SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Intragastric Balloon

Device Trade Name: Obalon Balloon System

Device Procode: LTI

Applicant's Name and Address: Obalon Therapeutics, Inc.
5421 Avenida Encinas, Suite F
Carlsbad, CA 92008

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160001

Date of FDA Notice of Approval: September 8, 2016

II. INDICATIONS FOR USE

The Obalon Balloon System (the "System") is a swallowable intragastric balloon system indicated for temporary use to facilitate weight loss in adults with obesity (BMI of 30 – 40 kg/m^2) who have failed to lose weight through diet and exercise. The System is intended to be used as an adjunct to a moderate intensity diet and behavior modification program. All balloons must be removed 6 months after the first balloon is placed.

III. CONTRAINDICATIONS

- Anatomical abnormalities or functional disorders that may inhibit swallowing or passage through any portion of the entire Gastrointestinal (GI) Tract.
- Prior surgeries that may have resulted in intestinal adhesions, narrowing of any portion of the digestive tract or any other condition that may inhibit passage through any portion of the GI tract.
- Persons whom have undergone any bariatric surgery procedure.
- Inflammatory and other pathophysiological conditions of the GI tract.
- Chronic or acute use of medications known to be gastric irritants or to otherwise alter function or integrity of any portion of the GI tract, including but not limited to NSAIDs and aspirin.
- Untreated *Helicobacter pylori* infection.
- Patients who are unable or unwilling to take prescribed proton pump inhibitor medication for the duration of the device implant.
- Allergies to products/foods of porcine origin.
- Patients diagnosed with bulimia, binge eating, compulsive overeating, high liquid calorie intake habits or similar eating related psychological disorders.

- Patients with known history of structural or functional disorders of the stomach including, gastroparesis, gastric ulcer, chronic gastritis, gastric varices, hiatal hernia (> 2 cm), cancer or any other disorder of the stomach.
- Patients requiring the use of anti-platelet drugs or other agents affecting the normal clotting of blood.
- Pregnant or lactating women, or women with an intention to become pregnant.
- Known history of duodenal ulcer, intestinal diverticula (diverticulitis), intestinal varices, intestinal stricture/stenosis, small bowel obstruction, or any other obstructive disorder of the gastrointestinal tract.
- Known history of irritable bowel syndrome, radiation enteritis, or other inflammatory bowel disease, such as Crohn's disease.
- Patients taking medications on specified hourly intervals that may be affected by changes in gastric emptying, such as anti-seizure or anti-arrhythmic medications.
- Alcoholism or drug addiction.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Obalon Balloon System labeling.

V. DEVICE DESCRIPTION

The Obalon Balloon System is a temporary implant intended to facilitate weight loss by occupying space in the stomach. The Obalon Balloon System is delivered by the patient swallowing a capsule attached to a thin inflation catheter. Once the capsule dissolves and the balloon location in the stomach is confirmed with radiography, the balloon is filled with a gas mixture via the attached inflation catheter. During the 6-month treatment period, a total of three (3) 250 mL balloons can be placed into the patient's stomach. At the conclusion of treatment, the Obalon balloons are removed using commercially available endoscopic tools defined in the Obalon Balloon System's labeling. An illustration of the Obalon Balloon System is provided in Figure 1.

	
Balloon Kit- Swallowable Capsule with Balloon and Catheter	Accessory Kit – Extension Tube and Ejection Syringe

<table>
<tr><td>  </td><td>  </td></tr>
<tr><td>Inflation System (EzFill Dispenser and EzFill Can) connected to an Extension Tube</td><td>Inflated Balloon</td></tr>
<tr><td colspan="2">  </td></tr>
<tr><td colspan="2">Practice Capsule (Sugar-Filled Gelatin Capsule)</td></tr>
</table>

Figure 1. Obalon Balloon System

A. Device Components

The Obalon Balloon System consists of the following components, which are packaged and supplied as individual models with separate labeling and instructions for use:

- Obalon Balloon Kit (consisting of the Obalon Balloon and Inflation Catheter)
- Obalon Accessory Kit (consisting of the extension tube and two (2) 3 mL syringes)
- Obalon EzFill Inflation System (consisting of the EzFill Dispenser and EzFill Can)
- Obalon Placebo Capsule

Obalon Balloon Assembly

The Obalon balloon is a thermoformed spheroid designed to occupy 250 mL when inflated. The balloon is manufactured using a composite of nylon and polyethylene. The balloon has a self-sealing valve made from titanium and silicone that is used to inflate the balloon during the administration procedure. The self-sealing valve is designed to allow for the balloon to be released from the Inflation Catheter after balloon inflation without introducing liquid. The balloon is pre-folded into a USP-grade porcine gelatin capsule. The capsule has a hydrophilic coating that is intended to enhance swallow characteristics. The capsule is approximately 1.32” long and 0.599” in diameter. The balloon is provided non-sterile and is pre-loaded onto the Inflation Catheter.

Obalon Inflation Catheter

The Inflation Catheter is intended to connect the balloon with the Extension Tube. The 30” long catheter is hydrophilically coated Pebax. There is also a stainless steel needle inside the distal end used to inflate the balloon. There is a luer connector at the proximal end to connect to the Extension Tube. There is a monofilament throughout the length of

the Inflation Catheter to provide structural strength, and strain reliefs that are designed to reduce kinking. The Inflation Catheter comes pre-attached to the balloon and is provided non-sterile. The Inflation Catheter is long enough that patients can swallow the capsule and provide physicians with enough room to use the inflation system.

Obalon Accessory Kit

The accessory kit consists of the Extension Tube and two (2) syringes. The Extension Tube is the connection between the Inflation Catheter and the EzFill Dispenser. The Extension Tube is intended to allow positioning of the EzFill Dispenser away from the patient's face. The Extension Tube has a 3-way stopcock. One position of the stopcock is used to deliver gas to the balloon. After gas delivery, the stopcock position is changed to the water-filled syringe. Depressing the syringe provides the hydraulic pressure necessary to release the balloon from the inflation catheter.

Obalon EzFill Inflation System

The EzFill Inflation System consists of the EzFill Dispenser and the EzFill Can. The Dispenser connects the proximal end of the Extension Tube to deliver gas to the balloon. The Dispenser is designed to engage the valve stem of the EzFill Can and seal the gas path. The Dispenser has a battery operated pressure gauge and regulator to display and control the gas pressure. Since balloon inflation is sensitive to elevation changes, each Dispenser is labeled for a specific location.

The Can is designed to fit snugly into the Dispenser's shuttle and depress the valve stem to deliver the correct amount of gas. The EzFill Can is an approximately 150 mL aluminum can filled with a mixture of nitrogen (N_2) and sulfur hexafluoride (SF_6). The EzFill Can is designed to provide a fixed volume of inflation gas to the balloon. The Can is for single use only.

Obalon Placebo Capsule

The Obalon placebo capsule is the same material, size, shape, and weight as the actual balloon capsule. However, it does not contain the balloon and is not attached to the Inflation Catheter. The placebo is used to help identify patients who will not be able to swallow the actual device without exposing them to the device and procedural risks. The placebo capsule is filled with food-grade table sugar.

B. Additional Components and Adjunct Devices

Other Obalon Balloon System components not supplied by Obalon Therapeutics, but used during the balloon administration and removal procedures include:

Radiography equipment

Fluoroscopy or digital x-ray is required during the balloon placement procedure to verify successful placement in the stomach prior to balloon inflation. Film x-rays are not acceptable because immediate verification prior to balloon inflation is required during the administration procedure.

