SUMMARY OF SAFETY AND EFFECTIVENESS (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Adjustable Silicone Gastric Band, Implanted
Device Trade Name:	LAP-BAND® Adjustable Gastric Banding (LAGB®) System
Applicant's Name and Address:	Allergan 71 South Los Carneros Road Goleta, CA 93117
Date of Panel Recommendation:	December 3, 2010
Premarket Approval Application (PMA) Number:	P000008/S017
Date of FDA Notice of Approval:	February 16, 2011

The original PMA application P000008 for the LAP-BAND® Adjustable Gastric Banding (LAGB®) System was approved on June 5, 2001, and is indicated for use in weight reduction for severely obese patients with a Body mass Index (BMI) of at least 40 or a BMI of at least 35 with one or more severe comorbid conditions, or those who are 100 lbs. or more over their estimated ideal weight according to the 1983 Metropolitan Life Insurance Tables (use the midpoint for medium frame). It is indicated for use only in severely obese adult patients who have failed one or more conservative weight-reduction alternatives, such as supervised diet, exercise and behavior modification programs. Patients who elect to have this surgery must make the commitment to accept significant changes in their eating habits for the rest of their lives. The SSED to support the indication is available on the CDRH website and is incorporated by reference here. Preclinical data from the original PMA application are applicable to the current PMA Supplement. The current supplement was submitted to expand the indication for the LAP-BAND® Adjustable Gastric Banding (LAGB®) System.

II. INDICATIONS FOR USE

The LAP-BAND® System is indicated for weight reduction for patients with obesity, with a Body Mass Index (BMI) of at least 40 kg/m^2 or a BMI of at least 30 kg/m^2 with one or more obesity related comorbid conditions.

It is indicated for use in adult patients who have failed more conservative weight reduction alternatives, such as supervised diet, exercise and behavior modification programs. Patients who elect to have this surgery must make the commitment to accept significant changes in their eating habits for the rest of their lives.

III. CONTRAINDICATIONS

1. Patients with inflammatory diseases of the gastrointestinal tract, including severe intractable esophagitis, gastric ulceration, duodenal ulceration, or specific inflammation such as Crohn's disease

2. Patients with severe cardiopulmonary diseases or other serious organic disease which may make them poor surgical candidates

3. Patients with potential upper gastrointestinal bleeding conditions such as esophageal or gastric varices or congenital or acquired intestinal telangiectases

4. Patients with portal hypertension

5. Patients with congenital or acquired anomalies of the GI tract such as atresias or stenoses

6. Patients who have/experience an intra-operative gastric injury during the implantation procedure, such as a gastric perforation at or near the location of the intended band placement

7. Patients with cirrhosis

8. Patients with chronic pancreatitis

9. Patients who are addicted to alcohol and/or drugs

10. Non-adult patients (patients under 18 years of age)

11. Patients who have an infection anywhere in their body or where the possibility of contamination prior to or during the surgery exists

12. Patients on chronic, long-term steroid treatment

13. Patients who are unable or unwilling to comply with dietary restrictions that are required by this procedure

14. Patients who are known to have, or suspected to have, an allergic reaction to materials contained in the system or who have exhibited pain intolerance to implanted devices

15. Patients or family members with a known diagnosis or pre-existing symptoms of autoimmune connective-tissue disease such as systemic lupus erythematosus or scleroderma

16. Pregnancy: Placement of the LAP-BAND® System is contraindicated for patients who currently are or may be pregnant. Patients who become pregnant after band placement may require deflation of their band

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the LAP-BAND® System labeling.

V. DEVICE DESCRIPTION

The LAP-BAND® System is a long-term implantable device intended to induce weight loss in obese patients by limiting food consumption (restriction rather than malabsorption). The device is surgically implanted, generally using a laparoscopic technique, to create a restricted opening (stoma) and a small gastric pouch to limit food consumption and induce early satiety. The main components (Figure 1) of the device are the silicone elastomer band, the access port and kink-resistant tubing used to connect the other two components. The inner surface of the silicone band, which is placed around the stomach, is inflatable and connected by the tubing to the access port (a remote injection site). The access port is placed in, or on, the rectus muscle to permit non-surgical, percutaneous adjustments to the band fill volume and thus, the stoma diameter, using sterile saline.

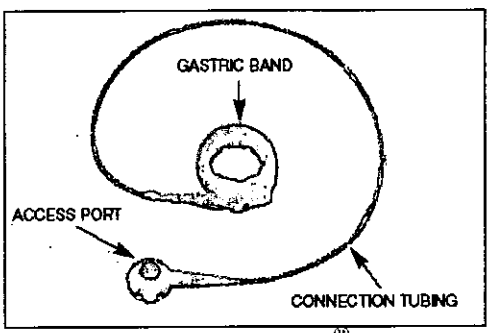


Figure 1: LAP-BAND® System

Five (5) LAP-BAND®® System models have been approved for use in the United States (Fig. 2).

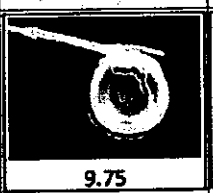
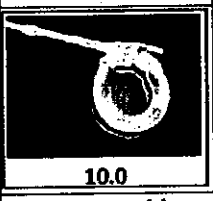
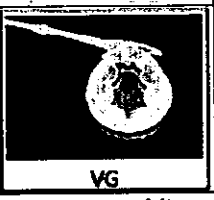
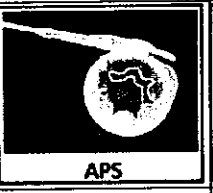
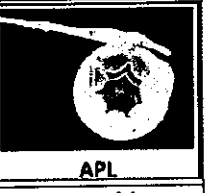
Design Features	LAP-BAND® 9.75	LAP-BAND® 10.0	LAP-BAND® VG	LAP-BAND AP® Standard	LAP-BAND AP® Large
	 9.75	 10.0	 VG	 APS	 APL
Belt and Buckle	Not Openable	Not Openable	Not Openable	Openable Locking Mechanism	Openable Locking Mechanism
Shell	Smooth Continuous	Smooth Continuous	Smooth, Pre-grooved (Omniform®)	Smooth, Pre-grooved (Omniform®)	Smooth, Pre-grooved (Omniform®)
	325° inflation area and no cushion effect under belt and buckle	325° inflation area and no cushion effect under belt and buckle	325° inflation area and no cushion effect under belt and buckle	360° inflation area with cushion effect under belt and buckle	360° inflation area with cushion effect under belt and buckle
Fill Volume	0-4 mL	0-4 mL	0-10 mL	0-10 mL	0-14 mL
Overall LAP-BAND®	Assembled injection molded components	Assembled injection molded components	Assembled injection molded components	One-piece injection molded	One-piece injection molded

Figure 2: Approved LAP-BAND® System Models

The implantable components of the LAP-BAND® System include:

Adjustable Gastric Band – a sterile band which, when fastened, forms a circular ring. Five (5) models are available: 9.75cm, 10.0cm, VG, AP Standard, and AP Large. Each band transitions to a length of kink-resistant tubing. The band's slip-through buckle facilitates laparoscopic placement around the stomach resulting in the formation of a small gastric pouch and stoma.

Access Port – a stainless steel component with a self-sealing injection site. This sterile port is designed to allow for post-operative percutaneous adjustment to the stoma diameter. The port is attached to the inner surface of the gastric band by the kink-resistant tubing. Saline can be injected into the access port causing the inner surface of the band to inflate and thus decreasing the size of the stoma. Saline can also be removed from the LAP-BAND® causing the band to deflate and increasing the size of the stoma. The access port is available in three (3) models: API (standard port), APII (low profile port), and RapidPort™ (for use with the RapidPort™ EZ System).

Kink-Resistant Tubing – a silicone tube which connects the inner surface of the gastric band to the access port.

Other components used during the implantation procedure of the LAP-BAND® System include:

Calibration Tube Assembly – a 157cm dual lumen, translucent, silicone tube with a 13mm-diameter sensor tip and an inflatable balloon attached to its distal end. The device is inserted into the patient's esophagus intraoperatively and used to position and size the stoma of the gastric pouch. The calibration tube is supplied separately from the LAP-BAND® System. It is provided clean, non-sterile, and for single use. The balloon is inflated via an inflation port, which is connected to the calibration tube's smaller lumen and remains external during the procedure.

Silicone End Plug with Stainless Steel Connector – used to temporarily seal the LAP-BAND® System while the band is being positioned around the stomach. The end plugs are then removed and the other components of the system connected.

Blunt tip flushing needles – provided to facilitate preparation of the LAP-BAND® System by operating room personnel prior to surgery. The 16 gauge band priming needle is used to flush and prime the band tubing and inflatable shell with sterile saline. The 22 gauge access port flushing needle is used to flush and prime the access port with sterile saline.

Access Port Needle – three (3) sizes of non-coring, deflected-tip access port needles designed to penetrate the access port during postoperative adjustment of the band are available: 20-gauge, 89 mm (3.5inches); 20-gauge, 51 mm (2 inches); and 22-gauge, 39 mm (1.5 inches). Access port needles are provided sterile and are also available separately.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of obesity (BMI of greater than 30 kg/m^2) and they can be divided into two (2) categories: non-surgical treatments and obesity surgery.

