adhesive peritonitis.
- Presence of localized or systemic infection at the time of surgery.

- Chronic use of aspirin and/or non-steroidal anti-inflammatory medications and unwillingness to discontinue the use of these concomitant medications.
- History of gastric or esophageal surgery.
- Use of weigh loss medications simultaneously.

NUMBER OF SUBJECTS: 120

PRODUCT NAME (USAN) LAP-BAND® Adjustable Gastric Band (LAGB®) System

TEST ARTICLE: LAP-BAND® System

DURATION OF THERAPY: 5 years

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1.0 INTRODUCTION

1.1 Background and Rationale

The Lap-Band System is approved by the FDA for use in adults. Studies have demonstrated that childhood obesity increases the likelihood of developing numerous co-morbid conditions, including: hypertension, diabetes mellitus, pulmonary complications, growth acceleration, dyslipidemia, musculoskeletal problems, psychosocial problems, and cancer [1-2]. The severely obese patient faces death without proper treatment of the condition. Furthermore, the economic impact of obesity is substantial. It is estimated that the cost of obesity in the U.S. in 2002 dollars is $117.1 billion, and, with estimates that obesity could affect two in five adults by the year 2025, the need to address obesity at an early age is clear.

It has been shown that the nutritional and behavior modifications necessitated by bariatric surgery, as evidenced by the reported success of the gastric bypass procedure in adolescents, are safe, and are associated with significant weight loss as well as correction of co-morbid conditions and improved self-image and socialization [3-5]. The use of the Lap-Band System results in clinically significant weight loss with significantly less operative morbidity and mortality than the gastric bypass procedure in adults [6]. Additionally, the adjustability to patient needs and the relative ease of reversal is unique to the Lap-Band System. This system has been used in adults in Europe and other countries since 1993; international publications report a mean Percent Excess Weight Loss (%EWL) of 52% in subjects with 1 year of follow-up and 68% after 2 years of follow-up [7-9]. In the first US clinical study a mean of 34.6% EWL in 221 subjects was reported with 1 year follow-up and 38.2% EWL in 122 subjects at 2 years of follow-up. However, the first published US experience by Rubinstein of 63 patients showed a 53% EWL at 3 years [10]. Currently, our experience in adults demonstrates a 44.3% EWL at 1 year [11]. Finally, the Lap-Band has been shown to be a safe and effective method of weight loss in morbidly obese adolescents by Dolan, et.al., in Brisbane, Australia [12]. In fact, when compared to matched controlled adults, adolescents did better in terms of weight loss and complications [13]. Mortality has been found to be only about 1 in 10,000 [0.01%]; this compares with a mortality rate among gastric bypass patients that approaches 0.5% [6].

At this time, there is only one surgical option for morbidly obese adolescents: Roux-en Y gastric bypass. We believe that the LAP-BAND®, which can be removed after sufficient weight loss and behavior modification, would be a better option for adolescents.

The lower age limit of children being offered LAGB surgery is open to conjecture. One of the obvious concerns in offering surgery to children as young as twelve years of age is the effect surgery may have on the child's growth. However, there are data available that encourage this concept. Obese children are known to grow faster than non- obese children [14-16]. They are taller by at least one standard deviation than their normal weight peers before puberty, and then normalize in their late teens. Furthermore, they have higher levels of lean body mass, as well as fat mass, corresponding with their height. Obese girls achieve puberty at a younger age than non-obese girls [17-19]. Also, it is typical for morbidly obese children to be taller than average, have heavier muscle mass, and for girls to be sexually developed by the age of 12.

In contradistinction to Roux-en Y Gastric Bypass (RYGB) and intestinal bypass procedures such as the biliopancreatic diversion (BPD) and duodenal switch, LAGB patients suffer no nutritional sequelae after surgery [20-23]. There has been no study that describes any nutritional deficiency after LAGB, despite a reduction in fat mass by up to 50%. In the first 3 months post-surgery, there is a small reduction (5-10%) in lean body mass, which stabilizes at 6 months, with no prolonged loss of lean mass thereafter [24-25]. The greatest disparity between LAGB and RYGB or BPD is in Vitamin D and calcium metabolism, which has only been studied in adults. Coates et al has recently shown increase in bone turnover and decreased bone mass 9 months after RYGB [26]. Newberry et al showed that after intestinal bypass operations, 50% of patients were depleted in Vitamin D, with associated hyperparathyroidism in 63% [27]. In concert with the data showing no caloric or nutrient malabsorption after LAGB, Pugnale et al showed no evidence of secondary hyperparathyroidism 1 year after LAGB [28]. The adult population effectively eat approximately 1200-1800 calories per day after LAGB, which equates with caloric intake of non-obese adults, and this would presume to be the same in children. In addition, all micronutrients and vitamins are completely absorbed.

In a 1975 report of 25 adolescents undergoing Roux-en Y gastric bypass surgery, a 25 % loss of body weight at 3 years was observed with no interruption in growth in height over that time period [4]. All published series of surgery for severe adolescent obesity, by vertical banded gastroplasty, RYGB, BPD or LAGB, include children 12 years of age [5, 12-13,30-33]. One includes children as young as 8 yrs old [29]. There is another case report of a 13 year old girl with severe renal failure having LAGB [34]. All were associated with severe obesity-related co-morbidity.

Dolan and Fielding have published two papers on their initial experience with the Lap–Band in morbidly obese adolescents [35, 36]. The first paper describes 17 children aged 12 – 19 years, weight 129 kg and BMI 45kg/m^2. At a median follow – up of 25 months (12–46), BMI fell to 30 kg/m^2, representing 60% EWL. One patient developed a slip needing revision, and another needed a port revision, both same day procedures. In a related paper, 17 adults matched for sex, weight and BMI were compared to the children, and the children performed marginally better in terms of weight loss.

In a subsequent assessment of 26 children aged 12–19 years, with mean 34 month follow up, Fielding found that BMI fell from 43 to 29 kg/m^2 at 3 years, and was maintained out to 5 years [37]. This represents 70% EWL at 3 years. Thirteen of 18 children are no longer obese after 3 years (BMI < 30kg/m^2). Furthermore, compliance for visits and adjustments was very high at 12.2 visits in 2 years (7–22 visits).

The following table is a brief weight loss report of 14 morbidly obese adolescents aged 13 to 17 years with BMI 43 to 64 who underwent laparoscopic adjustable gastric banding surgery by Dr. Christine Ren and Dr. George Fielding at New York University Medical Center. No deaths, re-operations, prolonged hospitalizations, or complications were occurred on those adolescents.

Age	Initial BMI	OP Date	6M BMI	6 M %E WL	1Y BMI	1Y %EWL	2Y BMI	2Y %EWL	3Y BMI	3Y %EWL
17	63	9/21/2001	52	26 %	47	39 %	42	53 %	42	51 %
17	64	4/18/2002	55	21 %	49	33 %	46	41 %		
17	47	8/15/2002	41	26 %	34	55 %	35	50 %		

13	61	4/26/2004	52	22 %						
17	59	6/10/2004	45	18 %						
17	51	6/28/2004	46	16 %						
15	44	8/5/2004								
13	43	8/6/2004	32	53 %						
16	43	8/6/2004								
16	44	8/13/2004								
17	44	8/13/2004	36	50 %						
15	42	10/7/2004								
16	51	10/21/2004	42	30 %						
17	44	10/22/2004								

There is an excellent opportunity in this proposed protocol to study the effect on growth of weight-loss after surgery in morbidly obese children as young as 14 years. Given that there is no evidence of nutritional sequelae or interruption of bone growth after LAGB and since we will be performing nutritional monitoring and bone density studies, there would seem to be minimal risk in including these younger children in the protocol.