Endoscope and Endoscope Injection Needle
An endoscope and endoscopic injector needle are necessary for the removal procedure. A 23 G x 6 mm or similar injector needle in a Teflon sleeve compatible with the endoscopic working channel is used for the balloon removal procedure.

Vacuum aspiration source
A vacuum is used to aspirate the gas once the balloon has been punctured during the removal procedure.

Endoscopic Rat Tooth Grasping Forceps with Alligator Jaws
Rat tooth grasping forceps with alligator jaws and a minimum opening width of 15 mm are necessary to retrieve the deflated balloon.

60 mL syringe
A syringe is necessary either for suction or to aspirate the balloon gas.

C. Principle of Operation

The Obalon Balloon System occupies space in the stomach for up to 6 months. Up to three (3) balloons are intended to be placed in the stomach within the first three (3) months of the 6 month treatment period. Each balloon is placed by a physician in an outpatient setting without anesthesia or endoscopy. The facility should have access to radiography equipment to confirm placement and access to endoscopic services in the event it is required.

The capsule is swallowed by the patient and begins to dissolve after exposure to water and fluids in the stomach. After radiographic verification that the capsule is in the stomach, a small pre-pulse of gas is delivered to ensure that the balloon is in the stomach. The physician then verifies successful placement using digital x-ray or fluoroscopy. Once placement is confirmed, the physician opens the valve on the Inflation System to inflate the balloon. The balloon inflation stops when the balloon and the EzFill Can reach equilibrium, and then the valve is closed. After gas delivery, the stopcock position is changed. A small amount of water provides the hydraulic pressure necessary to release the balloon from the inflation catheter. The inflated balloon is approximately 250 mL when pressurized to between 9-13 kPa (1.3-1.9 psi). The total volume of three (3) balloons placed in the stomach is 750 mL. The balloon implant procedure is shown in Figure 2.

The balloons are designed to act as a bezoar that can move freely within the stomach to occupy space. The balloon volume is intended to be sufficient to prevent passage through the pyloric sphincter. After the 6 month treatment, the physician uses an endoscopic procedure and tools present in an endoscopy suite to puncture, aspirate the gas, and remove the balloons from inside the patient.

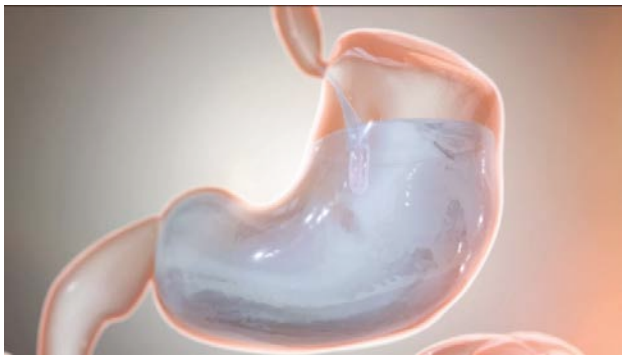
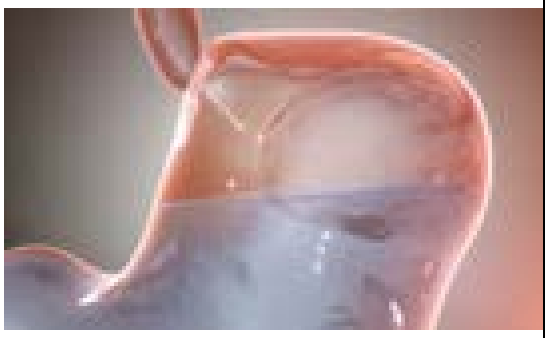
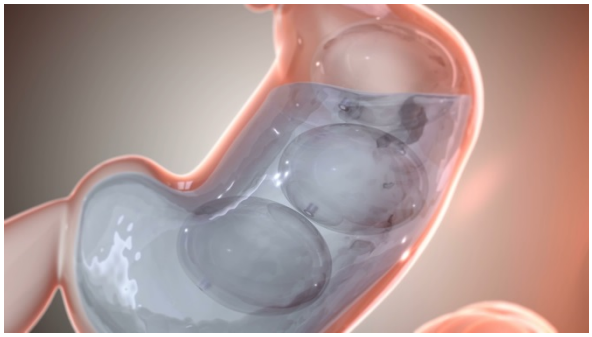
	
Swallowable Balloon Capsule	Verification of Capsule in the stomach
	
Inflated Balloon	Three (3) Balloons in the stomach with Radiopaque markers

Figure 2. Obalon Balloon System Implant Procedure

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for the treatment of obesity (BMI of > 30 kg/m^2), which can be divided into five (5) categories: non-surgical treatments, gastric banding, vagal blocking therapy, gastric emptying therapy, and obesity surgery. Some weight regain may occur with any weight reducing intervention. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with their physician to select the method that best meets expectations and lifestyle.

A. Non-Surgical Treatments

Non-surgical treatments for obesity include:

- Diet, exercise, and behavioral modifications, and
- Prescription weight loss medications.

B. Gastric Banding

Laparoscopic gastric banding is indicated for patients with a 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, who have failed more conservative weight reduction alternatives.

C. Vagal Blocking Therapy

Laparoscopic vagal blocking therapy is indicated for use in weight reduction in patients aged 18 years through adulthood who have a BMI of 40 to 45 kg/m^2, or a BMI of 35 to 39.9 kg/m^2 with one or more obesity related co-morbid conditions, and have failed at least one supervised weight management program within the past 5 years.

D. Gastric Emptying Therapy

Gastric emptying therapy is indicated for weight reduction in patients aged 22 years or older with a BMI of 35-55 kg/m^2 who have failed to achieve and maintain weight loss with non-surgical weight loss therapy.

E. Obesity Surgery

Bariatric surgery is typically recommended for patients with a BMI of at least 40 kg/m^2, or a BMI of at least 35 kg/m^2 with one or more obesity-related comorbid conditions. The most common types of bariatric surgery are described below.

Roux-en-Y Gastric Bypass
This procedure is 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 a gastric bypass, the surgeon first 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
Vertical sleeve gastrectomy is a restrictive 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
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.

VII. MARKETING HISTORY

The 6 month Obalon Balloon System has been approved in the European Union, Kuwait, and the United Arab Emirates.

The device has not been withdrawn from any market for any reason relating to the safety or effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Adverse events that may result from the Obalon Balloon System are both those associated with the device specifically and those commonly associated with gastrointestinal endoscopy procedures. Below is a list of the potential adverse effects (e.g. complications) associated with the use of the device.

Potential risks associated with an endoscopic procedure and sedation include abdominal cramps or discomfort, allergic or adverse reaction to sedation or anesthesia, aspiration, cardiac or respiratory arrest, digestive tract injury or perforation, sore or irritated throat, excessive sweating, hypotension, impaired judgment or reactions, and laryngospasm. Potential adverse events for the device include esophageal rupture, bowel obstruction, perforation or rupture of the stomach, gastric ulceration, gastric bleeding, esophageal bleeding, gastric irritation, peptic ulcer disease, allergic reaction, abdominal pain, nausea, vomiting, indigestion, bloating, and diarrhea.

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

The integrity and performance of the Obalon Balloon System was evaluated with the testing summarized in Table 1.