Non-Surgical Treatments (Medical Therapy)
Non-surgical treatments of obesity include:

- Diet, exercise, and behavior modification programs;
- Prescription weight loss medications; and
- Other procedures and practices, such as jaw-wiring, hypnosis, counseling, psychotherapy, nutritional supplements, etc.

Several reports have suggested a rather high incidence of failure for obese patients to sustain long-term weight loss with any form of non-surgical treatment.[1,2,3]

Obesity Surgery

Numerous surgical techniques have been developed for the treatment of obesity. Aside from LAGB®, the most common obesity surgery procedure performed in the United States is the Roux-en-Y Gastric Bypass. Other procedures that are not as common are the Vertical Sleeve Gastrectomy and the Biliopancreatic Diversion Duodenal Switch. Bariatric surgery is usually recommended for patients with a BMI of at least 40 kg/m^2 or 35 kg/m^2 with one or more comorbid conditions.

Roux-en-Y Gastric Bypass (GBP)

Gastric bypass is the most common of a group of restrictive-malabsorptive procedures. These procedures are considered to be restrictive (a small gastric pouch restricting the amount of food consumed), as well as having a malabsorptive component (bypassing some part of the intestines). In the GBP, the surgeon constructs a proximal gastric pouch, and then creates an outlet from the pouch to a limb of the small bowel. This results in a bypass of most of the stomach and duodenum.

Vertical Sleeve Gastrectomy (VSG)

Vertical sleeve gastrectomy is a restrictive obesity procedure which reduces the size of the stomach by surgical removal of a large portion of the stomach. The open edges are then sutured together to form a sleeve. The size of the stomach is permanently reduced without bypassing the intestines or causing malabsorption.

Biliopancreatic Diversion Duodenal Switch (BPDDS)

The biliopancreatic diversion with duodenal switch is a procedure in which stomach removal is restricted to the outer margin, leaving a stomach "sleeve" with the pylorus intact. The small intestine is divided with one end attached to the stomach pouch. The majority of the small intestine is bypassed, causing nearly complete malabsorption of food contents.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The LAP-BAND® System has been in use in Europe since 1993. In 1997, the LAP-BAND® System was CE-marked. Regulatory approval has also been obtained in Australia (1994), Canada (1998), Israel (1997), and Mexico (1996). Approval has also been obtained in several other countries including Turkey, New Zealand, Venezuela, Brazil, Saudi Arabia, Hong Kong, Russia, Switzerland, Korea, and Taiwan. No regulatory approvals have been withdrawn.

The use of the LAP-BAND® System in patients with BMI of 35 or greater, or BMI of 30 or greater with a comorbid condition was CE-marked and also received approval in Australia in 2010.

11

Over 600,000 LAP-BAND® Systems have been distributed globally, and it has been widely reported on in the medical literature.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Adverse events that may result from use of the LAP-BAND® System are both those commonly associated with obesity surgical procedures and others associated with the device specifically. Below is a list of the potential adverse effects (e.g., complications) associated with gastric restriction procedures;

- Perforation of the stomach and complications associated with laparoscopic surgery (e.g., spleen or liver damage, thrombosis and rupture of the wound, infection, and death).
- Ulceration
- Gastritis
- Gastroesophageal reflux
- Gas bloat
- Dysphagia
- Dehydration
- Constipation
- Nausea and vomiting
- Weight regain
- Elevated homocysteine levels have been found in patients actively losing weight after obesity surgery and may increase cardiovascular risk.
- The developing fetus of pregnant women with elevated homocysteine may be at risk for neural tube defects.
- During periods of rapid weight loss, patients may experience malnutrition, anemia, or other related complications, such as the development of cholelithiasis.

Below is a list of the potential adverse effects (e.g., complications) associated specifically with the LAP-BAND® System:

- Intolerance to the components (foreign body reaction)
- Mechanical malfunction (leakage and deflation of the inflatable section)
- Access port site pain and access port displacement
- Band slippage/pouch dilatation/dysmotility
- Peritonitis and death can occur as a consequence of a gastrointestinal perforation during implantation of the device.
- The LAP-BAND® System is a long-term implant, and the System or a component may need to be either explanted or replaced.
- Medical management of adverse events may necessitate reoperation to revise or explant the device.
- As with any revision procedures, the possibility of complications such as erosion and infection are increased.

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF PRE-CLINICAL STUDIES

The original PMA application P000008 for the LAP-BAND® Adjustable Gastric Banding (LAGB®) System was approved on June 5, 2001. Data from the original application are applicable to the current PMA Supplement and are therefore incorporated by reference.

X. SUMMARY OF CLINICAL STUDIES

Allergan, Inc. performed a clinical study to establish a reasonable assurance of safety and effectiveness of the LAP-BAND® System for use in obese adults (BMI 30-40 kg/m^2) in the United States under IDE G070039. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

Purpose of the Study:
This study evaluated the safety and effectiveness of the device for use in weight reduction for obese patients, BMI $\geq$ 30 kg/m^2 and < 35 kg/m^2 with or without comorbid conditions, or with a BMI $\geq$ 35 kg/m^2 and < 40 kg/m^2 without any severe comorbid conditions.

A. Study Design

Patients were treated between November 29, 2007 and July 16, 2009. The database for this PMA supplement reflected data collected through July 16, 2009 and included 160 patients. There were seven (7) investigational sites.

The study was a single-arm, multi-center study in which each patient served as his or her own control. Of those enrolled, 149 were implanted with the LAP-BAND® System following screening.

The primary effectiveness measure was the percent of patients who achieved clinically successful weight loss at one (1) year following LAP-BAND® implantation, where successful weight loss was defined as ≥30% excess weight loss (EWL). The study device was determined to be clinically effective if at least 40% of patients achieved an EWL of 30% or greater at one (1) year.

Secondary effectiveness measures included changes from baseline to 12 months in: percent total weight loss (%WL); comorbid conditions of type 2 diabetes, dyslipidemia, and hypertension; and health-related quality of life as measured by the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire.

Additional effectiveness analyses included changes in various other weight variables (weight, excess weight, BMI, percent BMI loss), health related quality of life (SF36 health survey), depressive symptoms (Beck Depression Inventory II), eating behavior (Three Factor Eating Questionnaire and Questionnaire on Eating and Weight Patterns – Revised) and the economic impact of the implantation (Economic Impact Survey (EIS) were examined. Select measurements were analyzed at time points other than month 12, and longitudinal analyses for mean %EWL changes from baseline were conducted.

The %EWL was defined as weight loss (baseline weight minus follow-up weight) divided by excess weight (baseline weight minus ideal weight) multiplied by 100. The %WL was defined as weight loss divided by baseline weight. Ideal weight was determined based on a BMI of 25 kg/m^2. Study patients were weighed prior to surgery (screening visit and 7 days before surgery), at surgery, at 1 week postoperatively, and at regular intervals over the next year (1, 2, 4, 6, 8, 10, 12 months). Baseline weight was the weight at screening for patients placed on the pre-surgical diet and at surgery for patients who were not placed on the diet.

Safety:
Incidence and severity of adverse events related to treatment.

Analysis Populations
All patients who underwent surgery for placement of the LAP-BAND® were included in the analysis of safety and effectiveness. Two (2) analysis populations were defined.

Intent-to-Treat (ITT) and ITT Evaluable populations: included all implanted patients, and was used in the main analysis for the primary and secondary effectiveness variables. Because the protocol specified that the primary analysis be performed without imputation, the applicant also evaluated the "ITT evaluable" dataset which included only the observed data from each study visit. Imputation of missing values (e.g., last observation carried forward) was not performed for patients who terminated prematurely or were lost to follow-up. As a sensitivity analysis the primary effectiveness endpoint was re-analyzed treating patients with no data as failures identified as "ITT all implanted."

Per Protocol (PP) population: included all patients in the ITT population who were not considered to be influential protocol violators (defined as any deviation from the protocol that could affect the effectiveness analyses). If a patient in the PP population missed a scheduled follow-up visit, the patient was excluded from the effectiveness analysis for that particular follow-up visit.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the LAP-BAND® Lower BMI study was limited to patients who met the following inclusion criteria:

- Age 18 to 55.
- BMI $\geq$ 30 kg/m^2 and < 35 kg/m^2 with or without obesity-related comorbid conditions or BMI $\geq$ 35 kg/m^2 and <40 kg/m^2 without any severe comorbid conditions.
- History of obesity for at least two (2) years.
- History of failure with non-surgical and more conservative weight-reduction alternatives.
- Physically and mentally able to comply with the visit schedule and behavior modification required for the LAP-BAND®.
- Successful completion of pre-operative screening, educational programs, and psychological assessment supporting that the patient is an appropriate bariatric surgical candidate.