1.2 Description of LAP-BAND® System Components

The implanted components of the Lap Band System include:

1. ADJUSTABLE BAND

The adjustable band component is a 13-mm wide band available in three sizes (an inside circumference of 9.75 cm, 10 cm, or 11 cm), which forms a circular ring around the stomach when closed. The band is made of silicone elastomer and the inner surface of the band is inflatable, allowing for stoma adjustments. Radiopaque, kink-resistant tubing is used to connect the inflatable section to the access port.

2. ACCESS PORT

The access port consists of a 31 mm-diameter titanium reservoir in polysulfone housing with a high-compression silicone septum. It is used for percutaneous adjustments of stoma diameter and is self-sealing when penetrated with the access port needle. The access port is also supplied individually packaged.

A component of the system used for adjustments post-operatively:

3. ACCESS PORT NEEDLE

The access port needles are a 20 gauge and a 22 gauge, 38 mm (1.1/2 inch), non-coring, deflected tip ("Huber Needle") needle designed to penetrate the access port for saline volume adjustment of the LAGB System. The access port needle is also available individually packaged in packs of 10 for additional stoma adjustments via the access port.

2.0 STUDY OBJECTIVES

2.1 Primary Objective

The primary objective of this research is to demonstrate the safety and efficacy of the use of the LAP-BAND® System in the morbidly obese adolescent population in the United States, and therefore provide these individuals with a significantly less morbid and reversible surgical option for weight loss.

2.2 Secondary Objective

The secondary objective is to assess the status of co-morbidities and changes in quality of life and the academic performance from baseline.

3.0 INVESTIGATIONAL PLAN

3.1 Study Design

This is a prospective, non-randomized, single-center study to be conducted under an FDA-approved Investigational Device Exemption (IDE). One investigational site will enroll and treat up to 120 subjects who meet the criteria for use of the LAP-BAND® System, except that they are adolescents ages 14 to 17. Subjects will be followed for five years.

3.2 Study Population

3.2.1 Inclusion Criteria

1. Be at least 14 and less than 18 years of age at the time of enrollment into the study, at Tanner developmental stage 4 or greater, and be past the point of peak height velocity. Bone age will be determined in this evaluation.
2. Have a BMI of at least 40 [BMI is calculated as follows: BMI = weight (Kg) divided by (height (m) squared); i.e. (W/H2) or Kg/m2)]. These criteria are the ones recommended by the NIH for adults. When applied to adolescents, they are more conservative than the criteria of BMI > 95th percentile for age because of the BMI curves for children and adolescents. We feel the criteria proposed in Pediatrics, 2004;114(1):217-223 are unnecessarily restrictive given the incidence of comorbidities starting at a BMI of 35, the likelihood of the development of comorbidities starting at a BMI of 35, and the poor results of therapies which do not include bariatric surgery for adolescents with a BMI of 35 or greater.
3. Have a history of obesity for at least 5 years, including failed attempts at diet and medical management of obesity.
4. Express willingness to follow protocol requirements which include signing an assent form, having the individual's legal guardian sign a consent form; completing 1-2 week, 6 week, 3 month, 6 month, 9 month, 12 month, and every 6 month follow-up visits for a total of five years, and completing all protocol-required laboratory and diagnostic tests.
5. Confirmation by a psychologist or psychiatrist experienced with adolescents that the subject is sufficiently mature emotionally to comply with the study protocol.

6. Assure investigators that subject, if female of childbearing potential, is using an appropriate form of contraception.

3.2.2 Exclusion Criteria

1. Intention or need to have another surgical procedure for weight reduction within 12 months of Lap Band placement.
2. History of congenital or acquired anomalies of the G.I. tract, such as; congenital or acquired intestinal telangiectasia, Crohn's disease or ulcerative colitis; severe cardiopulmonary disease or severe coagulapathy; hepatic insufficiency or cirrhosis.
3. Presence of dysphagia or documented esophageal dysmotility.
4. Patients with autoimmune connective tissue disorders.
5. Patients with acute abdominal infections.
6. Pregnancy or intention of becoming pregnant in the next 12 months.
7. Presence of psychiatric problems or immaturity which would compromise cooperation with the study protocol.
8. History of previous bariatric surgery, intestinal obstruction or adhesive peritonitis.
9. Presence of localized or systemic infection at the time of surgery.
10. Chronic use of aspirin and/or non-steroidal anti-inflammatory medications and unwillingness to discontinue the use of these concomitant medications.
11. History of gastric or esophageal surgery.
12. Use of weigh loss medications simultaneously

3.2.3 Patient selection equitability

We acknowledge the importance of equitability of research subjects in relation to patients' financial circumstances. Therefore, we will cover all costs for up to twenty percent of the study subjects who are unable to pay for professional fees, device fees and hospital costs and study-related costs.

Our staff will make every effort to obtain pre-authorization from the patient's insurance company for the surgery. If the insurance company refuses to pay the fees, the patients will be charged for the surgery and anesthesia. All study-related costs will be charged to the subject's family. Subjects and their parents will be notified of the payment arrangement very early on in the recruitment process. In the event that sufficient funds become available, we will cover all costs for whatever number of patients can be supported by these funds. We are actively seeking philanthropic funding to allow as many morbidly obese adolescents access to the study as possible.

3.2.4 Removal of Subjects from the Trial

A study subject or the parent of the study subject may end their participation in the study at any time. If a subject withdraws, the principal investigator will make reasonable effort to determine the reason for the subjects' withdrawal from the study and complete termination procedures as described in section 3.4.7. Telephone calls, registered letters and offers of transportation to the investigational site are considered reasonable effort.

In addition, the principal investigator may discontinue a patient's participation in the study if the patient fails to comply with the follow-up evaluation schedule (i.e., if patient missed 3 or more sequential follow-up visits.)

3.3 Study Duration

Subjects will be followed for a period of five years post-operatively.

3.4 Study Procedures

All parents or legal guardians of subjects must give their written informed consent in accordance with the informed consent regulations in Title 21 of the Code of Federal Regulations, Part 50. All subjects must give their written informed assent.

3.4.1 Subject Screening

Subjects will be recruited from among individuals referred to NYU Langone Weight Management Program for weight loss procedures. Both parents and children will be actively involved in the subject screening process. The information obtained from the parents will be about the child with minimal information on parent's weight history and family eating habits. Medical, social, psychiatric history and current psychological status, as well as weight history and eating disorders will be included in the subject screening.

3.4.2 Quality of Life and Psychological Evaluations

As part of the educational program, subjects and their parents will have visits with a nutritionist and psychologist before the surgery and at each follow-up visit (as listed below) after the operation, so they can be advised on dietary habit changes that will be needed. These scheduled visits will consist of an initial parent interview, initial child interview, questionnaires for the child assessing eating habits, degree of depression, degree of anxiety, subjective assessment of quality of life, body image satisfaction, self-esteem, and family environment. The parents will also be evaluated at scheduled follow-up visits with questionnaires assessing quality of life and family environment perceptions. Psychiatric Status will be evaluated by child study center psychologist with the use of an interview, a child behavior checklist (parent and self-report), a youth evaluation scale (parent and self-report), a three-factor eating questionnaire, and a child depression inventory.

