SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	Implant, Intragastric for Morbid Obesity
Device Trade Name:	REALIZE™ Adjustable Gastric Band (Model 2200-X)
Applicant's Name and Address:	Ethicon Endo-Surgery, Inc. 4545 Creek Road Cincinnati, OH 45242
PMA Number:	P070009
Date of Panel Recommendation:	None

Date of Notice of Approval to the Applicant: September 28, 2007

II. INDICATIONS FOR USE

The REALIZE™ Adjustable Gastric Band is intended for use in weight reduction for morbidly obese patients and is indicated for individuals with a Body Mass Index (BMI) of at least 40 kg/m^2, or a BMI of at least 35 kg/m^2 with one or more co-morbid conditions. The Band is indicated for use only in morbidly obese adult patients who have failed more conservative weight-reduction alternatives, such as supervised diet, exercise and behavior modification programs.

III. CONTRAINDICATIONS

- Inflammatory diseases of the gastrointestinal tract, including severe intractable esophagitis, gastric ulceration or duodenal ulceration, or specific inflammation such as Crohn's disease;
- Severe cardiopulmonary disease or other serious organic disease;
- Upper gastrointestinal bleeding conditions such as esophageal or gastric varices or intestinal telangiectases;
- Portal hypertension;
- Anomalies of the gastrointestinal tract such as atresia or stenosis;
- Cirrhosis of the liver;
- Chronic pancreatitis;
- Less than 18 years of age;
- Localized or systemic infection;
- Patients on chronic, long-term steroid treatment or steroids within 15 days of surgery

- Unable or unwilling to comply with dietary restrictions required by this procedure;
- Known allergy to materials contained in the Band or its Injection Port;
- Pregnancy: Women who are pregnant. Patients who become pregnant after Band placement may require fluid removal from their Band.

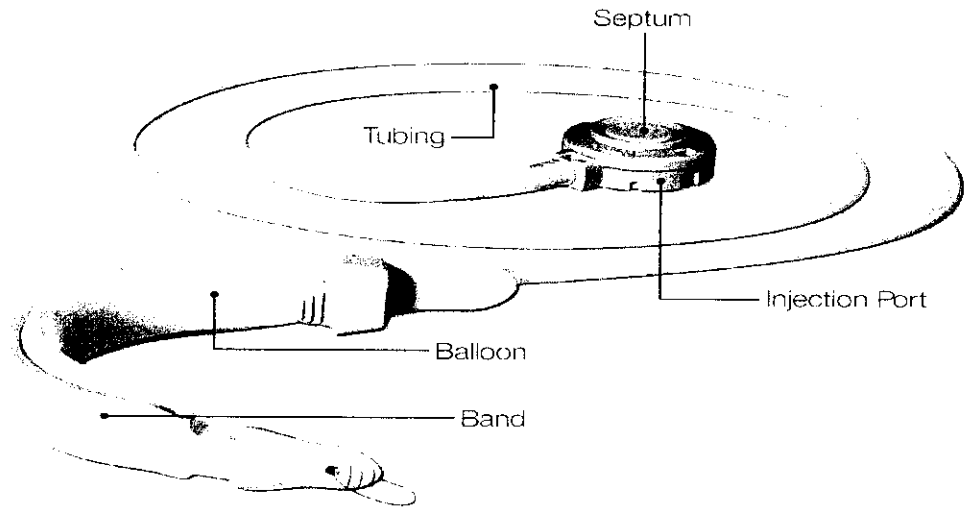
IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the REALIZE™ Adjustable Gastric Band labeling.

V. DEVICE DESCRIPTION

The REALIZE™ Adjustable Gastric Band (the Band) is a laparoscopically implanted medical device intended for use in the surgical treatment of morbid obesity. The Band is surgically implanted to create a restricted opening (stoma) and a small gastric pouch to limit food consumption and induce early satiety. There are three main device components; the reinforced band with balloon, kink resistant tubing, and the injection port (see Figure 1). The inner surface of the silicone band, which is placed around the stomach, is inflatable and connected by the tubing to the injection port (a remote injection site). The Band comes in one size, and the fit is customized by increasing or decreasing the amount of fluid in the balloon.

Figure 1 – REALIZE™ Adjustable Gastric Band and Injection Port



The reinforcing band provides structural support for the balloon and contains the mechanisms for joining the ends of the band together. The balloon is designed to hold between 0 to 9 ml of saline and provides 360° coverage around the stomach. One end of the tubing is pre-attached to the balloon and the other end must be connected to the Injection Port during surgery.

The Injection Port provides post-surgical access to the gastric band implant so that fluid can be added to or removed from the balloon. The Injection Port body is manufactured from polyetheretherketone (PEEK) and contains a silicone port septum and cobalt chromium fastening hooks (not visible in Figure 1). The port body also has three integral suture holes in the event that sutures, rather than fastening hooks, have to be used to secure the port in place. The locking connector on the Injection Port secures the tubing from the Band to the Injection Port. The Injection Port contains radiopaque components which enable visualization under radiographic imaging.

The Port Applier, which is supplied with the Band and Injection Port, is used to engage the fastening hooks on the Port and to secure the port on to the fascia of the anterior rectus sheath or the abdominal oblique muscles. The Injection Port is compatible ONLY with a REALIZE™ Adjustable Gastric Band.

The Band is wrapped around the upper stomach to form an artificial stoma. This placement creates a small pouch in the proximal stomach and a larger pouch in the distal stomach. After the band is in place, the patient cannot consume large quantities of food and weight reduction ensues. In general, clinical management goals are 0.5 to 1.0 kg (1 to 2 lbs.) weight loss per week along with the patient's ability to consume a recommended diet without vomiting. Close medical follow-up care is required as long as the Band remains in place.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Non-surgical and surgical alternatives to the Band are available for the treatment of severe obesity (body mass index greater than 35 kg/m^2).

Non-Surgical Treatments

Non-surgical treatments include diet, exercise, behavior modification and pharmacotherapy. Most individuals with severe obesity do not experience adequate weight loss with these methods alone.

Surgical Treatments

Gastric banding is a procedure where a device, the gastric band, is surgically implanted around the outside of the stomach to create a restricted opening (stoma) and a small gastric pouch to limit food consumption and induce early satiety. The size of the stoma can be changed by removing or adding fluid to the band through an injection port. The patient's anatomy remains intact and the gastric band can be surgically removed. One device, the LAP-BAND Adjustable Gastric Banding System, has received marketing approval.

The two most common surgical alternatives to gastric banding surgery include the Roux-en-Y gastric bypass (Roux-en-Y) and the biliopancreatic diversion with duodenal switch (BPD/DS). Each surgery (Roux-en-Y and BPD/DS) uses different methods to reduce stomach size and shorten the intestines.

Roux-en-Y Gastric Bypass (Roux-en-Y)
The Roux-en-Y gastric bypass procedure is the most common malabsorptive-restrictive procedure and comprises 80% of all bariatric procedures in the U.S. During the Roux-en-Y, the stomach is stapled to create a small (15-20 cc) stomach pouch. The outlet from this newly formed pouch empties directly into the lower portion of the jejunum, thus bypassing most of the stomach and the duodenum. A variation of this procedure is the long limb Roux-en-Y gastric bypass procedure which creates more malabsorption than the standard Roux-en-Y. Malabsorptive-restrictive procedures work by both reducing the number of calories absorbed and limiting the amount of food that can be eaten.

Biliopancreatic Diversion (BPD)
The BPD removes approximately three-fourths of the stomach. The small intestine is divided with one end attached to the stomach pouch to create an alimentary limb. Food moves through this alimentary limb with little absorption. Bile and pancreatic juices move through the biliopancreatic limb which is connected to the alimentary limb to form the common channel where nutrients are absorbed. The length of the common channel can be varied to regulate the amount of absorption. The Biliopancreatic diversion with duodenal switch (BPDDS) is a variation of the BPD in which stomach removal is restricted to the outer margin, leaving a stomach "sleeve" with the pylorus intact. The majority of the small intestine is bypassed, causing nearly complete malabsorption of food contents.

VII. MARKETING HISTORY

The REALIZE™ Adjustable Gastric Band has been registered and marketed in Europe since 1996. It became available to the European Union (EU) and other countries (excluding the U.S.) in 2004. The Velocity Injection Port has been marketed outside of the United States since 2005. The device has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Adverse events (AEs) that may result from use of the Band include those commonly associated with obesity surgical procedures and others associated specifically with laparoscopic implantation of gastric bands.