Patients were not permitted to enroll in the LAP-BAND® Lower BMI study if they met any of the following exclusion criteria:

- History of congenital or acquired anomalies of the gastrointestinal (GI) tract, such as intestinal telangiectasia, intestinal malrotation, duodenal ulceration, previously diagnosed Grade 3-4 esophagitis, congenital abdominal wall defects, or inflammatory bowel disease (i.e. Crohn's disease).
- Severe cardiopulmonary or other serious or uncontrolled organic disease (e.g. thyroid disease).
- Severe coagulopathy, hepatic insufficiency, or cirrhosis.
- History of bariatric, gastric, or esophageal surgery.
- History of intestinal obstruction or adhesive peritonitis.
- History of esophageal dysmotility disorders.
- Type I diabetes.
- Pregnancy or intention of becoming pregnant during the study (if female of childbearing potential).
- Uncontrolled psychiatric disorders (including untreated major depression, schizophrenia, substance abuse, bulimia nervosa), immaturity, or lack of family support which would potentially compromise the patient's ability to fully comprehend and/or cooperate with the study protocol.

- Chronic use of aspirin and/or non-steroidal anti-inflammatory medications and unwillingness to discontinue the use of these concomitant medications.
- Concurrent use of weight loss medications.
- Any condition that would be a contraindication in the LAP-BAND® System Directions for Use.

2. Follow-up Schedule

All patients were scheduled for three (3) preoperative examinations including one on the day of surgery (the baseline examination) and were scheduled to return for post-operative follow-up examinations at Week 1 and Months 1, 2, 4, 6, 8, 10, 12, 15, 18, 21, 24, 30, 36, 42, 48, 54 and 60, plus additional unscheduled visits as needed. Table 1 describes the preoperative and postoperative examinations and parameters measured during the study.

Table 1: Schedule of Follow-up Visits and Procedures

SC = Screening Visit BL = Baseline MO = Month WK = Week

					Month															
Procedures	**SC**	**-7 days**	**Surg. Day 0 BL**	**WK 1**	**1**	**2**	**4**	**6**	**8**	**10**	**12**	**15**	**18**	**21**	**24**	**30**	**36**	**42**	**48**	**54**	**60**
Informed Consent, HIPAA	X																				
Certification Page	X										X				X						X
Inclusion/ Exclusion	X																				
Demographics	X																				
Medical History	X																				
PFT, Chest x-ray, EKG	X																				
Vital Signs (BP, HR, Temp, RR)	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Comorbid Conditions	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical Exam	X										X				X		X	X	X	X	X
Nutritional Evaluation	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Patient Food and Exercise Diary	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine Pregnancy Test (if female of childbearing potential)	X		X			X					X		X		X	X	X	X	X	X	X
Gastrointestinal Evaluation	X																				
Esophagram	X										X				X		X		X		X

					Month															
Procedures	**SC**	**-7 days**	**Surg. Day 0 BL**	**WK 1**	**1**	**2**	**4**	**6**	**8**	**10**	**12**	**15**	**18**	**21**	**24**	**30**	**36**	**42**	**48**	**54**	**60**
Laboratory: Metabolic Hematologic Thyroid Panel Lipid Panel Liver Function Additional Pathology	X							X			X				X		X		X		X
Urinalysis	X							X			X				X		X		X		X
Weight, BMI, Height, Waist, and Hip Measurements	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Psychosocial Evaluation	X																				
BDI-II		X						X			X		X		X	X	X	X	X	X	X
IWQOL-Lite, SF-36		X						X			X		X		X	X	X	X	X	X	X
TFEQ, QEWP-R		X						X			X		X		X	X	X	X	X	X	X
EIS		X									X				X		X		X		X
LAP-BAND® System Surgery			X																		
Adverse Events			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Fluoroscopy (if necessary)				(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
LAP-BAND® Adjustments (if necessary)					(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)

The key time points are shown below in the table summarizing safety and effectiveness.

3. Clinical Endpoints

With regards to safety, the incidence and severity of adverse events related to the treatment were tabulated and presented at each of the time points as well as overall for all intent-to-treat (ITT) patients. Exact 95% binomial confidence limits were provided; no statistical hypotheses were evaluated.

With regards to effectiveness, the primary endpoint was the percent of patients who attained a clinically successful weight loss at one (1) year post LAP-BAND® placement where effectiveness was defined as having at least a 30% excess weight loss. At least 40% of the intent-to-treat (ITT) patients must have reached an excess weight loss of 30% or greater to achieve the primary endpoint.

Secondary effectiveness: all the secondary effectiveness analyses were conducted at 12 months. Two (2) of the secondary endpoints (percent total weight loss and Impact of Weight on Quality of Life-Lite (IWQOL-lite) Total Score) were tested against a null hypothesis of no change from baseline (i.e., a null hypothesis mean of zero). For the change in comorbid conditions, only descriptive statistics were reported and 95% confidence intervals for the rate of improvement and resolution were provided.

- *Percent weight loss (%WL)* – changes in weight were analyzed as %WL and were defined as weight loss divided by baseline weight multiplied by 100, where weight loss is equal to baseline weight minus month 12 weight. The mean change from baseline was evaluated by a paired t-test.

- *IWQOL-Lite Total Scores* – the IWQOL-Lite consists of 31 items to assess weight related quality of life over five (5) domains: *Physical*, *Self-Esteem*, *Sexual Life*, *Public Distress*, and *Work*. Scores ranged from 0 (worst) to 100 (best). The mean change in total IWQOL-Lite score from baseline to month 12 and its corresponding 95% confidence intervals were presented. The mean change from baseline was evaluated by a paired t-test or Wilcoxon signed-rank test, as appropriate. Effect size was calculated by Cohen's statistical test, dividing the difference between the means at baseline and one (1) year post implantation by the baseline standard deviation.

- *Comorbid conditions* – frequency of three (3) comorbid conditions related to obesity (type 2 diabetes, dyslipidemia, and hypertension) was presented by severity (none, mild, moderate, and severe) at each time point. Post operative changes in severity (resolved, improved, unchanged, or worsened) from baseline were examined at month 12. Resolved was defined as moving into the "none" category, improved was defined as moving down at least one (1) severity category, and worsened was defined as moving up at least one (1) category. Changes in severity of comorbid conditions were based on investigator assessments of the severity of the conditions, there were no standard criteria used by all investigational sites. The percentage was calculated using the number of patients with the existing comorbid condition at baseline as the denominator. Exact 95% binomial confidence limits were provided for the resolved and improved rate of the comorbid condition.

Other Effectiveness Analyses included:

- *%EWL* - Percent excess weight loss was summarized as a continuous variable at each of the follow-up time points. The mean change from baseline was evaluated by a paired t-test or Wilcoxon signed-rank test, as appropriate.

- *%weight loss, weight, excess weight (lb), BMI and % BMI loss* – were evaluated at all time points by a paired t-test or Wilcoxon signed-rank test, as appropriate.

- *Comorbid conditions* – 12 other comorbid conditions: back pain, depression, gallbladder disorder, gastroesophageal reflux, hypercholesterolemia,

hypertriglyceridemia, metabolic syndrome, osteoarthritis, respiratory abnormalities, sleep apnea, urinary incontinence, and venous stasis, were evaluated for changes at 12 months.

- *SF 36 Health Survey* – includes 36 questions that evaluate eight (8) discrete domains. The score for each domain ranged from 0 (poorest health status) to 100 (best health status). The mean change from baseline was evaluated by a paired t-test or Wilcoxon signed rank-test, as appropriate. Effect size was calculated by Cohen's d. The mean domain scores were also compared to general US population results by a two-sample t-test at baseline and month 12.

- *Beck Depression Inventory II* – consists of 21 questions to measure depressive symptoms and severity. Scores can range from 0 to 63 with higher total scores indicating more severe depressive symptoms. The patient's worst response at the respective time point was used for any missing responses. The mean change from baseline was evaluated by a paired t-test or Wilcoxon signed-rank test, as appropriate.

- *Three Factor Eating Questionnaire* – designed to assess three (3) dimensions of eating behavior: *Cognitive Restraint of Eating, Disinhibition* and *Hunger*. This is a two (2) part questionnaire. The mean change from baseline was evaluated by a paired t-test or Wilcoxon signed-rank test, if appropriate.

- *Questionnaire on Eating and Weight Patterns*-Revised – a self-reported measure used to assess binge-eating disorder. Changes from baseline were tested using the McNemar test.

With regards to success/failure criteria, a patient had to have at least a 30% EWL for the weight loss to be considered clinically successful. At least 40% of the intent-to-treat (ITT) patients must have reached an excess weight loss of 30% or greater for the study to be considered a success.

B. Accountability of PMA Cohort

At the time of database lock, a total of 160 patients were enrolled in the study (signed the informed consent) and, after screening, 149 patients underwent LAP-BAND® placement. Figure 3 shows the intent-to-treat (ITT) "evaluable" and per protocol (PP) populations through month 12. A total of 145 patients (97.3%) completed the 12-month followup. Four (4) patients discontinued their participation prior to 12 months.