Child Behavior Checklist (CBCL)

The Child Behavior Checklist (CBCL) is a device by which parents or other individuals who know the child well rate a child's problem behaviors and competencies. This instrument can

either be self-administered or administered through an interview. The CBCL can also be used to measure a child's change in behavior over time or following a treatment. The first section of this questionnaire consists of 20 competence items and the second section consists of 120 items on behavior or emotional problems during the past 6 months. The target age group of the test is 6 through 18 years old. Criterion validity was assessed and found to be acceptable.

The Youth Evaluation Scale (Y.E.S.)

The Youth Evaluation Scale (Y.E.S.) is a biopsychosocial assessment instrument for weight-related problems of boys and girls 12 to 20 years of age. Y.E.S. is designed for individual assessment and is a valuable component of the assessment of bulimia and anorexia nervosa. Subscales include physical, behavioral, fitness, depression, anxiety, self-esteem, family system, communication, and knowledge. Y.E.S. includes questionnaires for the adolescent and parent(s). Answers to over 600 questions are compared to established norms in each subscale. The analysis generates the Y.E.S. provider's summary report which presents historical, sensitive and specific information to the clinician. A separate Y.E.S. results report is also generated for parent(s) and adolescent education. Follow-up questionnaires and data summaries support the evaluation of post-treatment and long term changes. Using Y.E.S. involves administering the questionnaires to the adolescent and parent(s) and collecting data on weight, height and triceps skinfold.

Child Depression Inventory (CDI)

The CDI is a self-report, symptom-oriented scale which requires at least a first grade reading level and was designed for school-aged children and adolescents. The CDI has 27 items, each of which consists of three choices. The child or adolescent is instructed to select one sentence for each item that best describes him or her for the past two weeks. QuickscoreTM form scoring makes the inventories easy and economical to administer. The CDI profile contains the following five factors plus a total score normed according to age and sex: negative mood, interpersonal problems, ineffectiveness, anhedonia, and negative self-esteem. The assessment is designed for a variety of situations, including schools, child guidance clinics, pediatric practices, and child psychiatric settings.

Three-Factor Eating Questionnaires

51-item three-factor eating questionnaire is to measure three dimensions of human eating behavior; (1) 'cognitive restraint of eating', (2) 'disinhibition' and (3) 'hunger'.

(See Table I)

3.4.3 Baseline Evaluations

- Height and weight
- Blood pressure
- Baseline laboratory
    - Metabolic profile (Sodium, Potassium, Chloride, CO_2, BUN, Creatinine, Glucose, Calcium)
    - Hematologic profile (Hemogram)

  - Thyroid panel (T_3, T_4, TSH, Free T_4)
  - Lipid panel (Total cholesterol, LDL, HDL, Triglycerides)
  - Hepatic function panel (Albumin, Alkaline Phosphatase, Total Bilirubin, Direct Bilirubin, ALT, AST, Total Protein)
  - HbA1c and Insulin
  - Nutritional panel (Iron, Folate, B12, Vitamin D 25-Hydroxy, PTH, Magnesium, Phosphorus)
  - OGTT (Oral Glucose Tolerance Test) (excluding subjects who have Type I or II diabetes)
- Urinalysis
- Bone density
- Chest x-ray
- EKG
- Gall bladder ultrasound
- Serum pregnancy test (for female subjects)
- Pulmonary Function Testing (if indicated by history and physical)
- Sleep study (if indicated by history and physical)

Gastrointestinal evaluation will include:

- Esophagram
- Esophageal manometry, (if necessary, to evaluate for esophageal dysmotility if patient presents with dysphagia and abnormal esophagram indicating achalasia)

Nutritional evaluation will include:

- Initial nutritional assessment
- Follow up nutritional assessment

Psychiatric evaluation will be evaluated by:

- Psychiatric Assessment
- Child Behavior Checklist (parent and self-report, attached: Appendix C)
- Youth Evaluation Scale (parent and self-report, attached: Appendix D)
- Child Depression Inventory (CDI, attached: Appendix A)
- Three-Factor Eating Questionnaire (attached: Appendix B)
- SF-36 Health Survey (attached: Appendix E)

3.4.4 Surgery

Subjects and parents will be required to attend an intensive pre-op assessment by the bariatric team at NYU prior to the operative procedure. Placement of the Lap-Band System will be performed laparoscopically and with the patient under general anesthesia. Placement of the Lap-Band via laparotomy will be performed only in cases where conversion is needed. The surgery will be done on an inpatient or outpatient basis. All patients will receive prophylactic antibiotics.

3.4.5 Follow-Up Visits

3.4.5.1 Scheduled Visits

Study data will be collected at 1-2 week, 6 weeks, 3 months, 6 months, 9 months, 12 months, and every 6 months thereafter for a total of five years. Subjects will be weighed and given a physical examination. Parents and subjects will meet with the nutritionist at these same visits.

The subjects will maintain the behavior modification program worked out with the nutritionist and psychologist before surgery. These programs are individualized to each subject's dietary habits, eating habits, and quality of life issues. The subject will be encouraged and counseled to combine their Lap-Band tool with long-term modifications in their lifestyle, including exercise. Weight loss, status of pre-operative comorbidities and development of complications will be reviewed at every follow-up visit. This will include testing to follow pre-operative comorbidities. Baseline laboratory and nutritional parameters will be repeated every 3 months for the first year post op. OGTT will be performed at 1 year and 5 year on the subjects who have impaired glucose tolerance at baseline testing (excluding subjects who have type I or II diabetes who is not clinically safe to perform the test). However, if the HbA1c or fasting blood glucose tests show abnormal results or the subject develops polyuria or polydipsia, additional interval testing should be performed based on ADA guidelines.

All laboratory, gastrointestinal, EKG, nutritional, and psychiatric evaluations which were performed at baseline will be repeated every 12 months.

3.4.5.2 Band Adjustments

Fluid will be added to or removed from the band as indicated by the clinical progress, physical examination, and esophagram done at follow-up visit.

The adjustments will be performed as per study device manufacture’s DFU.

Visits for band adjustments can also be initiated by the patient or their course between scheduled visits. If they lose weight too quickly; develop symptoms such as heartburn, nausea, vomiting or overeating; or develop a condition or illness requiring them to eat more, they will be evaluated for removal of fluid from the band. If they lose weight too slowly or overeat, they will be evaluated for addition of fluid to the band. Each evaluation will involve review of their clinical progress, physical examination, and esophagram if necessary.

3.4.6 Diet

No calorie-specific diets
No weight loss medications
Eat slowly and chew thoroughly
Stop eating when full

3.4.6.1 POST OP Week 1 and 2

Liquids only moving to full liquids

3.4.6.2 POST OP Week 3 and 4

Blended diet with puree foods
Do not drink with meals

3.4.6.3 POST OP Weeks 5 and 6

Soft Diet
Do not drink with meals

3.4.6.4 POST OP Week 7 and beyond

No texture restrictions
Well balanced low-fat diet
Do not drink with meals
Include high fiber and high protein foods
Three small meals everyday
Drink 8 cups of liquid everyday

3.4.7 Termination

If a subject decides to withdraw from the study and desires the Lap-Band removed, this will be done using laparoscopic techniques when possible. The appropriate follow-up care will be provided for those cases, including hospital and clinic follow-up when necessary. In these cases, upper gastrointestinal studies will be performed when necessary.