Table 1: Non-Clinical Performance testing

Device Components	Test Description	Acceptance Criteria	Test Result
Obalon Balloon and Inflation Catheter	Balloon material evaluation Test to verify that the balloon film properties are acceptable for use in the gastric environment using the ASTM D638-01 dogbone test after 180 days.	The balloon film's mechanical properties shall not degrade by >30% over a minimum of 180 days.	Pass

Device Components	Test Description	Acceptance Criteria	Test Result
	Bond integrity Tests to verify tensile strength between the components of the balloon and Inflation Catheter.	The balloon shall not have any visible leaks after deployment. All device bonds must meet the following pre-specified minimum tensile strength requirements over the full product shelf life: • Re-sealable valve to film bond: > 5 lbf • Luer adaptor to filament: > 2.5 lbf • Sleeve to filament: > 2.5 lbf • Needle to needle holder: > 1 lbf • All strain reliefs: > 1 lbf	Pass
	Balloon accelerated fatigue testing Test to verify the balloon maintains volume over accelerated fatigue testing to simulate implantation period.	Balloon volume loss must be <15%. The balloon must not develop holes or defects.	Pass
	Balloon long term inflation Test to verify that the balloon maintains volume in simulated gastric space.	The balloon must meet the following pre-specified requirements after six months: • Volume loss: < 15% • Inflation pressure: > 3.5 kPa	Pass
	Balloon bond strength Test to verify that the balloon maintains structural integrity under exaggerated conditions.	Balloon must not have bubble leaks when inflated to 5 psi and placed under water.	Pass

Device Components	Test Description	Acceptance Criteria	Test Result
	Acute deployment Test to verify that the balloon and capsule meet dimensional, gravimetric, and performance specifications before and after simulated deployment.	The device must meet the following dimensional requirements: • Capsule diameter: ≤16 mm • Capsule length: ≤ 35 mm • Balloon kit mass: ≤ 15 g During and after simulated deployment, the device shall meet the following performance requirements: • Capsule separation time: ≤ 8 min after pre-pulse • Inflated balloon volume: 225-305 mL • Initial balloon pressure: 8.3-17.2 kPa • Inflated balloon mass: ≤ 15 g • Hydrogen leak rate: ≤ 10^{-4} mL/s • Catheter shall maintain pressure for 30 s without premature disconnection • Catheter shall not leak when pressurized to 70 psi • Catheter shall not leak or rupture during disconnection and hydraulic ejection	Pass
	Balloon film thickness Test to verify that the balloon thickness meets dimensional specifications after the manufacturing process.	The balloon film must be ≤ 0.006" after manufacturing in three (3) different locations on the balloon.	Pass
	Balloon film puncture resistance Test to verify the puncture force according to ASTM F1306 after 28 days in simulated gastric conditions.	The balloon film must have a <10% decrease in puncture force.	Pass

Device Components	Test Description	Acceptance Criteria	Test Result
	Balloon passability Test to determine whether the balloon could pass through the intestines using a simulated small intestine.	The balloon should pass through the simulated small intestines.	Pass
	Balloon retraction testing Test to verify that the balloon can be successfully retracted from the stomach using commercially available endoscopy tools.	The balloon must be retrievable using commercially available endoscopic tools.	Pass
	Balloon altitude performance Test to verify that the balloon can withstand simulated altitude changes over a seven day period.	The balloon shall meet the following performance requirements: • Balloon volume loss: < 15% • Balloon pressure > 5.5 kPa	Pass
	Changes in atmospheric pressure Test to verify that the balloon volume does not fluctuate in response to atmospheric pressure differences. The balloon was subjected to a simulated 8000 foot elevation gain.	The balloon shall remain within 225-304 mL when exposed to a simulated 8000 foot elevation gain.	Pass
	Inflation Catheter dimensional verification Test to verify that the Inflation Catheter meets its pre-defined dimensional specifications and is kink resistant.	The Inflation Catheter shall not kink when bent over a 5 cm mandrel and meet the following dimensional requirements: • Catheter length: 27-29” • Diameter: < 0.039”	Pass
	Inflation Catheter corrosion resistance Test to verify that the Inflation Catheter meets the corrosion resistance requirements of EN 1618, Annex A.	The Inflation Catheter shall not corrode when tested to the methods of EN 1618, Annex A.	Pass

Device Components	Test Description	Acceptance Criteria	Test Result
	Inflation Catheter pressure test Test to verify that when challenged with pressure, the Inflation Catheter does not leak.	The Inflation Catheter shall meet the following performance requirements: • No bubble leaks when pressurized to 70 psi • No premature disconnection or leaks during inflation or 35 psi challenge	Pass
Accessory Kit	Accessory kit leak test Test to verify that the accessory kit fittings can withstand exaggerated pressure conditions and not leak.	The accessory kit shall not leak when pressurized to 70 psi.	Pass
EzFill Can and Dispenser	EzFill Can verification Test to verify that the EzFill Can meets its design and performance requirements.	The EzFill Can shall meet the following requirements: • Volume: 161 ± 3 mL • Fill pressure: 60 ± 1 psi • No visual leaks via water immersion test • Mass: 1.6882 ± 0.025 g	Pass
	EzFill Dispenser Evaluation for Multiple Altitudes Test to verify that the EzFill Dispenser inflates balloons at the correct pressure over different simulated altitudes.	The EzFill Dispenser shall inflate balloons to 8.3-17.2 kPa for each altitude.	Pass
	Pre-Pulse Verification Test to verify that the pre-pulse verification technique can correctly detect constricted balloon inflation in a simulated esophagus fixture.	The pre-pulse technique shall meet the following requirements: • The dispenser shall read from 1-7 psi if the balloon is constricted • The dispenser shall read < 1 psi if the balloon is not constricted	Pass

Device Components	Test Description	Acceptance Criteria	Test Result
	EzFill Inflation System mechanical characteristics Test to verify that the EzFill Dispenser can successfully interface with the EzFill Can and deliver the correct amount of gas to the Obalon balloon.	The EzFill Inflation System shall meet the following performance requirements: • The Dispenser shall not leak against an ISO-594 reference fitting • Balloon inflation pressure: 13.8 ± 3.45 kPa • The regulator must vent within ± 3.45 kPa of true value • Dispenser depressurization time: < 30 s • Dispenser leakage rate: <0.1 psi over 5 minutes	Pass
	EzFill Dispenser 100,000 cycle test Test to verify that the EzFill dispenser is not adversely affected by fatigue using accelerated cycling.	The Dispenser shall meet the following performance requirements: • Fill balloons to 8.3-17.2 kPa after 5000 actuations • Be wiped every 100 uses without material degradation • Maintain pressure delivery within 3.45 kPa • Maintain pressure gauge accuracy within 0.25%	Pass
	EzFill Dispenser useful life Test to verify the useful life of the EzFill Dispenser	The Dispenser shall meet the following performance requirements: • Hold pressure and function for 5000 cycles • Vent in <30 s • Not leak for > 0.1 psi over 5 minutes • Gauge accuracy of 0.25% after 5000 cycles • Be wiped every 100 uses without material degradation	Pass

B. Animal Studies

The Obalon Balloon was tested in three (3) different animal studies to assess the safety using different prototype versions of the final device design. These studies were not completed in compliance with Good Laboratory Practices (GLP) (21 CFR Part 58).