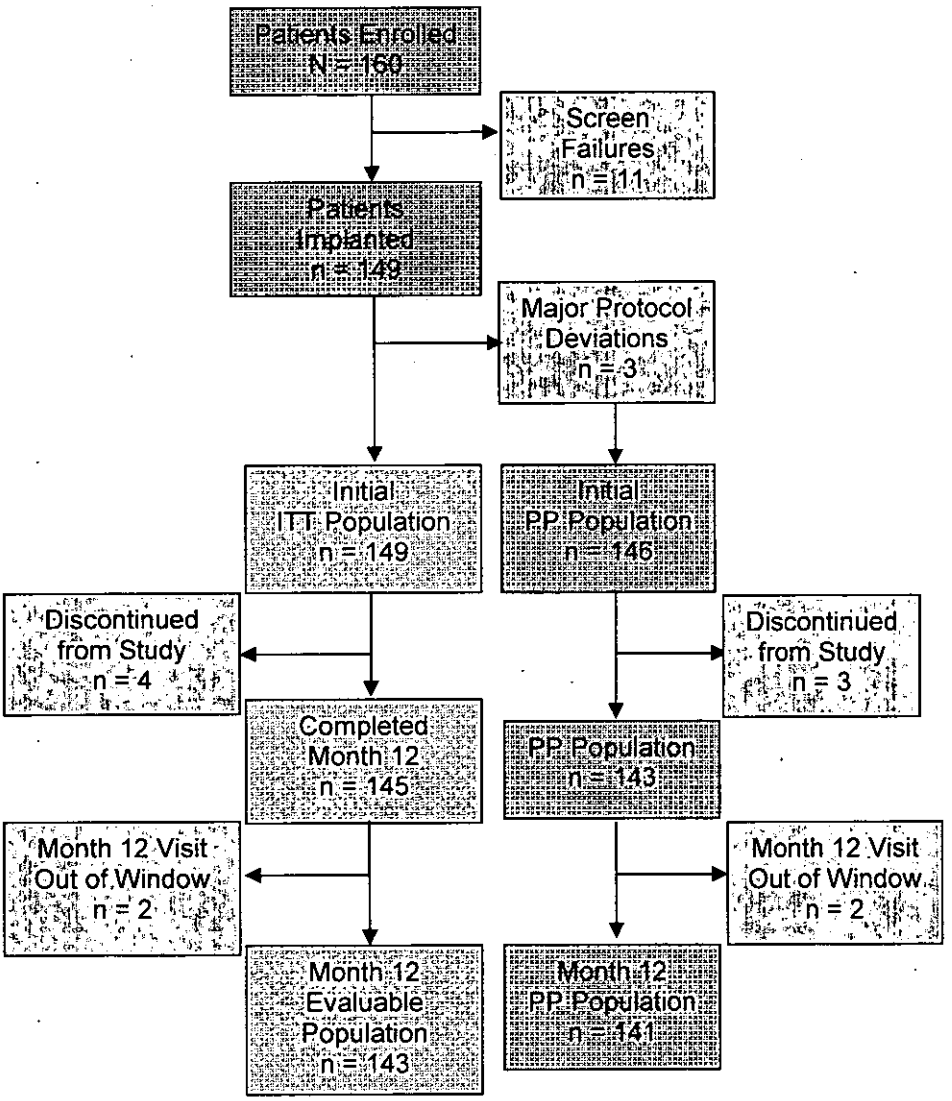


Figure 3: ITT and PP Populations through Month 12

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a single-arm, multi-center study in which each patient served as his or her own control performed in the US. A total of 160 patients were enrolled in the clinical study with 149 patients undergoing implantation with the LAP-BAND® System. The baseline demographics on the implanted patients are provided in Table 2.

Table 2: Subject Demographics and Baseline Characteristics (N=149)

Characteristic (n=149)	N	%
Gender		
Female	135	90.6%
Male	14	9.4%
Age at Surgery Visit (Average, Range)	39.3 (18.0 – 55.0)	
18-20	5	3.4%
21-29	19	12.8%
30-39	46	30.9%
40-49	57	38.3%
50-55	22	14.8%
Race		
Caucasian	115	77.2%
Hispanic/Latino	16	10.7%
Black (not of Hispanic origin)	14	9.4%
Asian	2	1.3%
Other	2	1.3%
BMI (Mean, Range)	35.4 kg/m^2 ($29.8\ kg/m^2$ - $39.9\ kg/m^2$)	
$\geq 29\ kg/m^2$ and $< 30\ kg/m^2$	1[a]	0.7%
$\geq 30\ kg/m^2$ and $< 35\ kg/m^2$	63	42.3%
$\geq 35\ kg/m^2$ and $< 40\ kg/m^2$	85	57.0%
Weight, pounds (Mean, Range)	214.9 (152.6 – 286.2)	
Ideal Weight, pounds (Mean, Range)	152.1 (121.7 – 216.3)	
Excess Weight, pounds (Mean, Range)	62.8 (28.8 – 100.7)	
Waist Circumference, inches (Mean, Range)	41.5 (33.5 – 53.5)	
Hip Circumference, inches (Mean, Range)	47.7 (37.0 – 55.9)	

[a] Patient BMI was $> 30\ kg/m^2$ at screening but $< 30\ kg/m^2$ at surgery

Following screening, 149 patients received LAP-BAND® implantation, of which 91% were female and 9% were male. Distribution by race was 77% Caucasian, 9% African-American, 11% Hispanic, 1.3% Asian, and 1.3% other. The average age at the time of surgery was 39.3 years. All 149 procedures were completed utilizing a pars flaccida technique, using the LAP-BAND AP® (Standard and Large) Systems, and were completed laparoscopically.

The mean weight at baseline was 215 pounds, with mean excess weight of 63 pounds and mean BMI of 35.4. Fifty-seven percent (57%) of patients had BMI ≥ 35 and < 40, and the remainder had BMI < 35. Subjects had significant obesity related comorbidities which included: osteoarthritis (38%), back pain (35%), gastroesophageal reflux (28%), depression (28%), respiratory abnormality (26%), dyslipidemia (20%), hypertension (18%), urinary incontinence (11%), venous stasis (7%), sleep apnea (7%), and type 2 diabetes (4%).

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the 149 obese patients with BMI ≥30 and <40 kg/m^2 who underwent LAP-BAND® System placement surgery in the lower BMI clinical study available at the one (1) year evaluation. Adverse effects for this study are reported in Tables 3 and 4 and Figure 4.

The severity of each event was rated as mild, moderate, or severe and then further rated as serious or not serious. These were defined as:

> *Mild* – symptom barely noticeable to the patient; does not affect performance or functioning. Prescription drugs not ordinarily needed for relief of symptom.
>
> *Moderate* – symptom of sufficient severity to make patient uncomfortable; performance of daily activities affected; patient is able to continue in study; treatment of symptoms is needed.
>
> *Severe* – symptom causes severe discomfort and may be of such severity that patient cannot perform daily activities. Severity may result in cessation of treatment or require removal of the device, or treatment of symptom may be given and/or patient hospitalized.

Adverse events were reported as *serious* if considered to be life threatening, permanently disabling, unexpected, fatal, requiring hospitalization, or prolonged hospitalization. All events categorized as serious in the US clinical study were associated with intervention that required hospitalization or prolonged hospitalization.

A total of 524 adverse events were reported in 131 patients (87.9%) and 215 of the adverse events were related or probably related to the device. These device related events occurred in 105 patients. Table 3 shows the number and percent of patients reporting an adverse event and the severity, for those events reported in 2% or more of patients.

Table 3: Device-Related Adverse Events that Occurred in ≥2% of Subjects in the US Lower BMI Study

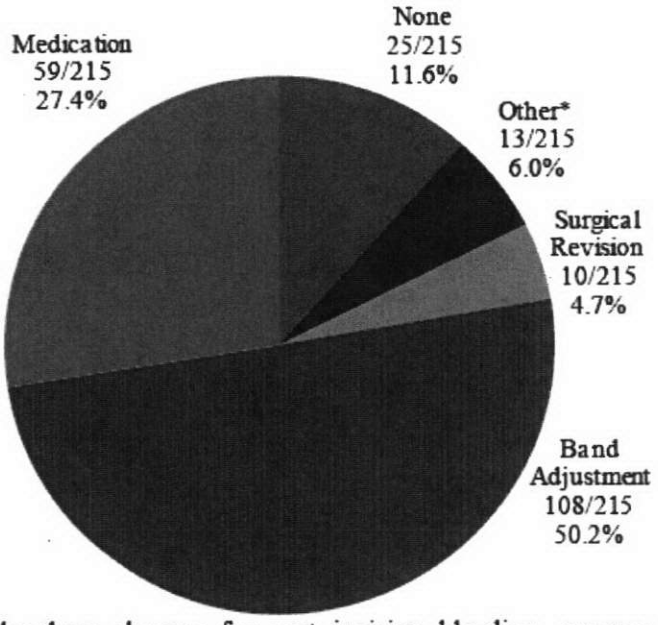
Preferred Term	Subjects		Events		Mild	Moderate	Severe
	N	(%)[a]	N	(%)[b]	n (%)	n (%)	n (%)
Vomiting	43	28.9%	43	(20.0%)	29 (67.4%)	13 (30.2%)	1 (2.3%)
Dysphagia	33	22.1%	33	(15.3%)	20 (60.6%)	12 (36.4%)	1 (3.0%)
Post procedural pain	28	18.8%	28	(13.0%)	1 (3.6%)	27 (96.4%)	0 (0.0%)
Gastroesophageal reflux disease	22	14.8%	22	(10.2%)	15 (68.2%)	7 (31.8%)	0 (0.0%)
Abdominal pain	8	5.4%	8	(3.7%)	2 (25.0%)	6 (75.0%)	0 (0.0%)
Nausea	8	5.4%	8	(3.7%)	5 (62.5%)	3 (37.5%)	0 (0.0%)
Dyspepsia	7	4.7%	7	(3.3%)	4 (57.1%)	3 (42.9%)	0 (0.0%)
Implant Site Pain	7	4.7%	7	(3.3%)	6 (85.7%)	1 (14.3%)	0 (0.0%)
Abdominal pain upper	4	2.7%	4	(1.9%)	3 (75.0%)	1 (25.0%)	0 (0.0%)
Constipation	4	2.7%	4	(1.9%)	3 (75.0%)	1 (25.0%)	0 (0.0%)
Medical device complication [c]	4	2.7%	4	(1.9%)	2 (50.0%)	1 (25.0%)	1 (25.0%)
Dehydration	3	2.0%	3	(1.4%)	1 (33.3%)	2 (66.7%)	0 (0.0%)
Device malfunction [d]	3	2.0%	3	(1.4%)	0 (0.0%)	2 (66.7%)	1 (33.3%)
Shoulder pain	3	2.0%	3	(1.4%)	1 (33.3%)	2 (66.7%)	0 (0.0%)