Potential adverse events associated with any general abdominal surgery include bleeding; pain; shoulder pain; pneumonia; complications due to anesthesia and medications; deep vein thrombosis (blood clot); injury to the stomach; esophagus; or surrounding organs; infection; pulmonary embolism; stroke or heart attack, and death.

Other adverse events reported with gastric restrictive procedures include ulceration, gastritis, gastroesophogeal reflux, bloating, dysphagia, dehydration, constipation, nausea, vomiting, and weight regain. Elevated homocysteine levels have been reported in patients actively losing weight after obesity surgery and may increase cardiovascular risk. In addition, the developing fetus of pregnant women with elevated homocysteine levels may be at risk for neural tube defects. During periods of rapid weight loss patients may experience malnutrition, hair loss, anemia or other related complications, such as the development of cholelithiasis.

Risks associated specifically with laparoscopic implantation of gastric bands are potential intolerance to the components (foreign body reaction), mechanical malfunction (leakage and deflation of the balloon), access port pain or displacement, band slippage, pouch dilatation, band erosion, gastric or esophageal perforation, stoma obstruction, esophageal dilatation and esophageal dysmotility. Peritonitis and death can occur either secondary to gastrointestinal perforation during implantation of the device or due to erosion of the gastric band into the stomach. Adjustable gastric bands are long-term implants and the management of adverse events may necessitate reoperation to revise or explant the device. As with any revisional procedure, the possibility of complications such as erosion and infection may be increased.

In the REALIZE™ U.S. clinical study, 266 of 276 (96.4%) subjects reported at least one adverse event. Peri-operative adverse events (onset $\leq$ 30 days post-implantation) were reported in 73% of the study subjects. The most commonly reported peri-operative adverse events were nausea, vomiting, constipation and post-procedural pain. Ninety-four percent (94%) of subjects reported one or more adverse events in the post-operative period. The most commonly reported adverse events in the postoperative period were nausea, vomiting, constipation and gastroesophageal reflux.

The most frequently reported adverse events (occurring with a frequency of $\geq$ 5%) are displayed in Tables 17 and 18. Many adverse events were mild and required no intervention. Some serious and severe adverse events required band adjustment or re-operation to revise, replace or remove the necessary component(s). Please refer to Section X, Summary of Clinical Studies, for further information.

IX. SUMMARY OF PRE-CLINICAL STUDIES

All subjects enrolled in the US clinical study were implanted with the Model 2100-X Band with titanium port. That device has been modified to the Model 2200-X Band with Velocity Injection Port. The modifications made to the Model 2100-X to make the Model 2200-X with Velocity Injection Port include:

1. Simplification of the locking mechanism by providing a buckle/tab closure on the reinforcement band;
2. A suture pre-tied to the end of the band for surgeon convenience (helps with placement of the device);

3. Change in the manufacturing process to allow for rounding of the reinforcement band edges;
4. Port now includes a connector sleeve integrated with the locking connector;
5. The port can be attached to the fascia using either sutures or by using fasteners which are an integral component of the port. The method of attachment is dependent on the surgeon's preference.

Testing of product samples was performed on the various components of the Model 2200-X Band and Velocity Injection Port to ensure that the product performed according to product specifications. Testing was performed to evaluate all levels of the manufacturing process (i.e., raw materials used to fabricate the device, components from which the device is assembled, the finished device, the device's packaging, sterilization process for the device, and product shelf life performance). Physical (engineering) tests, biocompatibility tests, sterility, product packaging and shelf-life tests were also performed.

Physical Testing
Mechanical testing was performed for all components. The data demonstrated that the components met design specifications and intended uses. The components were subjected to dimensional and visual inspection as well as break force and tensile strength testing. The finished assemblies were packaged and subjected to gamma sterilization prior to testing. Testing conducted on the Band and the Velocity Port included:

- Force to Pull the Band through 15mm Trocar
- Peel Force between Reinforcing Band and Balloon
- Band Suture-Hole Strength
- Suture Strength
- catheter Tensile Strength
- Force to Lock Band
- Force to Unlock Band
- Force to Disconnect Balloon and Catheter
- Burst Fill Volume
- Mechanical Integrity – Band Reliability
- Catheter-to-Port Connection Fatigue
- Force to Connect Catheter and Locking Connector to Septum Retainer Fitting
- Needle punctures of port septum
- Number of Needle Punctures that Port Septum Withstands
- Magnetic Resonance Imaging (MRI) Compatibility

The results of these tests demonstrated that the Model 2200-X Band and Velocity Injection Port met the requirements and specification for each of the tests. The results of the pre-clinical data support approval of the device.

Biocompatibility Testing
The materials and components of the Band and Port that contact the patient are fabricated primarily from silicone elastomers, polymers, cobalt chromium molybdenum and titanium. The Band and Injection Port are classified as "permanent implant, tissue/bone contacting." All patient contacting materials have been evaluated and tested for biocompatibility and toxicity.

The materials used to fabricate the components in contact with the body were tested and evaluated for biocompatibility per the FDA Modified "Use of International Standard 10993-1, "Biological Evaluation of Medical Devices, Part 1: Guidance on Selection of Tests." Tests were carried out in compliance with 21 CRF Part 58 Good Laboratory Practice Regulations. The results of the biocompatibility testing demonstrated that finished devices met the acceptance criteria for each of the tests.

Sterilization, Packaging and Shelf-Life
The gamma sterilization process was validated to provide a sterility assurance level (SAL) of 10^{-6}. Studies demonstrated that the packaging system maintains the sterile barrier and the devices remain sterile after being stored on the shelf for up to 5 years.

Accelerated aging shelf-life testing has been conducted. The Band has a five-year shelf life. Packaging validation of the sales unit consists of six phases: establishing a minimum seal strength; conditioning/environmental testing; simulating transit testing; final transit testing; package integrity testing; and functionality testing.

X. SUMMARY OF CLINICAL STUDIES

Objectives:
A clinical study was conducted within the United States under a significant risk Investigational Device Exemption (IDE) to evaluate the safety and effectiveness of the REALIZE™ Adjustable Gastric Band in the treatment of morbid obesity.

Study design:
The clinical study was a prospective, multi-center, single-arm trial in which each subject served as his or her own control. Subjects were followed for 3 years post-implantation.

Subjects were implanted using the Model 2100-X Band with Titanium Port at 12 clinical sites in the U.S. beginning June, 2003. The last subject was implanted in November of 2003. A total of 405 subjects were screened for the study and 276 were implanted with the device. Follow-up evaluations were conducted at discharge from the hospital (day 1-6), 7-10 days, 4-6 weeks, 2, 4, 6, 8, 10, 12, 15, 18, 21, 24, 28, 32 and 36 months after Band implantation.

Evaluation of the safety and effectiveness of the Band was based on the following clinical endpoints:

Effectiveness

1. Percent excess weight loss (%EWL) at three years post-implantation.
2. Changes in excess body weight (EBW) throughout the three-year postoperative period.
3. Changes in body mass index (BMI) throughout the three-year postoperative period.
4. Absolute weight loss and percent change in absolute weight throughout the three-year postoperative period.
5. Changes in Quality of Life (based on the Beck Depression Index and the SF-36) throughout the three-year postoperative period.
6. Changes in glycosylated hemoglobin (HbA1c), high density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol, and triglycerides throughout the three-year postoperative period.

Safety

1. Incidence (including severity, seriousness, and duration) of device-related adverse events (AEs) and device malfunctions in the subjects implanted with the Band throughout the three-year postoperative period.
2. Incidence (severity, seriousness, and duration) all AEs in subjects implanted with the device throughout the three-year postoperative period.
3. Subject discontinuations due to explantation of the device.
4. Incidence of conversion to open surgery.

Patient Selection

To qualify for enrollment in the study, patients met all the inclusion criteria and none of the exclusion criteria listed below.