After the five-year study is complete, subjects have the option of having the band surgically removed or keeping the band. If the subject chooses to keep the band, they will be followed with office visits every six months.

3.5 Interim Analysis

After the first 10 patients have completed 6 months of follow-up, an interim analysis of the safety and effectiveness data will be performed and the results submitted to the FDA.

3.6 Adverse Events

3.6.1 Adverse Events

Peri-operative adverse events include, but are not limited to, nausea and/or vomiting, pneumonia, thromboembolism, obstruction, bleeding, peritonitis, infection, and death.

Post-operative adverse events include, but are not limited to, nausea and/or vomiting, gastric prolapse, band erosion, dysphagia, tubing failure, port migration, esophageal dilation and band explantation.

Potential adverse events related to the Lap-Band® System surgery (per device labeling) include, but are not limited to, the following:

1. Inability to inflate band due to suspected band leak, access port leak, tubing leak, obstruction or other condition
2. Stomach/pouch slippage
3. Erosion
4. Suture disruption
5. Severe infections that require surgical interventions, such as those resulting from gastric perforation, subphrenic abscess, necrotizing fasciitis, pancreatic abscess and any infection that fails to respond to less invasive treatment (culture required)
6. Gastric perforation
7. Splenic injury
8. Hepatic injury
9. Pulmonary emboli
10. Deep vein thrombosis
11. Serious cardiac/respiratory adverse events (i.e. cardiac/respiratory arrest)
12. Adverse events, which in the opinion of a rheumatologist, may be related to the band (i.e. pain, swelling of joints, tightness, redness or swelling of skin, swollen glands or lymph nodes, unusual and unexplained fatigue, and unusual hair loss)
13. Rashes or other skin reactions
14. Pain resulting in hospitalization
15. Any other serious complication that poses a life-threatening condition to the subject
16. Blood loss resulting in a blood transfusion
17. Death

All adverse events will be recorded on appropriate case report form(s). A summary of the adverse events including frequency, type, and severity will be reported.

3.6.2 Adverse Event Recording

Adverse events are intended to be volunteered by subjects or observed by the investigator. All adverse events are to be recorded on appropriate case report forms. The investigator is instructed to report any serious adverse event immediately to the IBRA.

3.6.3 Serious Adverse Event Reporting

Any serious adverse event will be reported to the IRB within one business day by telephone. The Chairman of the Institutional Review Board will be notified within one business day.

1. Subject's initials and subject number
2. Investigator's name
3. Protocol title and number
4. Subject's date of birth, gender, and race

5. LAP-BAND® System date of implantation surgery
6. Concomitant medication(s): dose, route, duration of treatment, date of last dose
7. Information regarding the adverse event:

    - description
    - date(s) the event began and ended
    - whether the experience resulted in death or was life-threatening
    - whether hospitalization was required or prolonged
    - any treatment(s) required
    - outcome(s) of treatment(s)
    - investigator's determination of relationship to the test article(s)

3.7 Data and Statistical Analysis

3.7.1 Primary Efficacy Variable

The primary efficacy variable is weight loss evaluated in terms of % excess weight loss (EWL).

3.7.2 Secondary Efficacy Variable(s)

The secondary variables for evaluation are:

- Body mass index (BMI)
- Status of co-morbidities
    - Diabetes Mellitus or Impaired Glucose Tolerance
    - Hypertension
    - Asthma
    - Obstructive sleep apnea
    - Dyslipidemia
    - Gastroesophageal reflux disease
    - Urinary stress incontinence
    - Depression
    - Osteoarthritis
    - Back pain
    - Dyspnea and respiratory abnormalities
- Quality of life scores, depression degree, psychiatric evaluation

In general, the status of the comorbid conditions will be classified as unchanged, improved, resolved, or worsened. For the analysis of change in comorbidity status by the McNemar test, unchanged or worsened will be grouped into one category and resolved or improved will be grouped into a second category. For diabetes, this means whether there is change in serum HbA1c, insulin, OGTT, or fasting serum glucose or the amount of medication or no need for medication,. For hypertension, this means whether there is change in blood pressure or the amount of medication or no need for medication. For asthma, this means whether there is change in the amount of medication or no need for medication. For sleep apnea, this means

whether there is change in the sleep apnea study or a normal sleep apnea study. For hyperlipidemia, this means whether there is change in the lipid panel or the amount of medication or no need for medication. For gastroesophageal reflux, this means whether there is change in an annual esophagram or their symptoms. For urinary stress incontinence, this means whether there is change in clinical symptoms. For depression, this means whether there is change in the amount of medication or no need for medication or specified psychiatric evaluations.

3.7.3 Nutritional status

Nutritional status will be evaluated by a registered dietician with the use of initial nutritional assessment and follow up nutritional assessment. Nutritional panel (Iron, Folate, B12, Vitamin D 25-Hydroxy, PTH, Magnesium, Phosphorus) will be performed every 3 months for the first year and then annually for 5 years.

3.7.4 Psychiatric Status

Psychiatric Status will be evaluated by child study center psychologist with the use of an interview, a child behavior checklist (parent and self-report, a standard screen for general psychopathology), a youth evaluation scale (parent and self-report, YES has been utilized with a particular educational weight loss program to assess readiness for treatment as well as screen for psychopathology), a three-factor eating questionnaire (to measure three dimensions of human eating behavior, 1) cognitive restraint of eating, 2) disinhibition, and 3) hunger), and a child depression inventory (a standard screen for depression). Status of quality of life will be evaluated objectively with a standardized SF-36 Health Survey.

3.7.5 Safety Evaluations

Mortality:
Thirty day mortality will be evaluated to monitor death, which may have been directly related to the intervention.

Esophageal dilation:
The long-term effects of gastric banding on esophageal motility are unknown. The risk of chronic esophageal dilatation with loss of peristalsis is theoretical and unproven. Annual post-operative esophagrams will be performed to monitor esophageal anatomy and band positioning. If necessary, esophageal manometry will be performed to evaluate for esophageal dysmotility if patient presents with dysphagia and abnormal esophagram indicating achalasia.

Nutritional deficiency:
Although there has been no known nutritional deficiency linked with gastric banding, there have been no long-term studies that measure biochemical markers of nutrition or evaluation of eating behavior. Potential nutritional deficiencies will be monitored with annual blood work and nutritional evaluations, as described.

3.7.6 Statistical Methods

Change in the primary efficacy endpoint, % EWL, will be evaluated by a linear modeling in which the covariance among repeated measures of weight loss from month 6 to month 60 is

modeled. SAS PROC MIXED will be used in which two covariance structures will be examined by means of a REPEATED statement: unstructured (UN) and autoregressive (AR(1)). AIC will be examined to determine the most suitable structure. In the case that AR(1) is selected, a RANDOM statement for Subject will be included in the model. The predictive variable of greatest interest in the model is time. % EWL is expected to increase after surgery, more quickly initially, and then more slowly. To test for this decelerating trend, Time will be log transformed. The residuals of the model will be examined, especially those relative to predicted weight loss over time to ensure that the model is not over or under predicting over the course of follow-up. Systematic departures of the residuals from the predicted time course may require adding a quadratic trend to the model or the choice of a different transformation for time. Covariates used in the model will include baseline weight (as measured by BMI).