However, each study was approved by an Institutional Review Board and was performed with veterinary oversight. These studies were designed to evaluate the balloon performance, effect on gastric mucosa, balloon design changes to support continued studies in humans, tolerability, establish device radiopacity, and removal procedures.

These studies were designed to evaluate the device inflation, radiopacity, removal procedure, changes in fill gas mixture, balloon design, chronic effects on gastric mucosa, and overall tolerability. All three (3) animal studies were conducted using the porcine model (n=38 total). Balloon implantation times ranged from 31 days to 10 months in duration. Pigs were evaluated during these studies with in-life clinical observations, periodic endoscopic gastric evaluations, necropsy findings, histological analysis of the gastric wall, and analysis of the balloon materials and inflation.

The results from these studies demonstrate that later prototype balloon versions can be chronically implanted into healthy pigs without any significant morbidity or mortality. Though mucosal irritation was observed, this was likely due to the anatomic limitations of the porcine model. No new clinical risks were identified in these studies. The studies also support that the device can be inflated, removed, and will maintain inflation status using the final device gas mixture for the duration of the 6 month intended use period.

C. Additional Studies

Biocompatibility

The Obalon Balloon Kit, Inflation Catheter, and Delivery Capsule were subjected to biocompatibility testing in accordance with the requirements of ISO 10993-1:2009. All biocompatibility testing was conducted in compliance with GLP (21 CFR Part 58).

The Obalon Balloon Kit is categorized as a surface device that has permanent contact with the mucosal membrane (> 30 days). The results of biocompatibility testing for the Obalon Balloon Kit are summarized in Table 2.

Table 2: Obalon Balloon Kit Biocompatibility Testing

Biocompatibility Test	Acceptance Criteria	Test Results
Cytotoxicity (MEM Elution)	Must meet pre-specified criteria according to ISO 10993-5	Pass
Sensitization (Guinea Pig Maximization Test)	Must meet pre-specified criteria according to ISO 10993-10	Pass
Irritation (Intracutaneous Reactivity)	Must meet pre-specified criteria according to ISO 10993-10	Pass
Acute Systemic Toxicity (Oral Extract)	Must meet pre-specified criteria according to ISO 10993-11	Pass
Subacute Toxicity (14-Day Systemic Toxicity)	Must meet pre-specified criteria according to ISO 10993-11	Pass

Biocompatibility Test	Acceptance Criteria	Test Results
Genotoxicity (Bacterial Reverse Mutation Assay)	Must meet pre-specified criteria according to ISO 10993-3	Pass
Genotoxicity (*In Vitro* Mouse Lymphoma)	Must meet pre-specified criteria according to ISO 10993-3	Pass
Genotoxicity (*In Vivo* Mouse Micronucleus Assay)	Must meet pre-specified criteria according to ISO 10993-3	Pass
Materials Mediated Pyrogenicity (Rabbit Pyrogen)	Must meet pre-specified criteria according to ISO 10993-11	Pass
Muscle Implantation (2, 8, and 13 week with Histopathology)	Must meet pre-specified criteria according to ISO 10993-6	Pass
Establishment of Allowable Limits for Leachable Substances	Must meet pre-specified criteria according to ISO 10993-17	Pass
Chemical Characterization of Materials	Must meet pre-specified criteria according to ISO 10993-18	Pass

A toxicological risk assessment based on the extractable and leachable compounds identified from chemical characterization for the Obalon Balloon was conducted to address chronic systemic toxicity and carcinogenicity concerns. The toxicological risk assessment determined that the amounts of extracted chemical compounds are unlikely to pose significant risk of toxicological concern to patients.

The Obalon Inflation Catheter is categorized as a surface device that has limited exposure with the mucosal membrane (≤ 24 hours). The results of biocompatibility testing for the delivery catheter are summarized in Table 3.

Table 3: Obalon Inflation Catheter Biocompatibility Testing

Biocompatibility Test	Acceptance Criteria	Test Results
Cytotoxicity (MEM Elution)	Must meet pre-specified criteria according to ISO 10993-5	Pass
Sensitization (Guinea Pig Maximization Test)	Must meet pre-specified criteria according to ISO 10993-10	Pass
Irritation (Intracutaneous Reactivity)	Must meet pre-specified criteria according to ISO 10993-10	Pass
Materials Mediated Pyrogenicity (Rabbit Pyrogen)	Must meet pre-specified criteria according to ISO 10993-11	Pass

The Obalon Capsule is categorized as a surface device that has limited exposure with the mucosal membrane (≤ 24 hours). The results of biocompatibility testing for the delivery catheter are summarized in Table 4.

Table 4: Obalon Capsule Biocompatibility Testing

Biocompatibility Test	Acceptance Criteria	Test Results
Cytotoxicity (MEM Elution)	Must meet pre-specified criteria according to ISO 10993-5	Pass
Sensitization (Guinea Pig Maximization Test)	Must meet pre-specified criteria according to ISO 10993-10	Pass
Irritation (Intracutaneous Reactivity)	Must meet pre-specified criteria according to ISO 10993-10	Pass
Acute Systemic Toxicity (Oral Extract)	Must meet pre-specified criteria according to ISO 10993-11	Pass

A toxicological risk assessment based on the gas formulation was conducted to address the toxicity of sulfur hexafluoride and nitrogen gas. Based on a literature review, sulfur hexafluoride has a low order of acute and chronic systemic toxicity. Since nitrogen is present in atmospheric air, there are not any toxicological concerns about its use in the Obalon balloon. The toxicological risk assessment determined that the gases used to inflate the Obalon balloon are unlikely to pose significant risk of toxicological concern to patients.

Cleanliness, Packaging, and Shelf Life

The Obalon Balloon Kit, Accessory Kit, EzFill Can, and EzFill Dispenser are provided clean and non-sterile. The device is manufactured in an ISO Class 8 environment. The manufacturing environment is routinely monitored for bioburden levels. The bioburden method was validated and testing was completed in conformance with ISO 11737-1:2006. Appropriate alert and action limits were set to test for microorganisms during bioburden monitoring.

The Obalon Balloon, Inflation Catheter, and EzFill Can are intended for single use. The EzFill Dispenser is a reusable component. The Balloon Kit is supplied sealed in a foil package. The Accessory Kit is placed on a plastic card and sealed inside a Tyvek pouch. The Practice Capsules are packaged in foil pouches. The EzFill Can is provided in a small chipboard box. The EzFill Dispenser is individually packaged in a hard plastic case with a foam insert.

Packaging validation was performed on each component of the Obalon Balloon System. The Obalon Balloon Kit, Accessory Kit, and EzFill Can were subjected to accelerated aging for 12 months in accordance with ASTM F1980:2007 (R2011). The EzFill Dispenser was subjected to accelerated aging for a 24-month period. Real-time aging for all components was also included to support shelf life. The Balloon Kit and Accessory Kits were subjected to simulated shipping and distribution (preconditioning, drop, compression, and vibration). Package integrity was validated in accordance with ASTM D3078-02:2013, ASTM F2096-1:2011, and ASTM F88/F88M:2009. The EzFill Can and Dispenser were subjected to simulated shipping and distribution (manual handling, vehicle stacking, vibration, low

pressure hazard, and impact). The devices were also evaluated to determine whether device functionality was maintained. The shelf life and packaging testing demonstrated that the packaging protects the Obalon Balloon Kit, Accessory Kit, and EzFill Can over a 12-month shelf life (24 months for the EzFill Dispenser).