Inclusion Criteria

1. Able to comprehend, follow, and give signed informed consent;
2. 18 to 60 years of age (inclusive);
3. Five (5) year history of morbid obesity;
4. Body Mass Index (BMI) ≥ 40 kg/m^2 and ≤ 55 kg/m^2, or BMI ≥ 35 kg/m^2 and < 40 kg/m^2 with one or more significant medical conditions related to obesity (co-morbid conditions of type 2 diabetes, hyperlipidemia, obstructive sleep apnea, hypertension, metabolic syndrome, or osteoarthritis of the hip or knee) for which the subject was being treated, and which were generally expected to be improved, reversed, or resolved by weight loss.
5. 100 lbs overweight or 1.5 times their ideal body weight (IBW) as provided in the 1983 Metropolitan Life Height and Weight Table using the upper limit of the midpoint range;
6. Documented failure of conservative, non-surgical means of weight reduction within one year prior to the Screening Visit of this study, including failure of supervised diet, exercise and/or behavior modification programs, and pharmacologic therapy;

7. Willing to commit to significant lifestyle changes that included diet, eating, and exercise habits for the duration of the clinical trial;
8. Able to commit to long-term follow-up up to 3 years after device implantation, including Band adjustment visits;
9. Living within the contiguous U.S. and within a 100-mile radius of the study site;
10. Absence of significant psychopathology that could have limited the subject's ability to understand the procedure, comply with medical, surgical, and/or behavioral recommendations, as documented during screening assessment;
11. Agreed to refrain from any type of reconstructive surgery (such as abdominal lipoplasty or lipsosuction, mammoplasty, removal of excess skin) that would have affected body weight for three years following the Band placement; and
12. Candidate for surgical weight-loss intervention (i.e., met accepted health criteria for major surgery).

Exclusion Criteria

1. Women of childbearing potential who were not practicing an effective method of birth control or who were pregnant or lactating;
2. Previous malabsorptive or restrictive procedures performed for the treatment of obesity;
3. Documented history of drug and/or alcohol abuse within two (2) years of the Screening Visit;
4. History of impaired mental status by DSM4 criteria and including, but not limited to, active substance abuse, a history of schizophrenia, borderline personality disorder, uncontrolled depression, suicidal attempts within the past two (2) years, or current suicidal tendencies or ideations.
5. Presence of any of the following medical conditions:
    a. Inflammatory diseases of the gastrointestinal (GI) tract, including severe intractable esophagitis, gastric ulceration, duodenal ulceration, or specific inflammation such as Crohn's disease that had been active within the past 10 years;
    b. Congenital or acquired anomalies of the GI tract, including atresias or stenosis;
    c. Severe cardiopulmonary disease or other serious organic disease that makes the subject a high-risk surgical candidate;
    d. Uncontrolled hypertension;
    e. Portal hypertension;
    f. Uncontrolled diabetes mellitus;
    g. Chronic or acute upper GI bleeding conditions, e.g., gastric or esophageal varices;
    h. Cirrhosis;
    i. Congenital or acquired intestinal telangiectases;
    j. Esophageal or gastric disorders including severe preoperative reflux, dysmotility, or Barrett's esophagus;
    k. Presence of hiatal hernia;

l. Prior surgery of the foregut including hiatal hernia repair or prior gastric surgery;
m. Chronic pancreatitis;
n. Immunocompromised such as that resulting from chronic oral steroid use, chemotherapeutic agents, or immune deficiency disorders;
o. Conditions that, in the opinion of the investigator, may have jeopardized the subject's well-being and/or the soundness of this clinical study.

6. History or presence of pre-existing autoimmune connective tissue disease, i.e., systemic lupus erythematosus or scleroderma;
7. Presence of terminal illness with life expectancy ≤ 5 years;
8. Use of prescription or over-the-counter weight reduction medications or supplements within one month of the Screening Visit and for the duration of study participation;
9. Acute or chronic infection (localized or systemic);
10. Known or suspected allergy to silicone or other materials contained in the Band and Injection Port;
11. History of intolerance to implanted devices;
12. Not ambulatory; and
13. Participation in another clinical trial within 8 weeks of the Screening Visit and for the duration of this trial.

All patients signed an informed consent prior to being enrolled in the clinical study.

Demographic Data
Demographic data is summarized in Table 1. A total of 216 women (78.3%) and 60 men (21.7%) were implanted with the Band. The majority of patients were Caucasian (61.2%), while Black, Non-Hispanics and Hispanics comprised 12.0% and 24.3% respectively.

Co-morbidities included 118 (42.8%) subjects with a medical history of hypertension, 47 (17.8%) with diabetes mellitus, 24 (8.7%) with hyperlipidemia, and 74 (26.8%) with sleep apnea syndrome.

Forty-two of the 276 subjects (15.2%) had a baseline BMI between 35 and 40kg/m^2 and 234 subjects (84.8%) had a BMI of at least 40 kg/m^2.

The average age at the time of enrollment was 38.6 years (range 18 – 61). At baseline, the average weight was 276.5 pounds (range 194 – 415) and the average BMI was 44.5 (range 35 – 58).

Table 1
Demographic and Other Characteristics in the U.S. Trial
Intent-To-Treat Population (N= 276)

	Mean	SD	Median	Range
Age (Years)	38.6	9.4	39.0	18 – 61
Weight (lbs)	276.5	40.8	267.5	193.6 – 415.4
Ideal Body Weight (lbs)	146.5	13.4	144.0	121 – 197
BMI (kg/m^2)	44.5	4.7	43.7	35.0 – 58.1
Excess Body Weight (lbs)	130.0	33.1	121.8	61.6 – 233.8
Duration of Surgery (Min.)	73.8	21.8	70.0	35 – 184
Duration of Laparoscope (Min.)	52.9	19.2	50.0	15 – 184
Duration of Anesthesia (Min.)	115.7	28.4	112.0	21 – 222
Hospital Stay (Days)	1.2	1.3	1.1	0.1-21.2
	Count		**Percentage (%)**	
Gender:				
Male	60		21.7%	
Female	216		78.3%	
BMI				
≥ 35 and <40 kg/m^2	42		15.2%	
≥ 40 kg/m^2	234		84.8%	
Race:				
Caucasian, Non-Hispanic	169		61.2%	
Asian/Pacific Islander	4		1.4%	
Black, Non-Hispanic	33		12.0%	
Hispanic	67		24.3%	
Other	3		1.1%	

Device Implantation
Subjects were implanted with the Model 2100-X Band and the Injection Port. All but one of 276 patients (99.6%) had the Band placed laparoscopically.

Mean surgery time was 73.8 minutes. The mean hospital stay was 1.2 days (range 0.1 – 21.2).

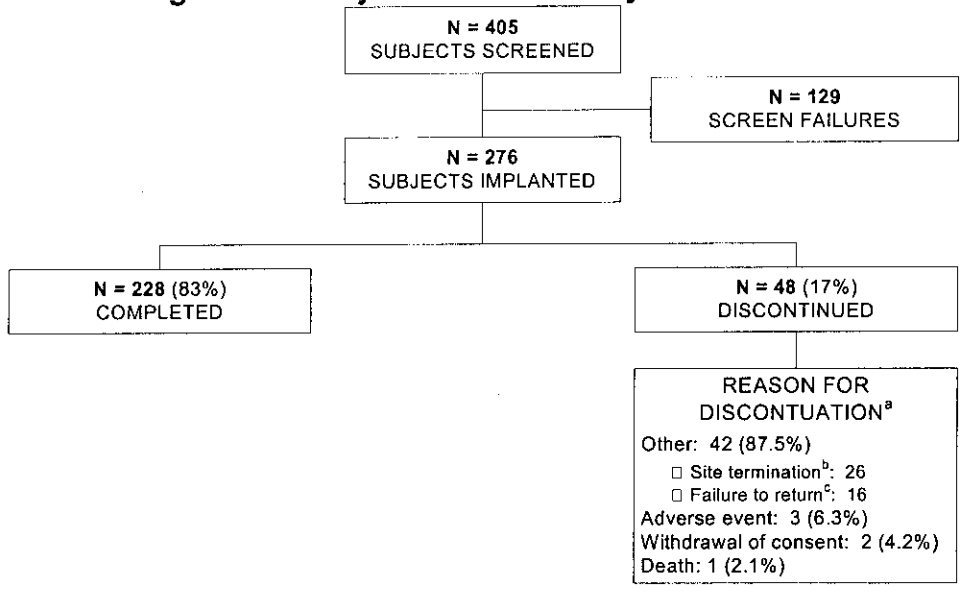
Saline was not introduced into the band at the time of surgery for any subject. The first band adjustment was performed at approximately 4-6 weeks post-implantation.

Study Results

Subject Accountability

A total of 405 subjects were screened for the study and 276 were implanted with the device. The first subject was implanted with the Band on June 24, 2003 and last subject on November 3, 2003. Complete, 36-month follow-up data are available for 228 subjects. The remaining patients are categorized as discontinued. Subject accountability is displayed in Figure 2.

Figure 2 – Subject Accountability in the U.S. Trial



[a] Mutually exclusive and exhaustive categories. Percentages are computed based on total number of discontinued subjects as the denominator.
[b] Site # 269/Martin/New Orleans - site was terminated after Hurricane Katrina.
[c] Subjects were able to be located and contacted, but unwilling to return for their final visit; subjects did not formally revoke consent to participate in the study.