The null hypothesis is that % EWL will remain unchanged (i.e., at zero) post surgery. The alternate hypothesis is that % EWL will be positive post surgery. An alpha of 0.05 will be used to determine if the null hypothesis is rejected. The form of the weight loss over time is not part of the hypothesis of the study, but instead is included to better understand the expected trend weight loss follows.

The secondary efficacy endpoint, BMI, will be tested using a model similar to that used to test % EWL. The covariance structure selected for the modeling of % EWL will be applied in the modeling of BMI. Similarly, the same transformation of time will be applied to this endpoint. Baseline BMI will not be included as a baseline covariate, but instead will be assigned a value of time 0 and will be included as an endpoint measure. The null hypothesis is that BMI will show no change from time of surgery. The alternate hypothesis is that BMI will decrease after surgery.

The secondary efficacy endpoint of change in co-morbidities will be examined by McNemar tests. The null hypothesis is that there is no change in each co-morbidity post surgery. The alternate hypothesis is that there will be a change in each co-morbidity.

The secondary efficacy endpoint of quality of life change, as measured by the SF36 scale, will be examined by testing the mean change against the null hypothesis of zero (no change) by means of a paired t-test. The alternate hypothesis is that improvements will be seen between pre and post surgery in SF36 scale scores. A further analysis will examine whether change in SF36 scale scores is correlated with amount of weight lost.

The secondary efficacy endpoint of depression change, as measured by the child depression inventory, child behavior checklist, and youth evaluation scale, will be examined by testing the mean change against the null hypothesis of zero (no change) by means of a paired t-test. The alternate hypothesis is that improvements will be seen between pre and post surgery in depression inventory scores. A further analysis will examine whether change in depression is correlated with amount of weight lost.

Descriptive statistics will be provided for secondary variables such as nutrition status, psychiatric evaluations, etc.

3.7.7 Data Collection

Data will be collected by the principal investigator, the nurse practitioner, or nutritionist and documented on a standardized data form. The data will be entered by a research coordinator or the principal investigator in a fashion that maintains patient anonymity, using a unique identification number. The data will be entered into a secure computerized database, which can be accessed only by the principal investigator and the research coordinator with the use of a password. Data collection and statistical analysis will be performed by assigned research personnel, who will access the data using the unique patient identification number assigned.

We will collect relevant life history information from the subject's medical records including illnesses and hospitalizations that occur while subjects are participating in the research, as well as age, ethnic background, marital status, medical history, weight loss, changes in weight-related medical conditions, and information about the surgery and information about lap-band adjustments, and complications. We will collect medical information from physicians and other healthcare providers in General Surgery, Pediatric Surgery, Pediatrics, Psychiatry, and Psychology and from the NYU hospital medical records.

All data will be recorded on case report forms and compared at 6, 12, 24, 36, 48, and 60 months with baseline. Results will be reported descriptively as well as by modeling weight loss in order to assess aggregate outcomes and address the issues of safety and efficacy.

3.7.8 Stopping Rules For Adverse Events

The trial will be terminated if two or more patients die due to the surgery. The trial will be terminated if during the follow-up period two or more of the first 25 patients implanted have developed esophageal dilation. The trial will also be terminated if during the follow-up period two or more of the first 35 patients implanted develop a nutritional deficiency.

3.7.9 Monitoring the Study

Dr. Christine Ren Fielding's designee will monitor the study progress as frequently as is necessary to assure compliance with Good Clinical Practices and protocol procedures and to monitor completion of case report forms. All records pertaining to the study will be made available to clinical research associate at each monitoring visit. The investigational facilities, case report forms, patient records, and all other study documentation will be available for detailed review. Arrangements for monitoring visits will be agreed in advance of planned visits, except in the case of an emergency. FDA representatives reserve the right to visit sites at any time.

3.7.10 Data Safety Monitoring Board

The data safety monitoring board will be composed of three independent physicians who expertise in the treatment of obesity, clinical trials, and statistical knowledge.

DSMB will meet quarterly and the location will be determined at least 2 weeks before the meeting date. The main responsibility of DSMB is to monitor data to provide evidence for

safety concerns and recommendations for study continuation, discontinuation, or modification due to benefit vs. harm.

The following data will be reviewed by DSMB.

1. baseline data
2. safety data
3. efficacy data

A third party surgeon, Dr. Evan Nadler, who is not affiliated with NYU SOM and NYU Hospital will serve as the safety monitor.

Evan P Nadler MD
Co-Director, Children's National Obesity Institute
Associate Professor of Surgery and Pediatrics
The George Washington University School of Medicine & Health Sciences
Children's National Health System
111 Michigan Avenue, NW
Washington, DC 20010

The appointed surgeon will monitor the safety data every year and will review all SAEs. All SAEs will be reported to the appointed surgeon within 10 days regardless the relationship to the study procedure.

4.0 Ethics

4.1 Ethical Principles

This study will be conducted in accordance with Title 21 of the Code of Federal Regulations, Part 812 on Investigational Device Exemptions. Specifically, this study is based on Good Clinical Practices; the study will be conducted under a protocol reviewed by the New York School of Medicine Institutional Board of Review Associates (IBRA); the study is to be conducted by scientifically and medically qualified persons; the benefits of the study are in proportion to the risks; the rights and welfare of the subjects will be respected; the physicians conducting the study will ensure that the hazards do not outweigh the potential benefits; the results to be reported will be accurate; subjects will give their informed consent and will be competent to do so and not under duress; and the ethical principles in Title 21 of the Code of Federal Regulations will be complied with.

4.2 Informed Consent

This study will be conducted in full compliance with the informed consent regulations in 21 Code of Federal Regulations 50. Written informed consent will be given by all subjects participating in this study in accordance with the 21 CFR 312, 600, and 812. The consent form must be reviewed and approved by the IBRA prior to initiation of the study. The consent form must contain a full explanation of the possible advantages, risks, alternate treatment options, and availability of treatment in the case of injury, in accordance with Title 21 of the Code of Federal Regulations. The consent should also indicate that, by signature, the subject, or where appropriate, legal guardian, permits access to relevant medical records by representatives of the FDA.

The investigator is responsible for obtaining written consent from potential subjects prior to performing any trial tests or assessments required by the protocol. A copy of the signed consent document will be given to the subject and the original retained by the investigator with the site's copy of the case report forms.

4.3 Institutional Board of Review Associates (IBRA)

This study will be conducted in full compliance with the New York University School of Medicine Institutional Board of Review Associates policies and procedures and the regulations in 21 CFR 812 and 56.

This protocol will not be initiated unless it has been reviewed and approved by, and remains open to continuing review by the IBRA meeting the requirements of 21 CFR 812.42. The IBRA shall review and have the authority to approve, require modification of (to secure approval), or disapprove the protocol. The IRB shall notify the investigator in writing of its decision. The IBRA shall require that the information given to subjects as part of the informed consent is in accordance with 21 CFR 812.43 and 50.25. The IBRA shall conduct continuing reviews of the protocol at intervals appropriate to the degree of risk, but not less than once per year. Further, at the completion or early termination of the trial, a final report should be made to the IBRA by the investigator within 90 days.