Magnetic Resonance (MR) Imaging Compatibility

Non-clinical testing of the Obalon Balloon in 3-Tesla magnetic fields demonstrated that the implanted balloon is MR Conditional. The Obalon Balloon can be scanned safely under the following conditions:

- Static magnetic field of 3-Tesla or less
- Maximum spatial field gradient of 4,000-guass/cm (40-T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 4-W/kg (First Level Controlled Operating Mode)

Under the scan conditions defined above, the Obalon Balloon is expected to produce a maximum temperature rise of less than 3 °C after 15-minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends approximately 5 mm from the Obalon Balloon when imaged with a gradient echo pulse sequence and a 3-Tesla MRI system.

The Obalon Inflation System (EzFill Can and EzFill Dispenser) are MR Unsafe and are known to pose hazards in all MR imaging environments.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

Clinical data supporting the safety and effectiveness of the Obalon Balloon System are available from three (3) clinical studies conducted under IDE G120083. Obalon conducted two (2) feasibility studies using previous versions of the device. The first two (2) feasibility studies investigated a 3 month balloon treatment period.

The data obtained from the pivotal 6-month "Six Month Adjunctive Weight Reduction Therapy" (SMART) study constitutes the main dataset to establish a reasonable assurance of safety and effectiveness of the Obalon Balloon System. A summary of the studies is presented below.

Feasibility Clinical Study 1

This feasibility study was a prospective, single-arm, two-center study on 41 patients with a BMI from 30-35 kg/m^2. Subjects underwent a 3-month treatment period followed by a 3-month follow-up period after device removal. Subjects were on a diet and exercise program for the entire 6 months. Thirty-two (32) subjects completed enrollment activities and attempted to swallow at least one device. There were no unanticipated adverse device effects (UADEs) or serious adverse device effects (SADEs) reported in this study. 87.5% of subjects reported adverse device effects (ADEs), which primarily consisted of stomach cramps, nausea, heartburn/reflux, stomach pain, sore throat, and

fullness/bloating. One patient during this study experienced gastroenteritis as a Serious Adverse Event (SAE), which occurred after the balloon therapy period. At 3 months, subjects experienced a mean percent excess weight loss (% EWL) of 16 ± 15.7%. Nine (9) of the 32 subjects met or exceeded the responder analysis at 5% total body loss (%TBL).

Feasibility Clinical Study 2

This feasibility study was a prospective, randomized, blinded, sham-controlled clinical study that took place at one clinical site. Fifty-two (52) subjects were enrolled and 23 were randomized to the Treatment (11) or Control (12) Groups. Subjects underwent a 3-month treatment period followed by a 3-month follow-up period after device removal. The Control Group obtained a sham capsule device without a balloon. Both Treatment and Control Groups were on a diet and exercise program for the entire 6 months. The co-primary effectiveness endpoints were the mean difference in %TBL and a 50% responder rate at a 5 %TBL performance goal. The study was not prospectively powered for these endpoints. Weight loss for the Treatment and Control Groups were 4.21 and 2.97 %TBL, respectively. The difference was not statistically significant at a 95% confidence level. 30% of subjects met the 5 %TBL responder rate. There were no balloon deflation, SAEs, SADEs, or UADEs reported in this study. The most common ADEs were abdominal cramping and nausea.

Pivotal Clinical Study

A. Study Design

The SMART study was a prospective, sham-controlled, double-blinded, randomized, multicenter clinical study. Patients in the SMART study were treated between March 2015 and May 2016. A total of 711 subjects were screened at 15 investigational sites in the United States. Screened subjects who met the inclusion and exclusion criteria were randomized in a 1:1 ratio to the Treatment (use of the Obalon Balloon System and a moderate intensity diet and exercise program) or the Control Group (sham Capsule device without a balloon and a moderate intensity diet and exercise program). The weight loss behavior modification program was designed for the SMART Trial prior to any subject enrollments. The program is a moderate intensity program and was developed in accordance with AHA/ACC/TOS 2013 Guidelines for the Management of Overweight and Obesity in Adults.[1]

A total of 430 subjects were randomized to receive the 6-month Obalon Balloon System or the sham device. Among the randomized subjects, 387 were treated with the Obalon Balloon (198) or sham device (189). Following the 24 week primary effectiveness endpoint assessments, the study blind was broken. Treatment Group subjects underwent endoscopic retrieval of the Obalon Balloon at Week 24, and were seen every 3 weeks by a registered dietician for an additional 24 weeks, for a total follow-up of 48 weeks (17 visits over 48 weeks). Control Group subjects who remained eligible were permitted to crossover and receive the Obalon Balloon System over Weeks 24-48 with diet and exercise counseling for an additional 24 weeks, for a total follow-up of 48 weeks. Control Group subjects who were

ineligible or who declined Obalon balloon treatment were exited from the study after Week 24. After 24 weeks of implantation, the Obalon Balloon was retrieved at Week 48 from the crossover Control Group. These subjects were then exited from the study. Additional safety information on the Control Group who elected to crossover to the balloon therapy was also collected.

The SMART study was a randomized 24 week comparison of treatment and control conditions, comparing the mean %TBL to the sham Control Group. The Treatment Group responder rate dichotomized at 5 %TBL was also assessed. Weight maintenance during the 6 months after device removal was evaluated for treated subjects who lost weight while the device was implanted.

The analyses for effectiveness were based on a comparison of subjects who successfully swallowed at least one balloon or sham device in either the Treatment or Control Group and were followed during Weeks 0 – 24 of their follow-up (Modified Intent-to-Treat or mITT cohort). An additional analysis for effectiveness is based on a comparison of subjects who received at least two (2) devices and participated in at least 18 weeks of use in either the Treatment or Control Group and were followed during Weeks 0 – 24 of their follow-up (Per Protocol or PP cohort). Treatment Group subjects who lost weight during Weeks 0 – 24 were also followed from Weeks 24 – 48 for weight loss maintenance assessments. The analysis for safety was based on all patients who received at least one balloon in the Treatment Group and the Control Group subjects who crossed over at Week 24, which is referred to as the Safety Population.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the SMART study was limited to patients who met the following inclusion criteria:

1. Male or female between the ages of 22-64 years
2. Current BMI of 30.0 – 40 kg/m^2
3. Previously attempted to lose weight unsuccessfully using a medically supervised or non-medically supervised diet
4. Willing to attend all protocol-specified follow-up visits plus any additional follow-up visits as required throughout the entire study period
5. Willing to avoid non-commercial air travel and scuba diving during the entire study period
6. Willing to avoid medications or other substances known to effect weight changes during the study
7. Willing to avoid Non-Steroidal Anti-inflammatory Drugs (NSAIDs), including Aspirin, Diclofenac, Ibuprofen, Naproxen, or other medications known to be gastric irritants during the study
8. Willing to use contraception (specifically a barrier method, surgical method, pharmacological or abstention method) and avoid pregnancy during the study if the subject is female with child bearing potential

9. Willing to provide written informed consent using the respective site's IRB approved consent form after being informed of the nature of the trial.