Primary Effectiveness Endpoint

The primary effectiveness endpoint for the U.S. clinical study was Percent Excess Weight Loss (%EWL), defined as:

(baseline weight – post-surgery weight) ÷ (baseline weight – ideal body weight)

The target, considered to be a clinically relevant mean %EWL, was 32.6%. Data for %EWL are provided in Table 2.

Table 2
Percent Excess Weight Loss by Visit in the U.S. Trial
Intent-To-Treat Population (Observed Non-imputed Values)

Visit	N	Mean	SD	Median	Range	95% CI
4-6 Weeks	265	15.3	6.4	14.9	0.7 – 40.5	14.6 – 16.1
2 Months	266	19.8	8.5	18.7	-2.1 – 48.2	18.8 – 20.8
4 Months	255	25.0	11.2	23.6	-6.7 – 56.9	23.6 – 26.4
6 Months	260	28.9	13.5	28.1	-7.5 – 64.1	27.2 – 30.5
8 Months	258	33.1	15.3	33.3	-9.5 – 88.5	31.2 – 35.0
10 Months	242	35.9	16.1	35.1	-10.5 – 89.7	33.9 – 37.9
12 Months	269	38.0	17.7	36.5	-5.2 – 105.0	35.9 – 40.1
15 Months	248	40.7	19.2	38.9	-13.1 – 125.9	38.3 – 43.1
18 Months	238	43.1	20.8	40.3	-7.7 – 133.1	40.4 – 45.7
21 Months	216	43.0	22.5	40.7	-27.1 – 123.3	40.0 – 46.0
24 Months	225	44.7	22.4	42.2	-30.8 – 122.9	41.8 – 47.7
28 Months	201	45.7	22.7	43.6	-22.2 – 130.4	42.5 – 48.8
32 Months	199	44.1	24.2	41.3	-22.2 – 141.1	40.7 – 47.5
36 Months	228	42.8	25.4	40.5	-25.6 – 129.3	39.5 – 46.1
36 Months[a]	276	41.1	25.1	39.2	-26.5 – 129.3	38.1 – 44.1

[a] Missing values were imputed using LOCF (Last Observation Carried Forward). This does not apply to all other values.

It should be noted that by 4–6 weeks after surgery, before the first post-implantation Band adjustment, patients had lost an average of 15.3% of their excess body weight. The reason for this is not known.

The mean %EWL at three years post-implantation was 42.8 (one-sided t-test; p-value < 0.001). The %EWL increased between 4-6 weeks and 28 months and remained relatively stable between 28 months and 36 months. Starting at 8 months post-surgery, the %EWL target of 32.6% was already achieved and this was maintained throughout the remainder of the study. Subjects who reached 36 months of follow-up lost, on average, 42.8% of their excess body weight.

Table 3 shows a categorical summary of %EWL for patients. There were 228 subjects (evaluable) with data at 36 months. In the intent to treat (ITT) category the last observed weight measured was used to calculate %EWL. Almost 75% of subjects lost at least 25% of the excess weight.

Table 3
Categorical Summary of Percent Excess Weight (EW) Loss at 3 Years in the U.S. Trial (N = 228)

Excess Weight Loss at 3 Years	Evaluable (%) N=228	Intent to Treat (%) N=276
Gained > 5% EW	2.2%	2.2%
No Change (-5% to 5%) EW	2.6%	2.9%
EW between 5% and 25%	18.0%	20.3%
Lost at least 25% EW	77.2%	74.6%
Lost at least 33% EW	62.7%	60.1%
Lost at least 50% EW	35.1%	33.0%
Lost at least 75% EW	10.5%	9.4%

Secondary Effectiveness Endpoints

Additional effectiveness endpoints included changes in excess body weight (EBW), changes in body mass index (BMI) and absolute weight loss throughout the 3-year study. These results are summarized in Tables 4, 5 and 6.

Table 4 shows that for those patients completing 36 months of follow-up, the mean excess body weight decreased by 54.3 pounds (from 130 pounds to 75.7 pounds).

Table 4
Excess Body Weight (lbs) by Visit in the U.S. Trial
Intent-To-Treat Population (Observed Non-imputed Values)

Visit	N	Mean	SD	Median	Range	95% CI
Baseline	276	130.0	33.1	121.8	61.6 – 233.8	126.1 – 133.9
4-6 Weeks	265	110.7	31.7	103.8	45.8 – 211.4	106.9 – 114.5
2 Months	266	104.9	31.7	97.8	39.4 – 205.2	101.1 – 108.7
4 Months	255	98.0	30.5	93.6	36.0 – 180.0	94.2 – 101.8
6 Months	260	93.4	32.8	87.3	28.0 – 209.6	89.4 – 97.4
8 Months	258	89.1	33.8	82.1	9.0 – 237.4	84.9 – 93.2
10 Months	242	84.1	33.1	78.7	8.0 – 230.2	79.9 – 88.2
12 Months	269	82.0	34.2	78.0	-4.6 – 229.0	77.9 – 86.1
15 Months	248	78.9	35.0	75.0	-20.2 – 245.6	74.5 – 83.3
18 Months	238	74.2	33.6	70.8	-29.8 – 184.0	69.9 – 78.4
21 Months	216	75.1	37.6	70.1	-21.0 – 241.2	70.0 – 80.1
24 Months	225	73.4	36.9	69.2	-20.6 – 194.2	68.6 – 78.3
28 Months	201	71.2	36.0	68.0	-27.4 – 176.0	66.2 –76.2
32 Months	199	73.4	38.2	68.4	-37.0 – 181.4	68.1 – 78.8
36 Months	228	75.7	39.8	73.5	-26.4 – 186.8	70.5 – 80.8
36 Months[a]	276	78.7	41.3	74.3	-26.4 – 241.2	73.8 – 83.6

[a] Missing values were imputed using LOCF. This does not apply to all other values.

The mean BMI at baseline was 44.5. As summarized in Table 5, the mean BMI decreased to 35.1 kg/m^2 at 24 months and then increased slightly to 35.7 kg/m^2 at 36 months for those completing follow-up.

Table 5
Body Mass Index (kg/m^2) by Visit in the U.S. Trial
Intent-To-Treat Population (Observed Non-imputed Values)

Visit	N	Mean	SD	Median	Range	95% CI
Baseline	276	44.5	4.7	43.7	35.0 – 58.1	43.9 – 45.0
4-6 Weeks	265	41.4	4.6	41.0	32.0 – 54.3	40.9 – 42.0
2 Months	266	40.4	4.6	39.9	31.6 – 54.1	39.9 – 41.0
4 Months	255	39.3	4.5	38.9	31.1 – 53.4	38.8 – 39.9
6 Months	260	38.6	4.9	38.0	27.8 – 52.8	38.0 – 39.2
8 Months	258	37.8	5.0	37.3	24.7 – 55.2	37.2 – 38.4
10 Months	242	37.1	4.9	36.4	24.5 – 54.3	36.4 – 37.7
12 Months	269	36.8	5.1	36.2	23.1 – 54.1	36.2 – 37.4
15 Months	248	36.2	5.3	35.7	20.0 – 56.4	35.6 – 36.9
18 Months	238	35.6	5.3	35.3	19.1 – 52.3	34.9 – 36.2
21 Months	216	35.8	5.7	35.2	20.6 – 55.8	35.0 – 36.5
24 Months	225	35.4	5.7	35.0	20.7 – 54.1	34.6 – 36.1
28 Months	201	35.1	5.5	35.0	19.5 – 52.2	34.3 – 35.9
32 Months	199	35.4	5.9	34.8	17.8 – 52.1	34.6 – 36.3
36 Months	228	35.7	6.2	35.3	19.7 – 53.5	34.9 – 36.5
36 Months[a]	276	36.2	6.3	35.6	19.7 – 55.8	35.5 – 37.0

[a] Missing values were imputed using LOCF. This does not apply to all other values.

As shown in Table 6, the mean absolute weight at baseline was 276.5 pounds. This decreased to 220 pounds at 24 months and to 222.2 pounds for those subjects who completed the entire 36 months of follow-up.