[a] Percentage is based on 149 patients.
[b] Percentage is based on 215 device-related adverse events
[c] Complications included band erosion, tubing palpated in umbilical hernia, and band slippage
[d] Malfunctions included partial slip, flipped port, and band slippage.

Other adverse events considered related to the LAP-BAND® System that occurred in fewer than 2% of study patients included: diarrhea (n=2), gastric pouch dilatation (n=2), gastritis (n=2), esophageal dilatation (n=2), syncope (n=2), and seroma (n=2). Other events reported to occur in only one patient per event included: abdominal discomfort, alopecia, anemia, arthralgia, decrease blood folate, flatulence, gastrointestinal motility disorder, bronchitis, chills, implant site infection, implant site irritation, implant site hemorrhage, night sweats, hypotrichosis, headache, nail infection, pyrexia, skin irritation, esophageal obstruction, esophageal spasm, postoperative infection, urinary tract infection, muscle spasms, depression, back pain, and hypertension.

Of the 215 device related adverse events (Figure 4), no action was taken for 25 events (11.6%), medication was prescribed for 59 events (27.4%), and band adjustment (fluid removal) was performed for 108 events (50.2%). Surgical revision was performed for 10 device related events in seven (7) patients and for one non-device related event (abdominal wall hernia repair).

The majority of device related adverse events resolved in less than a month (145/215, 67.5%), and the most common treatment for device related AEs was band adjustment (n=108, 50.2%).



*includes bandage changes for port incision bleeding, surgery to repair hernia, band removal, colonoscopy, walking to relieve gas pain, dietary changes, and seroma drainage

Figure 4: Treatment for Device-related Adverse Events

Reoperations – Seven (7) patients (4.7%, 7/149) each required one (1) reoperation and there were no intraoperative complications. Four (4) of these (57.1%, 4/7) were LAP-BAND® System explantations due to dysphagia (in two (2) patients), erosion of the band, or abdominal pain. Two (2) reoperations were access port revisions due to port flip or port site pain; the original ports were retained. One (1) reoperation was for repositioning of the original band to correct for band slippage. There were no deaths in the study.

Serious Adverse Events – Table 4 summarizes the incidence of serious adverse events that were reported to have occurred in the US clinical study that were, or may have been, related to the band. These seven (7) events occurred in three (3) patients (2%, 3/149). They were hospitalized for 7 days or less and discharged following band removal. There were no deaths or unanticipated adverse events.

Table 4: Serious Adverse Events Considered Related to the LAP-BAND® System for the US Lower BMI Study

Adverse Event	# of Patients	% of 149 Patients
Abdominal Pain	2	1.3
Shoulder Pain	1	0.7
Dysphagia	1	0.7
Medical Device Complication (Band Erosion)	1	0.7
Gastric Outlet Obstruction	1	0.7
Vomiting	1	0.7

2. Effectiveness Results

The analysis of effectiveness was based on the 143 "ITT evaluable" patients at the 12-month time point. Effectiveness was also evaluated using all implanted patients (n=149). Key effectiveness outcomes are presented in Tables 5-7.

- Primary Effectiveness Endpoint – Percent of patients with ≥ 30%EWL at one (1) year following LAP-BAND® System surgery

  The study device was determined to be clinically effective if at least 40% of patients achieved an excess weight loss of 30% or greater at one (1) year. As shown in Table 5, at one (1) year following LAP-BAND® surgery, 80.5% of all implanted patients (83.9% of ITT evaluable patients) achieved this goal. In Table 5 data are also provided as excess weight loss for subcategories of weight loss (i.e., at least 25%, at least 30%, at least 50%). Sixty-six percent (65.8%) of all implanted patients lost at least 50% of their excess weight.

Table 5: Percent Excess Weight Loss at Month 12

	N	At Least 25% EWL[a]	At Least 30% EWL[a]	At Least 50% EWL
ITT – All Implanted[b]	149	127 (85.2%)	120 (80.5%)[d]	98 (65.8%)
ITT - Evaluable at Month 12[c]	143	127 (88.8%)	120 (83.9%)[d]	98 (68.5%)
PP - Evaluable at Month 12	141	126 (89.4%)	119 (84.4%)[d]	97 (68.8%)

[a] Cumulative frequency.

[b] There were 6 patients who did not have a Month 12 visit within the analysis window - 4 patients discontinued (were explanted) prior to their Month 12 visit and 2 patients had a Month 12 visit that was outside the analysis window. These patients are treated as failures.

[c] The pre-specified analysis method was without imputation, so this analysis only includes patients who had a Month 12 visit within the analysis window (N=143).

[d] P-value from exact binomial test against a null value of 40% is < 0.0001

Table 6 provides information on the percentage of patients in the ITT evaluable group (without imputation) and the ITT all implanted group (with imputation) who achieved at least a 30% EWL by visit. Table 7 provides excess weight loss for subcategories of weight loss (i.e., at least 10%, at least 30%, at least 50%) in the ITT evaluable group.

Table 6: Percent of Subjects Achieving at least 30%EWL by Visit

Follow-up Visit	N	% of Subjects with ≥30% EWL (without imputation)[a]	% of Subjects with ≥30% EWL (with imputation)[b]
Month 1	149	16.1%	16.1%
Month 2	148	41.2%	40.9%
Month 4	146	70.5%	69.1%
Month 6	149	83.2%	83.2%
Month 8	147	86.4%	85.2%
Month 10	142	85.9%	81.9%
Month 12	143	83.9%	80.5%

N = Number of patients at follow-up visit

[a] Percentage based on observed cases

[b] Percentage with unobserved cases imputed as %EWL < 30%

Table 7: Distribution of Patients by EWL at 12 Months

%EWL	N	% of Patients*
≥10%	141	98.6%
≥30%	120	83.9%
≥50%	98	68.5%
≥70%	62	43.4%
≥90%	29	20.3%

N = 143 patients at 12 months.

*Rows are cumulative frequencies

- Secondary and Additional Effectiveness Endpoints

  Information on secondary weight related effectiveness endpoints are provided in Table 8. The mean weight loss was 39.7 pounds and the typical patient lost 18.3% of baseline total weight, 64.5% of excess weight and BMI declined by 6.5 points. Other endpoints also steadily decreased over time.

Table 8: Summary of Weight, BMI, and Body Changes at 12 Months

Parameter	Baseline Mean (SD) n[a] = 149	Month 12 Mean (SD) n = 143[b]	Mean Change from Baseline at Month 12	95% CI (Lower, Upper)	P-value[c]
Weight (lbs)	214.9 (24.3)	174.7 (24.5)	39.7	36.4, 43.0	<0.0001
%WL	N/A	18.3 (8.5)	18.3	16.9, 19.7	<0.0001
Excess Weight (lbs)	62.8 (16.1)	22.8 (19.4)	39.7	36.4, 43.0	<0.0001
%EWL	N/A	64.5 (30.3)	64.5	59.5, 69.5	<0.0001
BMI (kg/m^2)	35.4 (2.6)	28.8 (3.2)	6.5	6.0, 7.1	<0.0001
% BMI Loss	N/A	18.3 (8.5)	18.3	16.9, 19.7	<0.0001
Waist Circumference (inches)	41.5 (3.5)	35.4 (4.4)	5.9	5.4, 6.5	<0.0001
Hip Circumference (inches)	47.7 (3.0)	41.9 (3.5)	5.8	5.2, 6.4	<0.0001

[a] n is the actual number of patients at visit

[b] n=140 for waist circumference and hip circumference

[c] P-value is for the evaluation of mean change from baseline by paired t -test or Wilcoxon signed-rank test based on P-value of normality test <0.05

Change in BMI

Figure 5 shows the change in BMI by range of baseline BMIs at 12 months for all implanted patients. The data show that for all 149 implanted patients, there was an overall shift in the distribution of patients from the upper BMI range (≥ 35 kg/m^2) to the lower BMI range (< 30 kg/m^2).