Any change or revision in the protocol that significantly affects the safety of the subjects, the scope of the investigation, or the scientific quality of the trial must be approved by the IBRA prior to implementation. However, any protocol change intended to eliminate an apparent immediate hazard to the subject may be implemented immediately if the FDA is subsequently notified of the amendment by the investigator and the IBRA is informed by the investigator. [21 CFR 812.40]

It is the investigator's obligation to maintain an IBRA correspondence file, and to make this file available for review as part of the trial monitoring process. [21 CFR 812.140]

5.0 REFERENCES

1. National Institute for Health Care Management. Childhood Obesity - Advancing Effective Prevention and Treatment: An Overview for Health Professionals. National Institute for Health Care Management Foundation Forum, April 9, 2003.
2. United States Department of Health and Human Services. Health implications of Obesity. National Institutes of Health Consensus Development Conference, March 1991.
3. Greenstein R., Rabner J. Is Adolescent Gastric-Restrictive Antiobesity Surgery Warranted?, Obesity Surgery, 1995; 5(2): 138-144.
4. Breaux C. Obesity Surgery in Children, Obesity Surgery, 1995; 5(3): 279-284
5. Sugerman H., Sugerman E., DeMaria E., Kellum J., Kennedy C., Mowery Y., Wolfe L. Bariatric Surgery for Severely Obese Adolescents, Journal of Gastrointestinal Surgery, 2003; 7: 102-108.

6. Chapman, A.E.; Kiroff ,G.; Game, P.; Foster, B.; O'Brien, P.; Ham, J,.;Maddern GJ.Laparoscopic adjustable gastric banding in the treatment of obesity: A systematic literature review. Surgery, 2004,*135*,326-51
7. Belva P., Takieddine M., Lefebvre J.C., Vaneukem P., Laparoscopic Gastric Banding with Lap-Band® Results and Complications (Belgian and European Data), Obesity Surgery, 1997; 7, 299.
8. Fielding, G.A.; Rhodes, M.; Nathanson, L.K. Laparoscopic gastric banding for morbid obesity. Surg Endosc, 1999;*13*:550-554.
9. Vertruyen, M. Experience with LAP-BAND system up to 7 years. Obes Surg, 2002,*12*,569-572
10. Rubenstein, R.B. Laparoscopic adjustable gastric banding at a US center with up to 3-year follow-up. Obes Surg, 2002,*12*,380-384
11. Ren C., Horgan S., Ponce J. US Experience with the LAP-BAND System, The American Journal of Surgery, 2002; 184: 46S-50S.
12. Dolan K., Creighton L., Hopkins G., Fielding G. Laparoscopic Gastric Banding in Morbidly Obese Adolescents, Obesity Surgery, 2003; Feb; 13(1): 101-4.
13. Dolan K and Fielding G. A comparison of laparoscopic adjustable gastric banding in adolescents and adults. Surg Endosc. 2004;18:45-47.
14. Hypponen E, Virtanen SM, Kenward MG, Knip M, Akerblom HK; Childhood Diabetes in Finland Study Group. Obesity, increased linear growth, and risk of type 1 diabetes in children Diabetes Care. 2000 Dec;23(12):1755-60.
15. Vignolo M, Naselli A, Di Battista E, Mostert M, Aicardi G. Growth and development in simple obesity Eur J Pediatr. 1988 Apr;147(3):242-4.
16. Amador M, Bacallao J, Hermelo M. Adiposity and growth: relationship of stature at fourteen years with relative body weight at different ages and several measures of adiposity and body bulk. Eur J Clin Nutr. 1992 Mar;46(3):213-9.
17. Biro FM, Lucky AW, Simbartl LA, Barton BA, Daniels SR, Striegel-Moore R, Kronsberg SS, Morrison JA. Pubertal maturation in girls and the relationship to anthropometric changes: pathways through puberty. J Pediatr. 2003 Jun;142(6):643-6.
18. Wang Y. Is obesity associated with early sexual maturation? A comparison of the association in American boys versus girls. Pediatrics. 2002 Nov;110(5):903-10.
19. Morrison JA, Barton B, Biro FM, Sprecher DL, Falkner F, Obarzanek E Sexual maturation and obesity in 9- and 10-year-old black and white girls: the National Heart, Lung, and Blood Institute Growth and Health Study. J Pediatr. 1994 Jun;124(6):889-95.
20. Giusti V, Suter M, Heraief E, Gaillard RC, Burckhardt P. Effects of laparoscopic gastric banding on body composition, metabolic profile and nutritional status of obese women: 12-months follow-up. Obes Surg. 2004 Feb;14(2):239-45
21. Strauss BJ, Marks SJ, Growcott JP, Stroud DB, Lo CS, Dixon JB, O'Brien PE Body composition changes following laparoscopic gastric banding for morbid obesity Acta Diabetol. 2003 Oct;40 Suppl 1:S266-9.
22. Sergi G, Lupoli L, Busetto L, Volpato S, Coin A, Bertani R, Calliari I, Berton A, Enzi G. Changes in fluid compartments and body composition in obese women after weight loss induced by gastric banding Nutr Metab. 2003;47(3-4):152-7
23. Pontiroli AE, Pizzocri P, Librenti MC, Vedani P, Marchi M, Cucchi E, Orena C, Paganelli M, Giacomelli M, Ferla G, Folli F. Laparoscopic adjustable gastric banding for the treatment of morbid (grade 3) obesity and its metabolic complications: a three-year study. J Clin Endocrinol Metab. 2002 Aug;87(8):3555-61.

24. Wadstrom C, Backman L, Forsberg AM, Nilsson E, Hultman E, Reizenstein P, Ekman M. Body composition and muscle constituents during weight loss: studies in obese patients following gastroplasty Obes Surg. 2000 Jun;10(3):203-13
25. Dittmar M, Heintz A, Hardt J, Egle UT, Kahaly GJ Metabolic and psychosocial effects of minimal invasive gastric banding for morbid obesity. Metabolism. 200 Dec;52(12):1551-7.
26. Coates PS, Fernstrom JD, Fernstrom MH, Schauer PR, Greenspan SL. Gastric bypass surgery for morbid obesity leads to an increase in bone turnover and a decrease in bone mass. J Clin Endocrinol Metab. 2004 Mar;89(3):1059-60.
27. Newbury L, Dolan K, Hatzifotis M, Low N, Fielding G Calcium and vitamin D depletion and elevated parathyroid hormone following biliopancreatic diversion. Obes Surg. 2003 Dec;13(6):893-5.
28. Pugnale N, Giusti V, Suter M, Zysset E, Heraief E, Gaillard RC, Burckhardt P. Bone metabolism and risk of secondary hyperparathyroidism 12 months after gastric banding in obese pre-menopausal women. Int J Obes Relat Metab Disord. 2003 Jan;27(1):110-6.
29. Soper RT, Mason EE, Printen KJ, Zellweger H. Gastric bypass for morbid obesity in children and adolescents J Pediatr Surg. 1975 Feb;10(1):51-8.
30. Rand C, MacGregor A Adolescents having obesity Surgery: A six year follow up. Southern Med J 1994 87 1208 – 1213
31. Strauss RS, Bradley LJ, Brolin RE Gastric Bypass surgery in adolescents with morbid obesity J Pediatr. 2001 138 499 – 504
32. Capella JF, Capella RF Bariatric Surgery in Adolescence. Is this the best age to operate? Obesity Surg 2003, 13 826 ? 832
33. Stanford A, Glascock JM, Eid GM, Kane T, Ford HR, Ikramuddin S, Schauer PR Laparoscopic Roux-en-Y gastric bypass in morbidly obese adolescents J Pediatr Surg 2003 38 430 – 433
34. Knerr I, Horbach T, Plank C, Carbon R, Nusken KD, Rascher W, Dotsch J. Laparoscopically performed gastric banding in a 13 year-old girl with morbid obesity and end stage renal insufficiency allows lifesaving weight loss and hemodialysis J Pediatr Endocrinol Metab. 2003 Oct-Nov;16(8):1179-82
35. Dolan K. Creighton L, Hopkins G, Fielding GA Laparoscopic Gastric Banding in Morbidly Obese Adolescents Obesity Surg 2003 13 101 – 104
36. Dolan K, Fielding GA A comparison of laparoscopic adjustable gastric banding in adolescents and adults Surg Endosc. 2003 464 (1) 45 - 47 Epub ahead of print
37. Fielding GA, Duncombe J Laparoscopic adjustable gastric banding in teenagers – results at 3 years ASBS annual meeting 2004
38. Bruehl H, Sweat V, Hassenstab J, Polyakov V, Convit A. Cognitive impairment in nondiabetic middle-aged and older adults is associated with insulin resistance. *J Clin Exp Neuropsychol.* Jun 2010;32(5):487-493.
39. Hassenstab JJ, Sweat V, Bruehl H, Convit A. Metabolic Syndrome Is Associated with Learning and Recall Impairment in Middle Age. *Dement.Geriatr.Cogn Disord.* 2010;29(4):356-362.
40. Yau PL, Javier D, Ryan CM, et al. Structural and Functional Brain Complications in Obese Adolescents with Type 2 Diabetes Mellitus *Under Submission.* Under Submission 2008.