Table 6
Absolute Weight (lbs) by Visit in the U.S. Trial
Intent-To-Treat Population (Observed Non-imputed Values)

Visit	N	Mean	SD	Median	Range	95% CI
Baseline	276	276.5	40.8	267.5	193.6 – 415.4	271.7 – 281.3
4-6 Weeks	265	256.7	38.4	251.0	177.8 – 391.2	252.0 – 261.3
2 Months	266	251.3	38.6	246.0	171.4 – 384.6	246.6 – 255.9
4 Months	255	244.4	37.3	238.6	168.0 – 370.4	239.8 – 249.0
6 Months	260	239.6	39.1	232.6	162.8 – 379.6	234.8 – 244.4
8 Months	258	235.8	40.5	227.5	153.0 – 407.4	230.9 – 240.8
10 Months	242	230.1	39.5	223.6	145.2 – 400.2	225.1 – 235.1
12 Months	269	228.4	41.0	221.6	130.4 – 399.0	223.4 – 233.3
15 Months	248	225.8	41.9	219.5	123.8 – 415.6	220.6 – 231.0
18 Months	238	220.1	39.4	214.6	111.2 – 334.0	215.1 – 225.1
21 Months	216	221.1	44.0	213.6	120.0 – 411.2	215.2 – 227.0
24 Months	225	220.0	42.9	214.6	120.4 – 344.2	214.4 – 225.7
28 Months	201	217.4	42.2	210.6	113.6 – 326.0	211.5 – 223.3
32 Months	199	219.3	43.7	213.2	104.0 – 331.4	213.2 – 225.4
36 Months	228	222.2	45.8	218.1	114.6 – 336.8	216.2 – 228.2
36 Months[a]	276	225.2	47.8	219.6	114.6 – 411.2	219.6 – 230.9

[a] Missing values were imputed using LOCF. This does not apply to all other values.

Changes in Quality of Life as measured by the SF-36 and the Beck Depression Inventory are depicted in Table 7.

Table 7 shows that with the exception of the Mental Component score and the Role Emotional Domain score, there was a statistically significant improvement in the SF-36 Physical Component and the other Domain scores compared to baseline for all post-surgery visits.

Table 7
SF-36 Component Scores by Visit in the U.S. Trial
Intent-To-Treat Population (Observed Non-imputed Values)

	Baseline		12 Months		24 Months		36 Months	
SF-36	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
Physical Component	269	42.6 ± 9.8	265	53.5 ± 8.1	225	54.0 ± 7.3	226	53.5 ± 8.0
Physical functioning	275	59.6 ± 24.2	266	86.1 ± 19.7	226	89.5 ± 16.6	226	86.9 ± 18.7
Role Physical	276	67.0 ± 37.4	265	89.3 ± 26.2	226	92.6 ± 21.8	227	89.6 ± 25.6
Bodily Pain	275	67.0 ± 24.2	266	82.3 ± 23.0	226	81.2 ± 22.3	227	81.1 ± 24.2
General Health	274	61.0 ± 21.6	265	79.1 ± 18.1	227	81.6 ± 16.2	227	79.6 ± 18.5
Mental Component	269	52.8 ± 8.6	265	53.2 ± 9.9	225	54.6 ± 8.8	226	53.3 ± 9.7
Vitality	271	51.4 ± 21.7	266	70.0 ± 20.6	226	72.5 ± 19.1	227	70.5 ± 19.2
Social functioning	276	80.7 ± 22.9	266	89.5 ± 20.1	227	91.9 ± 16.7	227	89.3 ± 20.0
Role Emotional	275	84.8 ± 29.2	265	88.6 ± 27.8	225	92.7 ± 22.3	227	88.0 ± 28.3
Mental Health	271	78.0 ± 15.4	266	80.8 ± 16.7	226	83.1 ± 15.6	227	81.6 ± 16.6

Changes in the mean Beck depression scores at baseline and yearly during the clinical study are summarized in Table 8.

Table 8
Beck Depression Inventory II Score by Visit in the U.S. Trial
Intent-To-Treat Population (Observed Non-imputed Values)

	N	Mean ± SD
Baseline	276	7.6 ± 6.6 (range: 0 to 41)
12 months	265	4.5 ± 5.7 (range: 0 to 30)
24 months	227	3.7 ± 4.9 (range: 0 to 23)
36 months	227	4.8 ± 6.5 (range: 0 to 33)

Other secondary effectiveness endpoints included laboratory markers of co-morbidities including glycosylated hemoglobin (HbA1c), high density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol and triglycerides. Results for these endpoints are summarized in Tables 9 through 16.

Glycosylated hemoglobin (HbA1c)

Although there was minimal change in the HbA1c over the course of the study from a baseline of 5.9% ±1.1 (n=275) to 5.7 ± 0.7 (n=224), there was a statistically significant decrease in HbA1c in those subjects with an elevated HbA1c at baseline. This is summarized in Table 9. There were 60 subjects who had an elevated HbA1c at baseline. Of these, 48 subjects also had data at 36 months. The mean percentage of HbA1c fell from 7.55% to 6.4%.

Table 9
Glycosylated Hemoglobin (HbA1c) Elevated at baseline in the U. S. Trial
Mean Baseline (BL) vs. 36 months Post-Surgery

HbA1c (%)	N	Time point	Mean	SD	Range	% Change
Normal Baseline	176	Baseline	5.40	.033	4.7 - 6.1	-0.09
		36 months	5.49	.037	4.5 - 6.1	
Elevated Baseline	48	Baseline	7.55	1.33	6.2-11.8	1.15*
		36 months	6.40	0.93	5.3-9.5	

Normal reference range = 4.3-6.1% HbA1c * P <0.001 by t-test analysis

215 subjects had an HbA1c level within normal range at baseline, but only 176 had HbA1c test data at 36 months. 60 subjects had an HbA1c level outside normal range at baseline, but only 48 had HbA1c test data at 36 months.

There was a similar trend in subjects with a BMI ≥ 35 and < 40 kg/m^2. In this subgroup thirteen subjects had an elevated HbA1c at baseline, of these nine subjects also had data at 36 months. This data is summarized in Table 10.

Table 10
HbA1c Comparing at baseline and 36 months Post Surgery
in subjects with a BMI of between 35 and 40 kg/m^2

N	time point	mean, %HbA1c	SD	Range	% Change
9	baseline	7.40	2.0	5.5-11.8	1.01*
	36 months	6.39	1.2	5.5-9.5	

Normal reference range for HbA1c: 4.3-6.1%

* P=0.024 by t=-test analysis

Lipids

The change in Total Cholesterol is shown in Table 11. There was a statistically significant decrease in total cholesterol from 204.8 mg/dL at baseline to 193.5 mg/dL at 36 months.

Table 11
Total Cholesterol (mg/dL) Throughout 3-Year Post-Surgery Period in the U.S. Trial Intent-To-Treat Population (Observed Non-imputed Values)

Visit	N	Mean	SD	Median	Range	95% CI
Baseline	273	204.8	39.4	200.0	115–375	200.1– 209.5
2 Months	261	195.3	38.5	192.0	111–340	190.6– 200.0
6 Months	261	198.4	38.3	195.0	122–338	193.7– 203.1
12 Months	266	199.9	40.1	196.0	95–356	195.0– 204.7
18 Months	225	193.6	36.8	188.0	126–301	188.8– 198.4
24 Months	226	196.0	38.1	189.5	111–319	191.0– 201.0
36 Months	221	193.5	36.9	191.0	115–310	188.6– 198.4
36 Months[a]	276	196.0	37.6	192.0	115–356	191.5– 200.5

[a] Missing values were imputed using LOCF. This does not apply to all other values.

The data in Table 12 shows there was an increase in HDL from a baseline mean of 46.1 mg/dL (n=273) to 56.4 mg/dL (n=221) at 36 months. The data presented in Table 15 shows that there were 84 subjects who had an HDL below the normal range at baseline. Of these, 65 subjects also had data at 36 months. There was a 25% increase in HDL seen in these subjects from a mean of 34 mg/dl at baseline to 45 mg/dL at 36 months.

Table 12
High-Density Lipoprotein (mg/dL) throughout 3-Year Post-Surgery Period in the U.S. Trial Intent-To-Treat Population (Observed Non-imputed Values)

Visit	N	Mean	SD	Median	Range	95% CI
Baseline	273	46.1	11.9	45	23 – 120	44.6 – 47.5
2 Months	261	44.1	10.9	43	24 – 117	42.8 – 45.5
6 Months	261	47.9	11.8	46	27 – 112	46.4 – 49.3
12 Months	266	55.0	12.9	54	29 – 119	53.4 – 56.5
18 Months	225	57.8	13.5	57	28 – 101	56.0 – 59.6
24 Months	226	59.1	14.2	58	28 – 104	57.2 – 61.0
36 Months	221	56.4	14.7	54	23 – 109	54.5 – 58.4
36 Months[a]	276	56.2	14.8	54	23 – 119	54.4 – 57.9

[a] Missing values were imputed using LOCF. This does not apply to all other values.