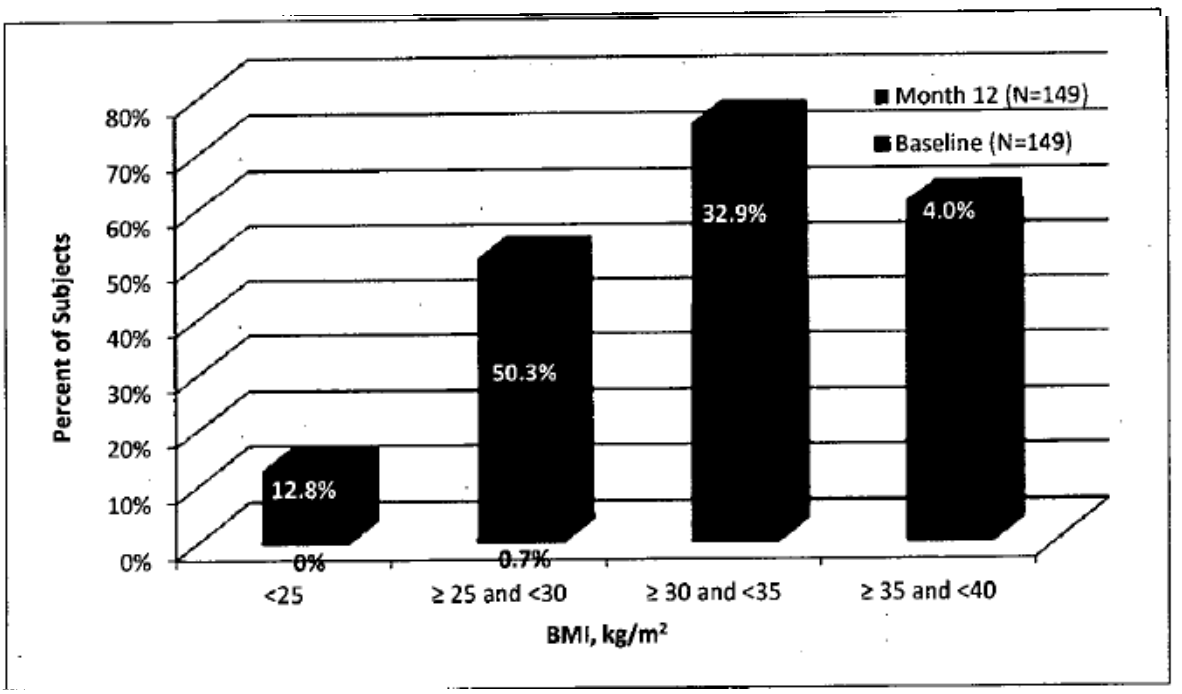


Figure 5: Change in BMI Range from Baseline to 12 months (with imputation)

As shown in Table 9, the number of patients with BMI ≥ 25 and < 30 kg/m^2 increased from 1 (0.7%) at baseline to 75 (50.3%) at Month 12, and the number of patients with BMI < 25 kg/m^2 increased from 0 at baseline to 19 (12.8%) at Month 12. The number of patients with BMI between 30 and 35 kg/m^2 decreased from 63 (42.3%) at baseline to 49 (32.9%) after 12 months, and the number of patients with BMI between 35 and 40 kg/m^2 decreased from 85 (57.0%) to 6 (4.0%) at Month 12. Overall, 148 patients (99.3%) had BMI ≥ 30 kg/m^2 at baseline, and this number decreased to 55 patients (36.9%) at 12 months. After one (1) year with the LAP-BAND® System, 19 patients (13.3%) were no longer overweight (BMI < 25 kg/m^2) and an additional 75 patients (52.4%) were no longer obese (BMI 25-30 kg/m^2). It should be noted that 36.9% of patients would still be eligible for enrollment in the study because their BMI remained greater than 30 kg/m^2.

Table 9: Change in BMI Range from Baseline to Month 12 (N=149)

BMI Group	Baseline n (%)	Month 12[a] n (%)
<25 kg/m²	0	19 (12.8%)
≥ 25 and <30 kg/m²	1 (0.7%)	75 (50.3%)
≥ 30 and <35 kg/m²	63 (42.3%)	49 (32.9%)
≥ 35 and <40 kg/m²	85 (57.0%)	6 (4.0%)
≥ 40 kg/m²	0	0
Total	149 (100.0%)	149 (100.0%)

[a] There were 6 patients who did not have a Month 12 visit within the analysis window - 4 patients discontinued (were explanted) prior to their Month 12 visit and 2 patients had a Month 12 visit that was outside the analysis window. For these patients, their worst outcome/highest weight during the study is used for missing values.

Change in Comorbid Conditions (Type 2 Diabetes, Dyslipidemia, and Hypertension)
In the study, changes in severity of comorbid conditions were based on investigator assessments of the severity of the conditions at each timepoint. At 12 months post-surgery (Table 10), improvement was noted in all three (3) of the secondary endpoint comorbidities: type 2 diabetes, dyslipidemia, and hypertension. The number of patients with each comorbid condition was small making it difficult to make any definitive statements regarding improvement in the conditions. These reported changes in comorbid conditions were consistent with changes in associated laboratory values, as shown in Tables 11-13.

Table 10: Change in Comorbid Conditions at 12 Months

Comorbid Conditions	Surgery Status N (%)*	Resolved n (%)**	Improved N (%)**	No Change N (%)**	Worsened n (%)**
Diabetes Type II	6 (4.0%)	2 (33.3%)	0 (0.0%)	4 (66.7%)	0 (0.0%)
Dyslipidemia	29 (19.5%)	8 (27.6%)	0 (0.0%)	21 (72.4%)	0 (0.0%)
Hypertension	27 (18.1%)	6 (22.2%)	2 (7.4%)	19 (70.4%)	0 (0.0%)

N is number of patients having comorbid condition at surgery.
* % is of total population (149).
** % is of N for each comorbid condition.

Table 11 shows the changes in fasting blood glucose and glycosylated hemoglobin (HbA1c) for the patients enrolled in the study and patients with abnormal baseline values.

Table 11: Changes in Fasting Plasma Glucose and Glycosylated Hemoglobin (HbA1c)

			Screening		Month 12 Change from Screening (Month 12-Screening)	
Lab Test	**Subject group**	**n[a]**	**Mean**	**SD**	**Mean**	**95% CI**
Fasting Plasma Glucose (mg/dL)	All Subjects	145	93.4	14.1	-3.6	-5.6, -1.6
	Subjects with Abnormal baseline values[b]	5	149.2	15.4	-40.4	-74.1, -6.7
HbA1c (%)	All subjects	145	5.4	0.5	-0.1	-0.1, -0.03
	Subjects with Abnormal baseline values[c]	2	7.5	0.5	-0.8	-13.5, 11.9

[a] n is the number of patients with values at Screening and Month 12
[b] n Abnormal Fasting Plasma Glucose is defined as $\geq$ 126 mg/dL
[c] Abnormal HbA1c is defined as $\geq$ 7%

Table 12 shows the overall values for dyslipidemia (total cholesterol, high density lipoproteins, low density lipoproteins, and triglycerides) for all patients enrolled in the study and patients with abnormal baseline values.

Table 12: Changes in Lipids [Total Cholesterol, High Density Lipoproteins (HDL), Low Density Lipoproteins (LDL), and Triglycerides]

			Screening		Month 12 Change from Screening (Month 12-Screening)	
Lab Test	**Subject group**	**n[a]**	**Mean**	**SD**	**Mean**	**95% CI**
Cholesterol (mg/dL)	All Subjects	143	204.5	38.1	-13.7	-18.6, -8.9
	Subjects with Abnormal baseline values[b]	24	258.9	20.7	-39.4	-52.8, -26.0
HDL (mg/dL)	All subjects	143	55.7	13.7	5.8	4.0, 7.6
	Subjects with Abnormal baseline values[c]	15	36.7	2.5	7.7	4.2, 11.3
LDL (mg/dL)	All subjects	143	121.3	30.4	-13.4	-17.6, -9.1
	Subjects with Abnormal baseline values[d]	16	171.3	14.8	-46.8	-58.3, -35.3
Triglycerides (mg/dL)	All subjects	143	137.2	67.5	-30.7	-40.0, -21.3
	Subjects with Abnormal baseline values[e]	22	261.4	61.5	-98.7	-135.9, -61.5

[a] n is the number of patients with values at Screening and Month 12
[b] n Abnormal Cholesterol is defined as ≥ 240 mg/dL
[c] Abnormal HDL is defined as < 40 mg/dL
[d] n Abnormal LDL is defined as ≥ 160 mg/dL
[e] Abnormal Triglycerides are defined as ≥ 200 mg/dL

Table 13 shows changes in blood pressure for all patients and patients with abnormal baseline values.