Patients were not permitted to enroll in the SMART study if they met any of the following exclusion criteria:

1. Significant weight loss in the past 12 months, defined as greater than or equal to 5% Total Body Loss
2. Use of medications or other substances known to induce weight gain or weight loss within the past 6 months
3. Participation in any clinical study (weight-loss or non-weight loss study) at the start of this trial or in the last year
4. Known history of endocrine disorders affecting weight, such as uncontrolled abnormal thyroid function, hypothalamic tumors, Cushing's syndrome, or other genetic syndromes
5. Currently receiving chronic steroid or immunosuppressive therapy or has previously been diagnosed with HIV
6. Subjects diagnosed with bulimia, binge eating, compulsive overeating, high liquid calorie intake habits, or similar eating related psychological disorders
7. Intent to undergo gastric surgery or gastric banding during the study period or within the 6 month period after completion of this study
8. Prior use of any weight loss medical device
9. Known history of structural or functional disorders of the esophagus that may impede passage of the device through the gastrointestinal tract or increase risk of esophageal damage during an endoscopic removal procedure, including, Barrett's esophagus, esophagitis, dysphagia, achalasia, stricture/stenosis, esophageal varices, esophageal diverticula, esophageal perforation, or any other disorder of the esophagus
10. Known history of structural or functional disorder of the esophagus, including any swallowing disorder, esophageal chest pain disorders, or drug refractory esophageal reflux symptoms
11. Known history of structural or functional disorders of the stomach including, gastroparesis, gastric ulcer, chronic gastritis, gastric varices, hiatal hernia (> 2 cm), cancer or any other disorder of the stomach
12. Known history of a structural or functional disorder of the stomach, including any symptoms of chronic upper abdominal pain, chronic nausea, chronic vomiting, chronic dyspepsia or symptoms suggestive of gastroparesis, including post-prandial fullness or pain, post-prandial nausea or vomiting or early satiety
13. Known history of duodenal ulcer, intestinal diverticula (diverticulitis), intestinal varices, intestinal stricture/stenosis, small bowel obstruction, or any other obstructive disorder of the gastrointestinal (GI) tract
14. Currently have ongoing symptoms suggestive of intermittent small bowel obstruction, such as recurrent bouts of post-prandial abdominal pain, nausea or vomiting

15. Known history irritable bowel syndrome, radiation enteritis or other inflammatory bowel disease, such as Crohn's disease
16. Known history of GI surgeries that may have resulted in anatomical GI tract abnormalities such as a stoma or narrowing of any portion of the digestive tract. Examples of these GI surgeries include, but are not limited to, gastric banding; however, uncomplicated appendectomies are acceptable. In addition, known history of any surgeries that may have resulted in anatomical GI tract abnormalities such intestinal adhesions, or any other condition that may inhibit passage through any portion of the GI tract must be excluded.
17. Type 1 diabetes
18. Type 2 diabetes requiring insulin or other hypoglycemic oral agents.
19. Experienced a myocardial infarction, has a known history of angina, a known history of congestive heart failure, or is currently being medically treated for any other cardiac condition
20. Poorly controlled hypertension, (≥ 160 mmHg Systolic and ≥ 100mmHg Diastolic).
21. End stage renal disease or requiring hemodialysis within the past 6 months
22. Unwilling or unable to avoid NSAIDs, including Aspirin, Diclofenac, Ibuprofen, Naproxen, or other medications known to be gastric irritants beginning two weeks prior to enrollment and throughout the entire study period
23. Subjects taking medications on specified hourly intervals that may be affected by changes to gastric emptying, such as anti-seizure or anti-arrhythmic medications
24. Subjects requiring the use of anti-platelet drugs or other agents affecting the normal clotting of blood
25. Untreated or unstable alcohol or illicit drug addiction
26. Known history of allergies to any component of the device materials, including but not limited to allergies to porcine proteins
27. Currently pregnant or breastfeeding or intention of becoming pregnant during the study
28. Life expectancy less than 1 year or severe renal, hepatic, pulmonary or other medical condition, in the opinion of the investigator
29. Subject is employed by the investigator, or is a close relative of the investigator, or the investigator's staff
30. Subject is a close relative of another subject already enrolled in the study.
31. Any other condition that, in the opinion of the investigator, would interfere with subject participation, may confound the study results, or interfere with compliance with the study (e.g., psychosocial issues).

2. Follow-up Schedule

Before screening, all study subjects were asked to sign informed consent. All study subjects were then screened over two visits, which are summarized in Table 5.

Table 5. Screening Period Activities After Informed Consent (Day -14 to Day 0)

Screening Visit #1 Activities	Screening Visit #2 Activities
• Inclusion & Exclusion Criteria • Demographics (Age, Gender, Race & Ethnicity) • Physical Characteristics (Weight, Height, & Waist) • Vital Signs (Blood Pressure, Pulse, & Temperature) • Placebo Capsule Test • Beck Depression Index (BDI) – II Questionnaire • Questionnaire on Eating and Weight Pattern – Revised (QEWP– R) • Pregnancy Test (Child Bearing Female Subjects) • Blood Lab Test (HbA1C, TSH, T3, Metabolic Panel, CBC, & Lipid Panel) • *H. Pylori* Breath Test	• Weight • Overall Readiness Assessment • ECG Assessment • Upper GI Assessment

After screening, randomization, and device administration on Day 0, follow-up visits occurred approximately every 3 weeks for both the Treatment and Control Groups. Table 6 and Table 7 summarize the scheduled visits and patient assessments for the Treatment and Control Groups, respectively.

Table 6. Schedule of Visits and Procedures – Treatment Subjects, Weeks 0 – 48

Visit	Weeks 0, 3, 9, & 12 ±3 days	Week 6 ±3 days	Weeks 15,18 & 21 ±3 days	Week 24 ±3 days	Every 3 Weeks 27-45 ±3 days	Week 48 ±3 days
Weight	x	x	x	x	x	x
Weight loss and behavior modification (WLBM) session[1]	x	x	x	x	x	x
Balloon administration[2, 3, 4]	x					
Dispense medication	x					
Radiographic imaging	x					
24 hour post procedure call[5]	x					
Vital signs[6]	x			x		
Endoscopic removal				x		
Waist				x		x
Blood lab tests[7]				x		x
Pregnancy test[8]	x			x		

[1]WLBM session must occur within 5 days of device administration procedures.
[2]Second balloon administered at Week 3 unless ongoing AE may be worsened.
[3]Third balloon administered at Week 9 if subject has gained weight since the last visit and reports a change in fullness and no ongoing AE may be worsened.
[4]Third balloon administered at Week 12 unless ongoing AE may be worsened (only for patients who do not have three balloons).
[5]Required after successful device administration.
[6]Vital signs: blood pressure, pulse, and temperature.
[7]Blood lab tests: HbA1C, TSH, T3, Metabolic Panel, CBC, & Lipid Panel.
[8]Pregancy test: women of child-bearing potential only

Table 7. Schedule of Visits and Procedures – Control Subjects, Weeks 0 – 48

Visit	Weeks 0, 3, 9, & 12 ± 3 days	Week 6 ± 3 days	Weeks 15,18 & 21 ± 3 days	Weeks 24, 27, and 36 ± 3 days	Weeks 30 & 33 ± 3 days	Weeks 39,42 &45 ± 3 days	Week 48 ± 3 days
Weight	x	x	x	x	x	x	x
WLBM session[1]	x	x	x	x	x	x	x
Device administration (sham)[2, 3, 4]	x						
Device administration (treatment)[5, 6]				x			
Dispense medication	x			x			
Radiographic imaging	x			x			
24 hour post procedure call[7]	x			x			
Vital signs[8]	x			x			x
Endoscopic removal							x
Waist				x			x
Blood lab test[9]				x			x
Pregnancy test[10]	x			x			x