Table 13 shows changes in LDL. There was a decrease in LDL from a baseline mean of 126.0 mg/dl (n=263) to 114.5 mg/dl (n=218) at 36 months. In addition, in Table 15 data show that there were 106 subjects who had an LDL above the normal range at baseline. Of these, 83 subjects also had data at 36 months. There was a 16% decrease in LDL seen in these subjects from a mean of 156 mg/dl at baseline to 131.6 mg/dl at 36 months (see Table 15).

Table 13
Low-Density Lipoprotein (mg/dL)
throughout 3-Year Post-Surgery Period in the U.S. Trial
Intent-To-Treat Population (Observed Non-imputed Values)

Visit	N	Mean	SD	Median	Range	95% CI
Baseline	263	126.0	34.2	121.0	55 – 277	121.8 – 130.1
2 Months	256	123.2	33.0	120.0	48 – 230	119.1 – 127.2
6 Months	260	125.3	34.1	123.0	56 – 255	121.1 – 129.4
12 Months	264	120.6	35.8	119.0	36 – 283	116.3 – 125.0
18 Months	225	114.1	31.7	110.0	52 – 216	109.9 – 118.3
24 Months	224	114.3	33.4	110.0	36 – 211	109.9 – 118.7
36 Months	218	114.5	32.3	113.5	44 – 219	110.1 – 118.8
36 Months[a]	275	116.6	34.0	115.0	36 – 283	112.6 – 120.7

[a] Missing values were imputed using LOCF. This does not apply to all other values.

Table 14 shows there was a decrease in triglycerides from a baseline mean of 172.7 mg/dl (n=273) to 114.9 mg/dl (n=221) at 36 months. There were also 35 subjects who had elevated triglycerides at baseline. Of these, 24 subjects also had data at 36 months. There was a 50% decrease in triglycerides seen in these subjects from a mean of 407.6 mg/dl at baseline to 205.8 mg/dl at 36 months (see Table 15).

Table 14
Triglycerides (mg/dL) Throughout 3-Year Post-Surgery in the U.S. Trial Intent-To-Treat Population (Observed Non-imputed Values)

Visit	N	Mean	SD	Median	Range	95% CI
Baseline	273	172.7	116.6	145.0	29 – 940	158.8 – 186.6
2 Months	261	139.9	81.5	123.0	37 – 749	130.0 – 149.9
6 Months	261	128.2	65.1	113.0	42 – 554	120.3 – 136.2
12 Months	266	122.5	68.7	104.5	41 – 711	114.2 – 130.8
18 Months	225	108.1	52.8	93.0	34 – 314	101.2 – 115.0
24 Months	226	115.5	65.0	100.0	38 – 507	107.0 – 124.0
36 Months	221	114.9	65.6	103.0	32 – 541	106.2 – 123.6
36 Months[a]	276	117.4	67.8	103.5	32 – 541	109.4 – 125.5

[a] Missing values were imputed using LOCF. This does not apply to all other values.

Table 15
Lipids Outside the Normal Range at baseline in the U. S. Trial
Mean Baseline (BL) vs. 36 month Post-Surgery

Lipid	Baseline	N	Time point	Mean	SD	Range	Change mg/dL (%)
Total Cholesterol[§]	Elevated	105	Baseline	233.8	25.7	201 - 306	21 (9%)*
			36 mo	212.8	34.3	138 - 310	
	Normal	110	Baseline	175.1	18.1	134- 200	-1.5 (1%)
			36 mo	176.6	29.9	115 - 279	
HDL Cholesterol[¶]	Decreased	65	Baseline	34.0	4.3	23 - 39	-11 (25%)*
			36 mo	45.0	10.2	23 - 72	
	Normal	153	Baseline	51.0	8.2	40 - 73	- 10.4 (20%)*
			36 mo	61.4	13.7	37 - 109	
LDL Cholesterol[£]	Elevated	83	Baseline	156.0	20.5	131 - 209	24.4 (16%)*
			36 mo	131.6	32.5	60 - 219	
	Normal	127	Baseline	103.3	18.1	55 - 130	-0.6 (<1%)
			36 mo	103.9	27.3	44 - 171	
Triglycerides[†]	Elevated	24	Baseline	407.6	180.0	256 - 940	201.8 (50%)*
			36 mo	205.8	125.3	65 - 541	
	Normal	192	Baseline	141.9	50.5	47 - 248	34.2 (24%)*
			36 mo	107.7	42.97	34 - 288	

*** P <0.001 by t-test analysis**

§ Normal reference range = 130-200mg/dL. At baseline, there were 135 subjects who had a total cholesterol above the normal range. Of these, 105 subjects had lipid panel data available at baseline and 36 months. At baseline, there were 134 subjects whose baseline total cholesterol was in the normal range. Of these, 110 subjects had lipid panel data at baseline and 36 months.

¶ Normal reference range = 40-80 mg/dL. At baseline, there were 84 subjects who had a HDL cholesterol **below** the normal range. Of these, 65 subjects had lipid panel data at baseline and 36 months. There were 183 subjects whose HDL cholesterol at baseline was in the normal range. Of these, 153 subjects had lipid panel data at baseline and 36 months.

£ Normal reference range = 0-130 mg/dL. At baseline, there were 106 subjects who had a LDL cholesterol above the normal range. Of these, 83 subjects had lipid panel data at baseline and 36 months. There were 157 subjects whose LDL cholesterol at baseline was in the normal range. Of these, 127 subjects had lipid panel data at baseline and 36 months.

† Normal reference range = 45-250 mg/dL. At baseline, there were 35 subjects who had a Triglyceride level above the normal range. Of these, 24 subjects had lipid panel data at baseline and 36 months. There were 235 subjects whose Triglyceride level at baseline was in the normal range. Of these, 192 subjects had lipid panel data at baseline and 36 months.

Similar findings were seen in the subjects with a lower BMI. In subjects with a BMI ≥ 35 and <40 kg/m^2 and a history of dyslipidemia, there were statistically significant changes in both HDL cholesterol and triglycerides. This is summarized in Table 16.

There were data for 18 of the 22 subjects at both baseline and 36 months. In these subjects, there was an increase in HDL from a mean of 45.7 mg/dl to 58.4 mg/dl at 36 months. There was a decrease in triglycerides from 194.2 mg/dl at baseline to 124.3 mg/dl at 36 months.

Table 16
Mean BL vs. 36 month Lipids in Subjects with Both Pre-implantation History of Dyslipidemia and BMI ≥35 and < 40

Lipid	N	Time point	Mean	SD	Range	Change mg/dL (%)
Total Cholesterol §	18	Baseline	212.3	32.1	159 - 276	3.1 (1.5%)
		36 mo	209.2	38.3	125 - 284	
HDL Cholesterol ¶	18	Baseline	45.7	8.0	31 - 59	-13 (28%)*
		36 mo	58.4	12.2	40 - 82	
LDL Cholesterol £	17	Baseline	132.3	36.3	72 - 203	6.5 (5%)
		36 mo	125.8	34.29	50 - 201	
Triglycerides†	18	Baseline	194.2	90.6	78 - 491	70 (36%)*
		36 mo	124.3	54.1	55 - 297	

§ Normal reference range = 130-200 mg/dL
£ Normal reference range = 0-130 mg/dL
One subject did not have LDL baseline data.
¶ Normal reference range = 40-80 mg/dL
† Normal reference range = 45-250 mg/dL
* P <0.001 by t-test analysis

Safety and Adverse Events

During the 3-year U.S. clinical study, 266 of 276 (96.4%) subjects reported at least one adverse event (AE). Twenty-four percent (24%) of subjects reported at least one severe adverse event. Note that new or worsening signs and symptoms were recorded separately as individual AEs. However, in many instances, several of these individual AEs were seen together in association with one common or "root cause." For example, band slippage may be associated with one or more of the following AEs: nausea, vomiting, and stoma obstruction.

AEs for patients implanted with the Band were evaluated throughout the course of the clinical study. Adverse events were categorized as peri-operative or postoperative. The severity of each AE was rated as mild, moderate or severe, then further rated as serious or not serious. Definitions for severity are listed below:

Mild: awareness of experience, but easily tolerated. No medical intervention required.

Moderate: enough discomfort to interfere with usual activities. Medical intervention required.

Severe: inability to carry out usual activities. Medical intervention (including hospitalization or prolongation of hospitalization) required.