41. Egger JR, Bartley KF, Benson L, Bellino D, Kerker B. Childhood Obesity is a Serious Concern in New York City: Higher Levels of Fitness Associated with Better Academic Performance. *NYC Vital Signs.* 2009;8(1):1-4.

6.0 Table I Schedule of Visits and Procedures

				Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7,9,11, 13	Visit 8,10,11,14	>18 yrs old (high school graduation)
Procedure	**Screening**	**PreOP**	**OP**	**Week 1-2**	**Week 6**	**3 m**	**6 m**	**9 m**	**1 Y**	**Every 6m**	**2 Y, 3Y, 4Y, 5Y**	
Informed Consent	X								X		X	
Additional IC for high school grades												X
Inclusion/Exclusion Criteria	X											
Complete Physical Exam	X								X		X	
Demographics Information	X											
Medical History	X											
Wt Loss History	X											
Co-morbidities and Concomitant Medications	X								X	X	X	
Lap-Band Implant/Revision			X									
Lap-Band Adjustment*				X	X	X	X	X	X	X	X	
Follow up Clinical Assessment				X	X	X	X	X	X	X	X	
Labs												
Metabolic Panel		X				X	X	X	X		X	
Hematology Panel		X				X	X	X	X		X	
Thyroid Panel		X				X	X	X	X		X	
Lipid Panel		X				X	X	X	X		X	
Hepatic Function Panel		X				X	X	X	X		X	
Nutritional Panel		X				X	X	X	X		X	
HbA1c & Insulin		X				X	X	X	X		X	
OGTT*		X							*X		*X	
Urinalysis		X							X		X	
Serum Pregnancy Test (If female)		X							X		X	
EKG		X							X		X	
Pulmonary Function Test (If indicated)		X							X		X	
Chest X-Ray		X										
Gall bladder ultrasound		X										
Bone Density		X										
Gastrointestinal Evaluation												
Esophagram		X							X		X	
Esophageal manometry (if necessary)		X							X		X	
Sleep Apnea Test (if indicated)		X							X		X	
Psychiatric Evaluation												
Psychiatric Assessment*	X					*X	*X		X		X	
Child Depression Inventory	X								X		X	
Three-Factor Eating Questionnaire	X								X		X	

Child Behavior Checklist	X								X		X	
Youth Evaluation Scale	X								X		X	
SF-36 Health Survey	X								X		X	
Nutritional Evaluation												
Initial Nutritional Assessment	X											
Follow up Nutritional Assessment		X	X	X	X	X	X	X	X	X	X	
Adverse Event Evaluation		X	X	X	X	X	X	X	X	X	X	

*OGTT will be performed at 1 year and 5 year on the subjects who have impaired glucose tolerance at baseline testing (excluding subjects who have type I or II diabetes wh is not clinically safe to perform the test). However, if the HbA1c or fasting blood glucose test show abnormal results or the subject develops polyuria or polydipisa, additional testing should be performed based on ADA guidelines.

*Additional follow up psychiatric assessment will be performed at 3 months and 6 months for the patients with antidepressants and moderate to severe psychiatric history.

Attachment for data sharing

Adolescent Lap-Band IDE (ALIDE) Study Group

Mission and Scope

Introduction

Obesity has become the most common life threatening disease affecting children in the United States. Bariatric surgery has been suggested as the only reliable means effecting significant weight loss in morbidly obese children, and protocol-controlled research into the application of the LapBand in treatment programs for adolescent obesity has been ongoing since 2005. The FDA will soon consider approving the use of the LapBand in treatment programs for adolescent obesity. Thus, results of the previous and ongoing research will be vital to the FDA considerations and to the obese adolescents who need access to surgery. These results need to be pooled, presented at the FDA panel, and published so as to best advocate for FDA extension of the indication for the device to ages less than 18, and to advocate for morbidly obese adolescents who currently have only the gastric bypass as a surgical option.

Independent IDE Studies

In 2001 the FDA approved the LapBand for use in morbidly obese adults. They specifically listed age less than 18 years as a contraindication to the use of the LapBand. In 2004, Dr. Mark Holterman of the University of Illinois at Chicago went to the FDA meeting regarding the LapBand and adolescents. Once again, use of the LapBand in children less than 18 years old was not approved. After that Dr. Mark Holterman worked with Dr. Ai-Xuan Holterman, Dr. Allen Browne and Dr Santiago Horgan to get an Investigational Device Exemption (IDE) from the FDA to study the LapBand in morbidly obese adolescents in a weight management program at the University of Illinois at Chicago – IDE #1. Subsequent to that, the group at the University of Illinois at Chicago worked with groups at New York University (Drs Ren, Fielding, Nadler), at Morgan Stanley Children's Hospital (Dr Zitsman), and at A.I. Dupont Children's Hospital (Dr Reichert) as they obtained IDE's number 2,3, and 4 respectively. The only support from Allergan for these studies was the donation of LapBands to the University of Illinois at Chicago. Each group developed unique methods to fund their studies. These 4 groups now have a

combined experience with over 150 morbidly obese adolescents who have used the LapBand in a multidisciplinary weight management program. These patients are 1-5 years out from the placement of their LapBand and have been managed with very similar protocols. All their studies are IRB approved at their local institutions and the pooled results will be acceptable for journal publication.

ALIDE Study Group
Recognition of the problem of morbidly obese children has increased greatly over the last ten years. Many organizations and many grants and studies have occurred to work on prevention of obesity in children. However, 20-50 % of different populations of children have BMI's that are already over the 95th %tile for their age and gender. These children are already obese and prevention is not appropriate for them. Very little work and study has been done on effective therapy for morbidly obese children. The TeenLabs study from the NIH has published data on comorbidities of morbidly obese adolescents, resolution of comorbidities with successful weight loss with gastric bypass surgery in morbidly obese adolescents, and the short term morbidity and mortality of gastric bypass surgery in morbidly obese adolescents.