[1]WLBM session must occur within 5 days of sham/device administration procedures.
[2]Second sham device administered at Week 3 unless ongoing AE may be worsened.
[3]Third sham device administered at Week 9 if subject has gained weight since the last visit and reports a change in fullness and no ongoing AE may be worsened.
[4]Third sham device administered at Week 12 unless ongoing AE may be worsened (only for patients who do not have sham devices).
[5] First, second, and third treatment devices (balloons) administered at Weeks 24 and 27 unless subject reports a change in fullness, has not lost or gained weight since the last visit, and no ongoing AE may be worsened.
[6]Third treatment device (balloon) administered at Week 36 unless ongoing AE may be worsened.
[7]Required after successful device administration (sham and treatment).
[8]Vital signs: blood pressure, pulse, and temperature.
[9]Blood lab tests: HbA1C, TSH, T3, Metabolic Panel, CBC, & Lipid Panel.
[10]Pregancy test: women of child-bearing potential only.

3. Clinical Endpoints

With regards to effectiveness, the SMART Pivotal Trial had two (2) co-primary effectiveness endpoints:

- An inferential test of whether the difference in the mean %TBL between the Treatment and Control Group at 24 weeks is significantly greater than 2.1%, and;
- An inferential test of whether the Treatment Group Responder Rate dichotomized at 5 %TBL ($\text{RESPONDER}_{5\%\text{TBL}}$) at 24 weeks is significantly greater than 35%.

There were no formal secondary effectiveness endpoints for the SMART Pivotal Trial. The observational analyses included percent excess weight loss (%EWL), BMI reduction, weight loss (lbs), changes in blood pressure and metabolic blood measurements, and waist circumference after 24 weeks. Each subject was also assessed for weight loss maintenance, changes in blood pressure and metabolic blood measurements, and changes in waist circumference at 48 weeks.

With regards to safety, a review was completed of reported adverse events and serious adverse events, as well as device and procedure-relatedness of adverse events. There were no pre-specified safety endpoints for the SMART Pivotal Study.

B. Accountability of PMA Cohort

Seven hundred and eleven (711) subjects were consented and formally screened for the SMART Pivotal Trial. A total of 281 subjects did not meet the inclusion and exclusion criteria. The remaining 430 subjects were randomized 1:1, 11 of whom exited prior to a device placement day. A total of 419 subjects attempted at least one balloon swallow (216 Treatment and 203 Control). A total of 198 Treatment and 189 Control subjects successfully swallowed one balloon. At Week 24,182 Treatment and 179 Control subjects remained in the study. Of these subjects, 12 Treatment withdrew and 40 Control subjects either withdrew or were ineligible for crossover. Of the 139 Control subjects in the study at Week 24, one of them failed to successfully swallow the balloon. Therefore, 170 Treatment and 138 Control subjects continued into the second phase of the study. Ten (10) subjects each from both the Treatment and Control arms did not finish Week 48. At Week 48, 160 Treatment and 128 Control subjects remained in the study and recorded a weight at Week 48. A subject accountability flowchart is shown in Figure 3.

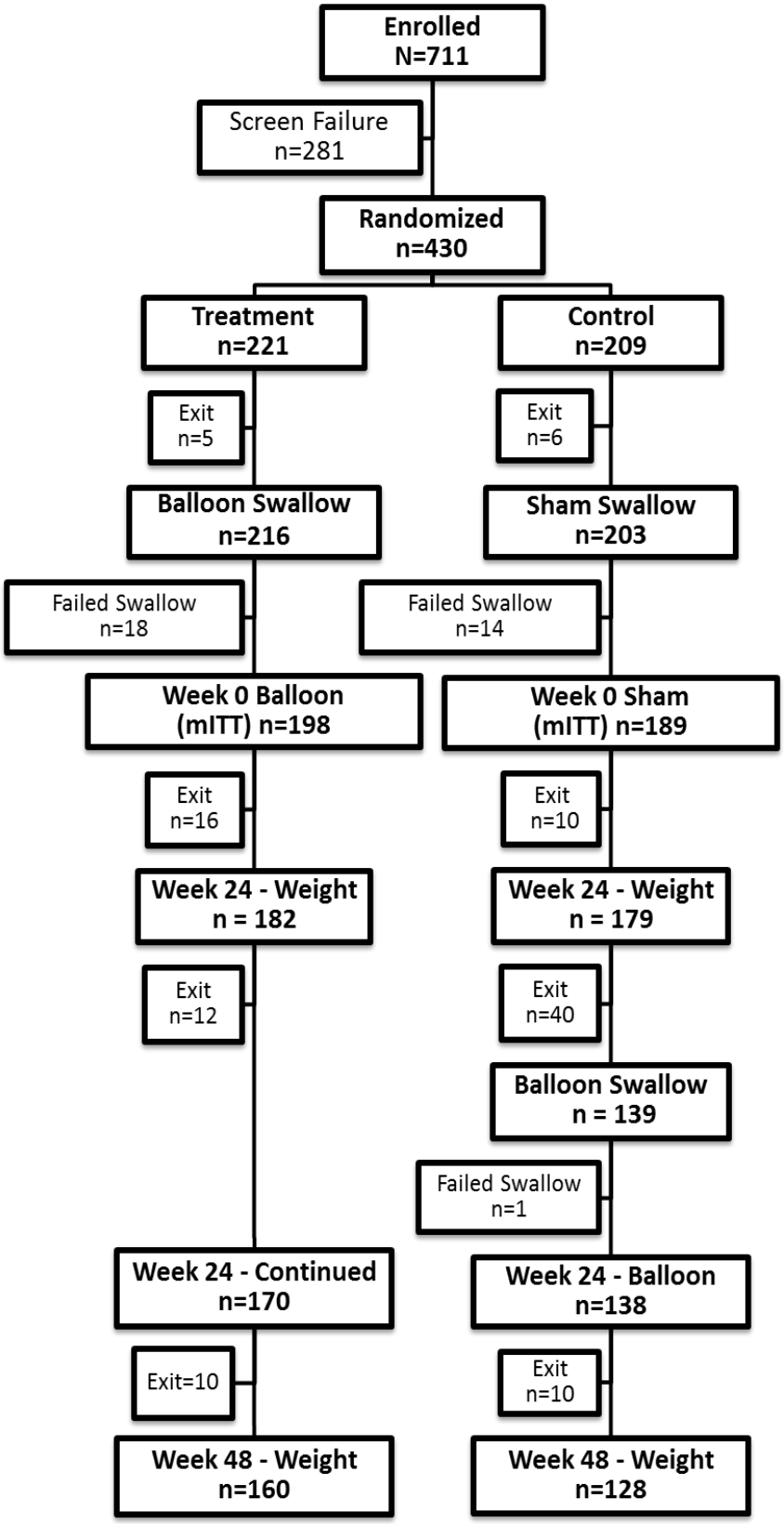


Figure 3. Subject Accountability Flowchart

C. Study Population Demographics and Baseline Parameters

A review of demographic data from the SMART Pivotal Trial showed no statistical differences in baseline characteristics between Treatment and Control subjects who received at least one device. For both groups, the baseline demographic assessment showed that both the Treatment and Control Groups had a mean age of 42.5 years, 35.2 mean BMI, 216 lb enrollment weight, and a 43.3 inch mean waist circumference. The baseline physical characteristics are shown in Table 8.