All adverse events in the U.S. clinical study that occurred with a frequency > 5% are listed below in Table 17. A total of 73.2% (202) of the study subjects experienced one or more AEs peri-operatively. Postoperative AEs were reported in 93.8% (259) of study subjects.

Table 17
Adverse Events (Frequency > 5%) in the U.S. Trial

System Organ Class MedDRA Preferred Term[A]	# (%) Subjects (N=276)
Gastrointestinal Disorders	
Vomiting	124 (44.9%)
Nausea	88 (31.9%)
Constipation	69 (25.0%)
Gastroesophageal Reflux Disease	53 (19.2%)
Abdominal Pain	29 (10.5%)
Abdominal Pain Upper	28 (10.1%)
Flatulence	28 (10.1%)
Diarrhea	26 (9.4%)
Dysphagia	26 (9.4%)
Dyspepsia	23 (8.3%)
Post Procedural Nausea	14 (5.1%)
General Disorders And Administration Site Conditions	
Fatigue	29 (10.5%)
Port Site Pain	18 (6.5%)
Migration of Implant*	17 (6.2%)
Catheter Related Complications	15 (5.4%)
Chest Pain	14 (5.1%)
Infections And Infestations	
Nasopharyngitis	31 (11.2%)
Influenza	26 (9.4%)
Sinusitis	23 (8.3%)
Upper Respiratory Tract Infection	21 (7.6%)
Urinary Tract Infection	21 (7.6%)
Injury, Poisoning And Procedural Complications	
Post Procedural Pain	66 (23.9%)
Musculoskeletal And Connective Tissue Disorders	
Back Pain	41 (14.9%)
Arthralgia	27 (9.8%)
Nervous System Disorders	
Headache	38 (13.8%)
Psychiatric Disorders	
Depression	28 (10.1%)
Insomnia	17 (6.2%)
Skin and Subcutaneous Tissue Disorders	
Alopecia	24 (8.7%)

System Organ Class MedDRA Preferred Term[A]	# (%) Subjects (N=276)
Vascular Disorders	
Hypertension	15 (5.4%)
Post-operative Hypertension	15 (5.4%)

[A] MedDRA is the acronym for Medical Dictionary for Regulatory Activities, which is a pragmatic, medically valid terminology with an emphasis on ease of use for data entry, retrieval, analysis, and display.
* "Migration of Implant" refers to band slippage, port displacement, and band erosion; should not be considered the same as "device migration," which is a term frequently used in the clinical literature to refer to the "erosion" of the band into the GI tract.

All AEs in the U.S. clinical study that occurred with a frequency > 5% are categorized by severity in Table 18. **Note:** A subject may have experienced a specific AE more than once.

Table 18
Common Adverse Events (> 5%) by Severity in the U.S. Trial

System Organ Class Preferred Term	Total (%) (N = 276)	N per Severity (% from Total per Event)[a] Mild	Moderate	Severe
Subjects with at least 1 Adverse Event	266 (96.4%)	74 (28%)	128 (48%)	64 (24%)
Total Number of Adverse Events	2400	1406	853	141
Gastrointestinal Disorders	**224 (81.2%)**			
Post Procedural Nausea	14 (5.1%)	4 (29 %)	10 (71%)	0 (0%)
Dyspepsia	23 (8.3%)	15 (65%)	8 (35%)	0 (0%)
Diarrhea	26 (9.4%)	15 (58%)	9 (35%)	2 (8%)
Dysphagia	26 (9.4%)	7 (27%)	16 (62%)	3 (12%)
Abdominal Pain Upper	28 (10.1%)	16 (57%)	10 (36%)	2 (7%)
Flatulence	28 (10.1%)	18 (64%)	9 (32%)	1 (4%)
Abdominal Pain	29 (10.5%)	19 (66%)	7 (24%)	3 (10%)
Gastroesophageal Reflux Disease	53 (19.2%)	32 (60%)	19 (36%)	2 (4%)
Constipation	69 (25.0%)	56 (81%)	12 (17%)	1 (1%)
Nausea	88 (31.9%)	45 (51%)	39 (44%)	4 (5%)
Vomiting	124 (44.9%)	70 (56%)	45 (36%)	9 (7%)
General Disorders And Administration Site Events	**113 (40.9%)**			
Chest Pain	14 (5.1%)	5 (36%)	6 (43%)	3 (21%)
Catheter Related Complication	15 (5.4%)	5 (33%)	5 (33%)	5 (33%)
Port Disconnection	12 (4.3%)	5 (41%)	4(33%)	3(25%)
Catheter Kinking	3 (1.1%)	0 (0%)	1(33%)	2(67%)
Injection Site Pain[b]	18 (6.5%)	17 (94%)	0 (0%)	1 (6%)
Migration Of Implant	17 (6.2%)	3 (18%)	8 (47%)	6 (35%)
Band Erosions	1 (0.4%)	0 (0%)	0 (0%)	1 (100%)
Band Slippage	9 (3.3%)	1 (11%)	3 (33%)	5 ((56%)
Port Displacement	7 (2.5%)	2 (29%)	5 (86%)	0 (0%)
Fatigue	29 (10.5%)	23 (79%)	6 (21%)	0 (0%)

Table 18 (Continued)
Common Adverse Events (> 5%) by Severity in the U.S. Trial

System Organ Class Preferred Term	Total (%) (N = 276)	N per Severity (% from Total per Event)[a] Mild	Moderate	Severe
Infections And Infestations	**123 (44.6%)**			
Upper Respiratory Tract Infection	21 (7.6%)	14 (67%)	6 (29%)	1 (5%)
Urinary Tract Infection	21 (7.6%)	12 (57%)	9 (43%)	0 (0%)
Sinusitis	23 (8.3%)	12 (52%)	11 (48%)	0 (0%)
Influenza	26 (9.4%)	12 (46%)	12 (46%)	2 (8%)
Nasopharyngitis	31(11.2%)	30 (97%)	1 (3%)	0 (0%)
Injury, Poisoning And Procedural Complications	**111 (40.2%)**			
Post Procedural Pain	66(23.9%)	25 (38%)	39 (44%)	2 (3%)
Musculoskeletal And Connective Tissue Disorders	**92 (33.3%)**			
Arthralgia	27 (9.8%)	10 (37%)	15 (56%)	2 (7%)
Back Pain	41 14.9%)	20 (49%)	17 (41%)	4 (10%)
Nervous System Disorders	**76 (27.5%)**			
Headache	38(13.8%)	19 (50%)	19 (50%)	0 (0%)
Psychiatric Disorders	**51 (18.5%)**			
Depression	28(10.1%)	11 (39%)	17 (61%)	0 (0%)
Insomnia	17 (6.2%)	6 (35%)	11 (65%)	0 (0%)
Skin And Subcutaneous Tissue Disorders	**52 (18.8%)**			
Alopecia	24 (8.7%)	22 (92%)	2 (8%)	0 (0%)
Vascular Disorders	**46 (16.7%)**			
Hypertension	15 (5.4%)	8 (53%)	7 (47%)	0 (0%)
Post-operative Hypertension	15 (5.4%)	5 (33%)	10 (67%)	0 (0%)

[a] Terms reported multiple times (per subject) are counted once in the highest severity.

[b] The term "Injection Site" refer to the "Port Site."

Description of Adverse Events

Abdominal Pain

Abdominal pain was reported as either lower or upper, or location unspecified. Only upper abdominal pain and abdominal pain (not otherwise specified) were reported at an incidence greater than 5%. Upper abdominal pain and abdominal pain (not otherwise specified) were reported in 28 (10.1%) and 29 (10.5%) subjects respectively (see Table 18).

Dysphagia (difficulty swallowing)

Twenty-six (9.4%) subjects reported 56 episodes of dysphagia; of these, 15/26 reported multiple (2–5) episodes (see Table 18).

Gastroesophageal Reflux (GERD)/Dyspepsia

Gastroesophageal reflux was reported in 53 (19.2 %) subjects. Symptoms of heartburn were reported in 23 (8.3%) subjects. Eight subjects reported both GERD and heartburn (see Table 18).

Adverse events specifically associated with the Band are identified in Table 19 and discussed below.

Table 19
Device-Related Adverse Events Reported in the in the U.S. Trial

Adverse Event	# of Events	#(%) of Subjects	Peri-operative ≤30 days following surgery N=subjects	Post-operative > 30 days following surgery N=subjects
port site pain	21	18 (6.5%)	4	15
band slippage/pouch dilatation	23	17 (6.2%)	0	17
catheter related complications	17	15 (5.4%)	0	15
stoma obstruction	12	12 (4.3%)	1	11
esophageal dilatation/dysmotility	10	10 (3.7%)	0	10
port displacement	9	7 (2.5%)	0	7
band erosion	1	1 (0.4%)	0	1

Injection Port Site Pain

Eighteen subjects (6.5%) reported Injection Port site pain. Four (1.4%) reported Injection Port site pain during the peri-operative period and 15 (5.4%) in the post-operative period. One subject reported this event at some point during both study periods.