Table 13: Changes in Blood Pressure [Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)]

			Screening		Month 12 Change from Screening (Month 12-Screening)	
Lab Test	**Subject group**	**n[a]**	**Mean**	**SD**	**Mean**	**95% CI**
SBP (mm Hg)	All Subjects	142	127.6	14.8	-8.1	-10.9, -5.3
	Subjects with Abnormal baseline values[c]	27	150.9	10.0	-21.0	-28.2, -13.9
DBP (mm Hg)	All subjects	142	79.1	9.3	-3.1	-4.8, -1.3
	Subjects with Abnormal baseline values[d]	16	94.3	4.9	-9.4	-15.2, -3.7

[a] n is the number of patients with values at Screening and Month 12
[b] P-value is from Wilcoxon signed-rank test, testing against a difference of 0
[c] n Abnormal SBP is defined as ≥ 140 mm Hg
[d] Abnormal DBP is defined as ≥ 90 mm Hg

Impact of Weight-related Quality of Life-Lite (IWQOL-Lite)
Quality of life significantly improved as measured by the IWQOL-Lite assessment. The mean IWQOL-Lite score for all patients was 62.8 at baseline, and improved to 90.6 at 12

months. One hundred and forty two (142) patients had IWQOL scores both at baseline (mean 62.5) and month 12 (mean 90.5). The analysis, shown below in Table 14, showed significant improvements in all five (5) scale domains, as well as the total score (p<0.0001).

Table 14: Change in IWQOL-Lite Score at 12 Months

Domains	N	Baseline Mean	Month 12 Mean	Mean Change	*p*-value
Physical Function	142	60.9	92.7	31.8	<0.0001
Self-Esteem	141	43.6	80.4	36.8	<0.0001
Sexual Life	139	66.3	89.0	22.7	<0.0001
Public Distress	143	79.0	96.6	17.6	<0.0001
Work	143	75.8	95.7	19.9	<0.0001
Total Score	142	62.5	90.5	28.0	<0.0001

N = Number of Patients with scores at both baseline and 12 months

Changes in Other Comorbid Conditions

In addition to the comorbidities of dyslipidemia, Type 2 diabetes, and hypertension, additional comorbidities were assessed by the Investigator for severity at baseline and Month 12. All comorbid conditions demonstrated some improvement or resolution at Month 12 with the LAP-BAND® System, as shown in Table 15.

Table 15: Month 12 Change in Status of Other Comorbid Conditions

Comorbid Condition	Present at Baseline n (%)[a]	Resolved[b] n (%)[e]	Improved[c] n (%)[e]	Unchanged N (%)[e]	Worsened[d] n (%)[e]
Back Pain	52 (34.9%)	18 (34.6%)	2 (3.8%)	31 (59.6%)	1 (1.9%)
Depression	41 (27.5%)	9 (22.0%)	1 (2.4%)	30 (73.2%)	0 (0.0%)
Gastroesophageal Reflux	42 (28.2%)	30 (71.4%)	0 (0.0%)	9 (21.4%)	0 (0.0%)
Metabolic Syndrome	1 (0.7%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Osteoarthritis	57 (38.3%)	18 (31.6%)	0 (0.0%)	38 (66.7%)	1 (1.8%)
Respiratory Abnormality	38 (25.5%)	18 (47.4%)	1 (2.6%)	19 (50.0%)	0 (0.0%)
Sleep Apnea	11 (7.4%)	4 (36.4%)	1 (9.1%)	6 (54.5%)	0 (0.0%)
Urinary Incontinence	16 (10.7%)	8 (50.0%)	0 (0.0%)	8 (50.0%)	0 (0.0%)
Venous Stasis	11 (7.4%)	6 (54.5%)	0 (0.0%)	5 (45.5%)	0 (0.0%)

[a] n is the number of patients having comorbid conditions at Surgery; percent is of total population;
[b] Resolved is defined as patients moving to the None category
[c] Improved is defined as patients improving by at least one category but not Resolved
[d] Worsened is defined as patients worsening by at least one category
[e] n is the number of patients with status Resolved/Improved/Unchanged/Worsened at Month 12; percent is of patients who had condition at Surgery; sum of change in status (Resolved + Improved + Unchanged + Worsened) may not equal Baseline status due to missing data at Month 12.

Other Patient Reported Outcomes

Consistent with improvements seen in IWQOL-Lite, improvements from baseline were seen at Month 12 in other patient reported outcomes including the SF-36, Beck Depression Inventory-II, Three Factor Eating Questionnaire, and Questionnaire on Eating and Weight Patterns – Revised.

- Subgroup Analyses

  Table 16 presents a summary of the BMI and % EWL subpopulation analysis by gender, age, baseline BMI, and ethnicity. Substantial weight loss was observed in all subpopulation groups.

Table 16: Subpopulation Analyses of BMI and % EWL

	Baseline[a]	Month 12[b]			
Subpopulation	BMI Mean (SD)	N	BMI Mean (SD)	Change in BMI from Baseline Mean	%EWL Mean (SD)
Age, years					
18-29 (n=24)	35.90 (2.739)	22	28.65 (3.650)	7.21	66.27 (31.212)
30-39 (n=46)	35.79 (2.740)	44	28.73 (3.389)	6.97	66.28 (31.596)
40-49 (n=57)	35.15 (2.237)	55	29.14 (3.006)	6.04	61.17 (29.446)
50-55 (n=22)	34.41 (2.672)	22	28.25 (2.943)	6.16	67.61 (30.138)
Race					
Caucasian (n=115)	35.27 (2.580)	112	28.56 (3.216)	6.71	66.69 (30.420)
Non-Caucasian (n=34)	35.67 (2.556)	31	29.70 (3.042)	5.87	56.68 (28.961)
Gender					
Female (n=135)	35.43 (2.511)	132	28.86 (3.239)	6.51	64.31 (30.361)
Male (n=14)	34.74 (3.133)	11	28.17 (2.796)	6.71	66.98 (30.800)
BMI					
< 35 (n=64)	32.91 (1.566)	62	27.57 (2.764)	5.35	69.11 (34.289)
≥ 35 (n=85)	37.21 (1.330)	81	29.74 (3.213)	7.42	61.00 (26.524)
BMI and Baseline Comorbidity Status					
< 35 with comorbidities (n=56)	32.99 (1.539)	54	27.55 (2.735)	5.46	69.34 (33.025)
< 35 without comorbidities (n=8)	32.35 (1.748)	8	27.74 (3.145)	4.61	67.57 (44.550)
≥ 35 with comorbidities (n=71)	37.14 (1.267)	68	29.72 (3.157)	7.38	60.88 (26.338)
≥ 35 without comorbidities (n=14)	37.55 (1.621)	13	29.86 (3.627)	7.62	61.65 (28.576)
Investigational Site					
HL001 (n=14)	35.42 (2.543)	11	28.12 (2.213)	6.88	66.98 (25.384)
HL002 (n=15)	35.91 (2.597)	15	29.06 (3.289)	6.85	64.50 (28.418)
HL003 (n=30)	34.89 (2.716)	30	29.24 (2.876)	5.65	58.81 (26.409)
HL004 (n=15)	35.31 (2.145)	13	29.44 (3.161)	6.09	56.75 (30.329)
HL005 (n=15)	34.47 (2.969)	15	27.34 (3.614)	7.13	78.85 (34.065)
HL006 (n=30)	36.21 (2.096)	30	28.79 (2.997)	7.42	64.36 (29.420)
HL007 (n=30)	35.16 (2.783)	29	28.96 (3.798)	6.09	65.73 (35.356)

[a] Baseline is defined as screening visit for patients placed on the pre-surgery diet and surgery visit for patients not on the pre-surgery diet.

[b] Month 12 is based on the analysis visit window as defined in SAP. The pre-specified analysis method was without imputation, so this analysis includes the Month 12 Evaluable Population (N=143). There were 6 patients who did not have a Month 12 visit within the analysis window - 4 patients discontinued (were explanted) prior to their Month 12 visit and 2 patients had a Month 12 visit that was outside the analysis window.

Overall conclusions regarding the safety and effectiveness of the LAP-BAND® System for weight reduction in patients with a BMI of ≥ 30 to < 40 kg/m^2 with one or more comorbid conditions:

The data provide reasonable assurance of the safety and effectiveness of the LAP-BAND® System for use in weight reduction for obese patients, when used in accordance with its labeling.