The groups at the University of Illinois at Chicago and New York University have individually published short term safety and efficacy, as well as resolution of comorbidities, in morbidly obese adolescents after LapBand surgery. The opportunity now exists for the groups with IDE's #1,2,3, and 4 to pool their data on the safety and efficacy of the LapBand in morbidly obese adolescents. This data would be useful for the upcoming FDA panel consideration of the LapBand in morbidly obese adolescents as it will have as many, if not more, patients as the industry-sponsored multicenter trial and many patients will have longer follow-up. Furthermore, these data should published as the most extensive data so far from weight management programs for morbidly obese adolescents that utilize a surgical approach.

Project Plan and Output:
The adolescent LapBand IDE Study Group (ALIDE) was formed to achieve pooling of the data from the IDE's at the University of Illinois at Chicago, New York University, Morgan Stanley Childrens Hospital, and A.I. Dupont Children's Hospital. Also included in ALIDE study group are Dr. Allen Browne and Dr. Evan Nadler, who were part of the initial IDE work but have since left the institutions listed above.

The ALIDE study group will contact and coordinate with each of the investigators and institutes to acquire a copy of their study data which will be provided to the ALIDE Study group in a de-identified manner, such that no patient can be identified by the ALIDE Study group. The ALIDE Study group will then pool the data from each institute, further de-identifying the patients prior to evaluating and analyzing the data by linear modeling. The data will then be prepared for publication, in a peer-reviewed journal. The data will also be presented to the FDA Pediatric Advisory Committee in the fall of 2010 to support the use of the LabBand in adolescents.

Plan of Action

1. IRB Approval

The ALIDE Study Group project coordinator, Bonnie Kuehl, will work with each site to achieve IRB approval for the ALIDE Study group project which is to acquire a copy of the de-identified patient data from the four institutions, followed by pooling and analysis of the data and then publication.

Key Personnel at each Site:
NYU: Youn (Allison) Heekoung
UIC: Sandra Gomez and Melissa Satterlee
A.I. Dupont: Dr. Kirk Reichard
Morgan Stanley:

2. Data Transfer

The data will be transferred electronically in a secure manner from each study site as laid out in the ALIDE Study Group Data Transfer Protocol dated March 31, 2010 (Appendix 1). This SOP ensures that patient data is deidentified by the participating site such that any information that can be used to independently identify the identity of any patient will be removed or replaced with non-specific information prior to the data transfer to ConscienHealth. The data will then be deidentified again prior to the pooled data analysis. Note, the data will not be transferred from the ALIDE Study Group secure site once received.

3. Data Analysis

The data from each institute will be pooled and further de-identified prior to evaluating and analyzing the data by linear modeling. The ALIDE study group has identified and agreed upon the data fields (Appendix 2) for which they hope to acquire data from each institute to complete the pooled analysis. The agreed upon data fields will not include date of birth, if needed age will be calculated or estimated.

4. Publication/Presentation

Once the data analysis is complete the data will then be prepared for publication in a peer reviewed journal deemed appropriate by the ALIDE study group and the investigators from each site. The data will also be presented to the FDA Pediatric Advisory Committee in the fall of 2010 to support the use of the LabBand in adolescents. In all publications/presentations the lead investigator from each site and the institution will be acknowledged for their involvement in the project.

APPENDIX 1

ALIDE Study Group Data Transfer Protocol

Approved: March 31, 2010

Prior to transfer

- Each participating site will be provided with the specific data element requirements that will need to be included with the submission package.
- All data will be submitted in an electronic format.
- Prior to submission, the data will be de-identified by the participating site such that any information that can be used to independently identify the identity of any patient will be removed or replaced with non-specific information.
- Each patient will be assigned an identification number and the information linking an identification number with the patient will be held by the participating site and not distributed to any groups outside the participating site.
- Following the collection and preparation of the data in a suitable electronic format, the data will be transferred, as follows.

Data Transfer

- Each site will be provided with a URL (address) for a secure web server.
- Security will be established using SSL and identification accomplished by using self-signed certificates. Each site will be provided with a guide to ensure that the certificates are accepted by the browser and a connection with the web server is established. Due to the limited number of participating sites, a certificate signed by an outside agency will be not obtained.
- Prior to allowing data transfer, the web server will ensure that a secure connection is established; if the connection is established using an insecure mechanism, the client will be redirected automatically to the secure mechanism.
- The participating site will be presented with an authentication page to provide both a user ID and a password; both will be provided with the data requirements package.
- Upon successful authentication using user ID, the site will be presented with a page to select a file to download. The participating site will then download a file with the de-identified data to the secure web server.

Following Transfer

- Following transfer, the web server will move the copied file to a secure, web non-accessible location. Following transfer, the data file will no longer be available to the participating site, or any other public site.
- The information package will no longer be distributed through the public internet but will be physically transferred using portable electronic methods or using private and secure networks.

Data Safeguards

- File transfer will be only allowed using SSL encrypted file transfer protocols.
- Authentication and data upload will be only allowed for participating sites and will be secured by unique passwords and user information.

- In the unlikely event that the transferred data is intercepted or otherwise is obtained, the information will not contain information that will allow for the independent identification of individual patients, but will require further information held by the participating site to allow patient information.
- The information to allow identification of patients will not be requested by the study and will not be transferred outside of the study site.

APPENDIX 2

Data Field Request- June 2010

1	Age at surgery (Date of birth will not be given, if needed age will be calculated or estimated)	
2	Height at surgery	
3	Weight at surgery – before preop diet	
4	BMI at surgery - before preop diet	
5	Duration of surgery (if data exists)	
6	Age at onset of obesity (if data exists)	
7	Length of preop preparation – months (not needed for FDA)	
8	Length of hospitalization - days	
9	Operative complications – list	
10	Readmissions within 30 day post op – Y/N	
11	Preop comorbidities a) OSA b) Pseudotumor cerebri c) Hypertension d) Abnormal EKG e) Abnormal cardiac ECHO f) Asthma g) GERD h) NASH	i) PCOS j) SCFE k) Diabetes l) Prediabetes – abnormal GTT or elevated fasting insulin m) Hyperlipidemia n) Kidney disease
12	Preop Evaluations a) EKG (if data exists) b) Cardiac ECHO (if data exists) c) Fasting glucose d) Fasting insulin e) GTT f) LFT's	g) Lipids h) Nutritional Panels (if data exists) i) Quality of life evaluations (if data exists) j) Depression questionnaire (f data exists)
13	Items monitored post op – 3 months, 6 months, 9 months, 12 months, 18 months, 2 years, 2.5 years, 3 years, 3.5 years, 4 years, 4.5 years, 5 years a) Height b) Weight c) BMI d) EKG (if data exists) e) Cardiac ECHO f) Fasting glucose (yearly only) g) Fasting insulin (yearly only)	k) Nutritional Panels (if data exists) l) Quality of life evaluations (if data exists) m) Depression questionnaire (if data exists) n) GTT (yearly only) o) LFT's (yearly only) p) Lipids (yearly only) q) Nutritional Panels (if data exists) r) Quality of life evaluations (if data exists)

	h) GTT (yearly only) i) LFT's (yearly only) j) Lipids (yearly only)	s) Depression questionnaire (if data exists)
14	Healthcare issues post op a) Hospitalizations b) Operations c) New medical problems	
15	Post op care (if data exists) a) Scheduled visits to weight management program – each year b) Unscheduled visits to weight management program – each year c) AGB adjustments – each year	