Migration of Implant

Due to limitations on the availability of appropriate device-specific preferred terms in the MedDRA encoder, the term "migration of implant" was used for events involving *any* kind of displacement of the band components from their original implantation position (which included band slippage, port displacement, and band erosion). It should be noted, however, that this definition of "migration of implant" differs from the clinical literature where the term "device migration" more typically refers specifically to the "erosion" of the band into the GI tract.

Table 20 summarizes the actual incidence of each specific type of "migration of implant" based on verbatim reports.

Table 20
Classification of Events Coded as "Migration of Implant" in the U.S. Trial

MedDRA Term Used	Classification	N = Subjects	%
"Migration of Implant"	Band Erosion	1	0.4
	Band Slippage	9	3.3
	Port displacement	7	2.5
	Total	17	6.2

Note: "Migration of Implant" refers to band slippage, port displacement, and band erosion; and should not be considered the same as "device migration," which is a term frequently used in the clinical literature to refer to the "erosion" of the band into the GI tract.

Band Slippage and/or Pouch Dilation

If "band slippage" occurs (the sliding of the stomach upwards and through the band, rather than the downward sliding of the band on the stomach), it can lead to an enlargement of the stomach pouch which in turn results in excessive food volume capacity and a change in the relative position of the band from the original implantation position.

In this study, radiographic changes in the relative position of the band from the original implantation position were reported as band slippage. Routine limited upper GI series were required in association with band adjustments; therefore, band slippage and pouch dilation were primarily radiological findings reported by the study sites. Pouch enlargement without change in baseline band position was reported as 'pouch dilation.'

Eleven events of band slippage were reported in nine (3.3%) subjects. Twelve events of pouch dilation were reported in 10 (3.6%) subjects. In two subjects, both band slippage and pouch dilation was reported. Therefore, overall 17 subjects (6.2%) reported band slippage and/or pouch dilation.

All subjects with band slippage were symptomatic. Seven subjects required surgical revision and two resolved with band adjustment. Two subjects each had two separate events of band slippage. In both subjects, the first event in both subjects was reported to have resolved with band adjustment and the second event required surgical revision.

Eight of ten subjects with pouch dilation reported associated symptoms. Six resolved with band adjustment and one required surgical revision. In three subjects, the AE was still ongoing at end of study.

Five of the ten subjects (50%) reported with pouch dilatation had the Band implanted by one investigator.

Stoma Obstruction
Stoma obstruction (gastric outlet obstruction) was reported in 12 (4.3%) of subjects. Signs and symptoms associated with stoma obstruction included nausea/vomiting, heartburn/reflux, abdominal pain, dehydration, coughing, band slippage.
Note: These signs and symptoms of stoma obstruction are not mutually exclusive; some subjects could have exhibited a combination of them.

In four subjects, the signs and symptoms associated with stoma obstruction were not reported.

In ten subjects, the event resolved after removal of saline from the band. In one subject, the event resolved with no intervention and one other (reported as food impaction) with nutritional counseling.

Esophageal Dilatation/Dysmotility
Esophageal dilatation was reported in 9 (3.3%) subjects. Seven of the nine cases resolved after band deflation. The other two cases, which were reported approximately 35 months post-operatively, were also treated with band deflation but were still ongoing at time of study completion. No cases of esophageal dilatation were reported as serious, required surgical revision, or required device explantation.

Esophageal dysmotility was reported in one (0.4%) subject.

Band Erosion
Band erosion into the gastric lumen was reported in one subject (0.4%). The gastric defect secondary to the erosion was surgically closed without complications.

Malfunctions – Band Leaks and Catheter-Related Complications

Band Leaks
Investigators reported band leakage in only one (0.4%) subject. The band was replaced laparoscopically and no further problems were reported.

During routine Band adjustment, the investigator noted there was less fluid in the band than previously observed. The subject reported lack of restriction and weight gain. The leak was confirmed radiographically, and the Band was subsequently replaced laparoscopically without further incident.

Catheter-Related Complications
Fifteen (5.4%) subjects reported 17 complications related to the catheter, all noted during the post operative period. catheter related complications include port disconnections and catheter kinking.

- Port Disconnections: There were a total of 14 port disconnections reported in 12 (4.3%) subjects. All required surgical reconnection. In two subjects the investigator replaced the port.

- Catheter Kinking (Inability to Inflate/Deflate the Band) Based on the inability to withdraw saline from the band (to resolve band overfill) during an adjustment, investigators assumed and reported a catheter kink in three subjects (1.1 %). All three required surgical revision of the port.

Re-operations: Revisions, Replacements and Explants
Forty-three subjects (15.6%) required re-operations involving the Band including 2 band replacements, 10 band revisions, 4 band explantations, 5 port replacements, and 22 port revisions.

Serious Adverse Events
One hundred fifteen (115) serious adverse events (SAEs) were reported during the U.S. study in 78 (28.3%) subjects. Of these events, only 13 (11.3%) were considered unanticipated and related to the gastric band; 46 (40%) were considered unanticipated, but not related to the gastric band; and the remaining 56 (48.7%) were considered anticipated.

There was one death in the study. The patient was seen approximately 23 months post-implantation with an incarcerated hernia at a trocar site. The trocar site was in close proximity to the port site. The patient underwent an uneventful hernia repair. Following the hernia repair, a chronically draining wound developed at the trocar site, which did not respond to standard antibiotic therapy. Seventeen months later the patient underwent surgery to relocate and replace the port and tubing. Twelve hours following the port surgery, the patient became acutely ill and died of multi-organ system failure. The peri-operative clinical course and subsequent post mortem identified a gastric perforation suggesting intra-abdominal sepsis as a major contributing factor to the patient's death. This may have been an acute process, as suggested by the post mortem finding, however, an unrecognized band erosion resulting in a chronically discharging wound site may have been a contributing factor.

No other SAEs were reported as life-threatening or associated with disability.

XI CONCLUSIONS DRAWN FROM THE STUDIES

Effectiveness
The results of the US clinical study demonstrated that the REALIZE™ Band is effective in reducing excess weight in morbidly obese subjects. At three years post implantation the %EWL in the 228 subjects who completed the study was 42.8% with 77% of subjects having a %EWL of at least 25%.

A statistically significant reduction from baseline was seen in HbA1c, total cholesterol, LDL cholesterol, and triglyceride laboratory assessments at three-years

post implantation. There was also a statistically significant increase in HDL cholesterol levels at three years post-surgery compared to baseline.

Adverse Events

During the study, 266 (96.4%) of the subjects reported one or more adverse events. Specific adverse events associated with gastric banding reported during the course of the study included 1 band erosion (0.4%), 7 port displacements (2.5%), 9 band slippages (3.3%), 10 pouch dilatations (3.6%), 9 esophageal dilatations (3.3%), 1 esophageal dysmotility (0.4%), 18 injection port site pain (6%), 1 band leak (0.4%), 12 port disconnections (4.3%), and 3 kinking of catheter (1.1%).

Forty-three subjects (15.6%) required re-operations involving the Band including 2 band replacements, 10 band revisions, 4 band explantations, 5 port replacements, and 22 port revisions.

There was one death in the study. Causality was probably related to port replacement surgery. No other serious adverse events were reported as life-threatening, associated with disability, or resulting in a congenital anomaly.

XII PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the Act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology and Urology Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

The Center for Devices and Radiological Health (CDRH) reviewed the PMA and concluded that there is a reasonable assurance of safety and effectiveness for the REALIZE™ Adjustable Gastric Band based on the pre-clinical testing and the results of the clinical study.

The sponsor has agreed to conduct a post-approval study to evaluate the long-term safety and effectiveness of their device. The study will be conducted in the US at up to 12 centers. The objectives of the study are to determine the re-operation rate and to continue to evaluate changes in excess body weight, Quality of Life measures and changes in glycosylated hemoglobin (HbA1c) and serum lipid levels at 4 and 5 years post implantation.

The applicant's manufacturing facilities were also inspected and found to be in compliance with the Quality System Regulation (21 CFR 820).

FDA issued an approval order on September 28, 2007

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See the Labeling

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.

Post-approval Requirements and Restrictions: See approval order.