Results from the pivotal U.S. clinical study in obese adults demonstrated:

- The primary effectiveness endpoint was achieved ($p < 0.0001$); 80.5% of all patients implanted with the LAP-BAND® System lost at least 30% of their excess weight. One hundred and twenty (120) patients implanted with the LAP-BAND® System met the primary effectiveness endpoint.
- For all 149 patients implanted with the LAP-BAND® System, 98 patients (66%) lost at least 50% of their excess weight, 62 patients (42%) lost at least 70% of their excess weight, and 29 patients (19%) lost at least 90% of their excess weight.
- The proportion of patients who were obese ($\geq$ 30 kg/m^2) decreased from 99.3% at baseline to 36.9% at 12 months. At baseline there were 85 patients (57%) with a BMI between 35 and 40 kg/m^{2}and at 12 months the number of patients had decreased to six (6) (4%). At baseline there were 63 patients (42.3%) with a BMI between 30 and 35 kg/m^2 and at 12 months the number of patients had decreased to 49 (32.9%). At 12 months there were 75 patients (50%) who had a BMI between 25 and 30 kg/m^2, and 19 patients (12.8%) with a BMI less than 25 kg/m^2.
- Mean percent EWL at 12 months for patients with a BMI <40 kg/m^2 was greater than weight loss previously reported for patients with a BMI >40 kg/m^2 (from the device labeling) (64.5% vs. 34.5%, respectively); however, patients in the lower BMI group have to lose less weight to obtain the same percentage of excess weight loss. In addition, the lower BMI study was conducted using a BMI of 25kg/m^2 as the ideal weight whereas the study of patients with a BMI >40 kg/m^2 was based on an ideal weight on the mid point of the Metropolitan Life Tables.
- Other weight related endpoints also showed improvement at 12 months:
    - The mean amount of weight loss in the study was 39.7 pounds
    - The percentage of total weight loss was 18.3%
    - The mean percent of excess weight loss was 64.5%
    - BMI decreased from a mean of 35.4 to 28.8, a decrease of 6.4 points from baseline.
    - Waist circumference decreased by a mean of 5.9 inches (41.5 to 35.4)
    - Hip circumference also decreased by a mean of 5.8 inches (47.7 to 41.9)
- In the original clinical study protocol, patients with a BMI of $\geq$30 and <35 kg/m^2 could be enrolled with or without a comorbid condition. Patients with a BMI of $\geq$35 to <40 could also be enrolled with or without a severe comorbid condition. For each comorbid condition evaluated in the study the number of patients with that condition was small. In addition, improvement or resolution of the condition

was evaluated by each investigator, there was no standard criteria used by all investigational sites.

  - Comorbid conditions evaluated as secondary endpoints, Type II diabetes, hypercholesterolemia, and hypertension showed improvement although the number of patients with each of these comorbid conditions was small making it difficult to make any definitive conclusions..
  - Additional comorbidities were also assessed by the investigators for severity at baseline and Month 12. All comorbid conditions demonstrated some improvement or resolution at Month 12.

- Health-related quality of life was significantly improved after implantation with the LAP-BAND® System. The Impact of Weight-related Quality of Life-Lite (IWQOL-Lite) assessment showed significant improvement. The mean IWQOL-Lite score for all patients was 62.8 at baseline, and 90.6 at 12 months. Significant improvements from baseline were seen at Month 12 in other patient reported outcomes including the SF-36, Beck Depression Inventory-II, Three Factor Eating Questionnaire, and Questionnaire on Eating and Weight Patterns – Revised.

- Adverse events related to the device (n=215) were reported to have occurred in 105 patients.
  - The most commonly reported events were vomiting, dysphagia, post procedural pain, and gastroesophageal reflux disease. The majority of device related adverse events resolved in less than a month (145/215, 67.5%), and the most common treatment for a device related adverse event was band adjustment (n=108, 50.2%).
  - Seven patients each required one reoperation, and there were no intraoperative complications. Four of the reoperations were LAP-BAND® System explantations due to dysphagia (in 2 patients), erosion of the band, or abdominal pain. Two reoperations were access port revisions due to port flip or port site pain. One reoperation was for repositioning of the original band to correct for band slippage.
  - There were seven events occurring in three patients that were considered serious adverse events. They were hospitalized for 7 days or less and discharged following band removal. There were no deaths or unanticipated adverse events.

- Risks of the LAP-BAND® include those associated with any surgical operation, including risks of undergoing anesthesia, problems with placement of the band (e.g., bleeding, damage to internal organs, deep vein thrombosis, infection), post-operative complications (e.g., nausea and vomiting, swelling, erosion, pouch dilation), rapid weight loss issues (e.g., nutritional deficiencies, gallstones, bone density decrease), and other discomforts (e.g., blood draws, needle pain during band adjustment, scars).

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

A. Panel Meeting Recommendations

At an advisory meeting held on December 3, 2010, the Gastroenterology and Urology Devices Panel voted 8-2 that there is reasonable assurance the device is safe, 8-1 that there is reasonable assurance that the device is effective, and 8-2 that the benefits of the device do outweigh the risks in patients who meet the criteria specified in the proposed indication.

The panel recommended a Post Approval Study to evaluate the long term safety and effectiveness of the LAP-BAND in this expanded patient population. Because of the low number of males and non-Caucasians in the clinical study, the panel recommended that these demographic groups be evaluated in the post approval study.

The meeting transcript may be accessed at the following webpage:
http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/ucm234224.htm

B. FDA's Post-Panel Action

In the 35 to 40 kg/m^2 patient group enrolled in the clinical study there were only 14 patients who did not have a comorbid condition; however, most of the comorbid conditions present in this patient population were not considered "severe." Since almost all patients had some type of comorbid condition that can be associated with obesity, FDA believes that the Indication for Use should state that all patients in the 30-40 kg/m^2 should have at least one (1) obesity related comorbid condition in order to be eligible for the LAP-BAND® System.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The primary effectiveness endpoint was achieved ($p < 0.0001$); 80.5% of all patients implanted with the LAP-BAND® System lost at least 30% of their excess weight. Implantation with the LAP-BAND® System resulted in statistically significant decreases in all measures of weight loss. Secondary weight related effectiveness endpoints also showed significant decreases: mean weight loss was 39.7 pounds, patients lost a mean18.3% of baseline total weight, 64.5% of excess weight, and BMI declined by 6.5 points. There was some improvement in comorbid conditions, although there were limited numbers of patients with each condition. Patient reported outcomes (IWQOL-Lite, SF 36, Beck Depression Inventory-II, Three Factor Eating Questionnaire, and Questionnaire on Eating and Weight Patterns – Revised) also showed improvement.

B. Safety Conclusions

The risks of the device are based on data collected in a clinical study conducted to support PMA approval as described above. Although the majority of patients in the clinical study experienced at least one (1) device related adverse event (n=105, 70.5%), adverse events were generally mild, lasted less than a month, and resolved without sequelae. Seven (7) serious device related adverse events occurred in three patients (3/149, 2%). Seven (7) patients each required one (1) reoperation; four (4) were explants without replacement, two (2) were access port revisions and one (1) reoperation was a revision to reposition the band. The adverse events seen in this study are expected based on the current device labeling.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The risks seen in this study were similar to that seen in the original study evaluating the use of the LAP-BAND® in patients with a BMI of at least 40 kg/m^2. Most patients (68%) lost a substantial amount of weight, at least 50% EWL. The majority of the FDA Advisory Panel and the FDA agree that the data support the expansion of the indication for use of the LAP-BAND® Adjustable Gastric Banding System to include patients with a BMI between 30-40 kg/m^2 who have at least one (1) obesity related comorbid condition. The sponsor will continue to evaluate the safety and effectiveness of the LAP-BAND® in two (2) Post Approval Studies.

XIII. CDRH DECISION

CDRH issued an approval order on February 16, 2011. The final conditions of approval are described below and include an agreement from Allergan to conduct two (2) post-approval studies that will evaluate the long-term effectiveness of the device and the incidence of adverse events. The first study will continue to follow patients enrolled in the investigational device exemption (IDE) pivotal study. The second study will enroll new patients from the Bariatric Outcomes Longitudinal Database (BOLD) registry database.

1. Study LBMI-002: This study will be a multi-center, single arm, prospective, longitudinal study designed to gather data on the explant rate, adverse event rates, and successful weight loss. This study will continue to follow the 149 patients who were implanted during the investigational device exemption (IDE) pivotal study for five (5) years post LAP-BAND® implantation. At five (5) years, at least 112 patients will be included in the follow-up. The null hypotheses are: 1) the 5-year explant rate is not higher than 18% with a 14.5% superiority margin; 2) the 5-year successful weight loss (defined as 30% excess weight loss (EWL)) will be noted in at least 60% of patients; and 3) data to be collected will include a yearly

X-ray examination with barium swallow, hemoglobin A1c and lipid profile, in addition to all the data points in the pivotal study.

2. Study BOLD-001: This will be an observational, prospective, longitudinal study using the BOLD registry. The objective of this post-approval study is to evaluate the safety and effectiveness of the LAP-BAND® System in an obese population with a body mass index (BMI) of $\geq 30 kg/m^2$ and $< 40 kg/m^2$ and one or more obesity related comorbidities. Specifically, the study will assess long-term improvement in obesity-related comorbid conditions and percent excess weight loss. Other objectives are to evaluate safety (explant rate and other adverse events) by age, gender, and race/ethnicity. The study duration will be 10 years. The null hypotheses are: 1) the explant incidence rate at five (5) years is less than 6.5 per 100 person years; 2) the 5-year successful weight loss (defined as >30% EWL) will be noted in at least 60% of patients; 3) the 10-year successful weight loss (defined as >30% EWL) will be noted in at least 50% of patients; and 4) there will be a significant decrease in the leading comorbidity factors of diabetes, hyperlipidemia and hypertension. A sample size of at least 845 patients will provide five (5) year data and 90% power to detect a decrease of five (5) percentage points in the prevalence of diabetes (i.e., from a baseline rate of 30% to a follow-up rate of 25%). A sample of 845 patients would also provide sufficient information to analyze more than 80 variables that may predict or confound outcomes, or to identify potential subgroup differences.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-Approval Requirements and Restrictions: See approval order.

XV. REFERENCES

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