Table 8. Baseline Physical Characteristics

Parameter	Obalon Treatment (n=198) Mean ± SD (Median)	Obalon Control (n=189) Mean ± SD (Median)	p-value
Age (years)	42.6 ± 9.6 (43.2)	42.5 ± 9.3 (43.8)	0.8707
Enrollment weight (lbs.)	215.7 ± 29.3 (211.1)	216.8 ± 25.9 (216.4)	0.6851
BMI (kg/m^2)	35.1 ± 2.7 (35.0)	35.4 ± 2.7 (35.5)	0.3452
Waist circumference (in)	43.1 ± 3.8 (43.0)	43.6 ± 4.0 (43.7)	0.2453

A baseline demographic assessment showed that both Treatment and Control groups had over 85% females. The demographics of the SMART Pivotal Trial are similar to other obesity studies performed in the United States. The baseline sex, ethnicity, and races of the SMART Pivotal Trial participants are shown in Table 9.

Table 9. Baseline Sex, Ethnicity, and Race

Parameter	Obalon Treatment (n=198) Mean ± SD (Median)	Obalon Control (n=189) Mean ± SD (Median)	p-value
Sex (female)	171 (86.4%)	170 (89.9%)	0.2762
Ethnicity: Not Hispanic or Latino	183 (92.4%)	165 (87.3%)	0.0943
Race:			
Black/African American	21 (10.6%)	29 (15.3%)	0.1648
White or Caucasian	165 (83.3%)	155 (82.0%)	0.7310
Other	12 (6.1%)	5 (2.6%)	0.1013

Study subjects in the Treatment Group had comparable medical histories in comparison to the Control Group. Additionally, baseline blood pressure and metabolic blood measurements were not statistically different between the Treatment and Control Groups.

D. **Safety and Effectiveness Results**

1. Safety Results

The safety assessment of the Obalon Balloon System included a complete review of reported adverse events and serious adverse events, as well as device- and procedure-relatedness of adverse events. There were no pre-specified primary safety endpoints for the SMART Pivotal Study. The safety analysis was based on the 198 Treatment Group subjects in Weeks 0-24 who received ≥1 balloon and 138 Control Group subjects who opted to receive the Obalon Balloon System from Weeks 24-48 of the SMART Pivotal Study (Safety Population, n=336).

a. Serious Adverse Events

One subject had one device or procedure-related Serious Adverse Event (SAE). This SAE is reported in Table 10. The proportion of the Obalon Balloon Safety Population with any device or procedure-related SAE was 0.3% (1/336, 95% CI 0.0, 1.6%). There were no deaths, Unanticipated Adverse Device Effects, no device migrations out of the stomach, and no bowel obstructions in the SMART Pivotal Study. The SAE was peptic ulcer disease that resulted in gastrointestinal bleeding 6 weeks after receiving the third balloon. The patient had undergone an orthopedic surgery unrelated to the Obalon Balloon System. The patient took a large dose of nonsteroidal anti-inflammatory drugs (NSAIDs). This SAE was concluded to be NSAID-induced gastropathy that was also device-related. There were no additional SAEs recorded in the Smart Pivotal Study.

Table 10. Device or Procedure-Related Serious Adverse Events

	Safety Population (n=336)		
Serious Adverse Events[1]	**# of Events**	**Subjects % (n)**	**Device Removed Due to SAE # Subjects (% Subjects)**
Peptic ulcer disease	1	0.3% (1)	1/1 (100%)

[1]SAEs were defined as any adverse event that: resulted in death; was life-threatening; required hospitalization (initial or prolonged); caused a substantial disruption of the subject's ability to conduct normal life functions; required intervention to prevent permanent impairment or damage; resulted in a congenital anomaly or birth defect; may require medical or surgical intervention to prevent a serious medical event.

b. Adverse Events

A summary of the most common device-related adverse events is presented in Table 11.

Table 11. Gastrointestinal System Device-Related Adverse Events Occurring in 10% or More of Subjects (Safety Population, n=336)

Device Related Adverse Event	Events	Subjects (%) (N=336)	Mild[1] # Events (%)	Moderate[2] # Events (%)	Severe[3] # Events (%)	Day of Onset[4]	Event Duration (Days) # Events (%)
Abdominal Pain	494	244 (72.6%)	414 (83.8%)	79 (16.0%)	1 (0.2%)	Median: 0 Mean: 10 Range: 0-112	0-7: 323 (65.4%) 8-14: 37 (7.5%) >14: 134 (27.1%)
Nausea	311	188 (56.0%)	261 (83.9%)	50 (16.1%)	0 (0.0%)	Median: 0 Mean: 11 Range: 0-90	0-7: 225 (72.3%) 8-14: 25 (8.0%) >14: 61 (19.6%)
Vomiting	71	58 (17.3%)	56 (78.9%)	15 (21.1%)	0 (0.0%)	Median: 1 Mean: 14 Range: 0-134	0-7: 59 (83.1%) 8-14: 5 (7.0%) >14: 7 (9.9%)
Indigestion/ Heartburn	69	57 (16.7%)	48 (70.6%)	20 (29.4%)	0 (0.0%)	Median: 5 Mean: 15 Range: 0-67	0-7: 22 (31.9%) 8-14: 4 (5.8%) >14: 43 (62.3%)
Bloating	54	49 (14.6%)	49 (90.7%)	5 (9.3%)	0 (0.0%)	Median: 2 Mean: 14 Range: 0-61	0-7: 22 (40.7%) 8-14: 3 (5.6%) >14: 29 (53.7%)

[1]Mild: Subject has an awareness of signs or symptoms, which are easily tolerated and causing no loss of time from normal daily activities; symptoms do not require prescription medications, other than those previously specified; actions taken are limited to clinical observations or diagnostic tests.
[2]Moderate: Subject experience transient periods of discomfort, interfering with normal daily activities; actions taken may include prescription medications beyond what is pre-specified; actions taken do not require hospitalization or invasive interventions.
[3]Severe: Subject is experiencing non-transient discomfort inhibiting performance of normal daily activities; actions taken require hospitalization or invasive interventions.

[4]Day of Onset

A summary of all device-related adverse events is presented in Table 12 along with their severity and early removals. Table 12 also includes device-related adverse events that were identified at removal. A summary of all adverse events related to the removal procedure is shown in Table 13. The severity breakdown of all device-related adverse events is shown in Table 14. The reasons for patients who did not receive all three balloons is included in Table 15.

Table 12. All Device Related Adverse Device Effects With Severity by Balloon Placement and Early Removal as a Result of Event for all Subjects in the Control and Treatment Cohorts that received a Balloon (Safety Population, n = 336 Subjects)

Device Related Adverse Event	Safety Population (n= 336)				1st Balloon (n=336)		2nd Balloon (n=328)		3rd Balloon (n=315)	
	Events*	Subjects* (%)	Severity of Events % of Events	Subjects w/ Early Removal (%)	Events	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)
ALL Gastrointestinal Events	**1,146**	**300 (89.3%)**	**Mild: 82.7% Moderate: 16.9% Severe: 0.3%**	**11 (33%)**	**442**	**256 (76.2%)**	**293**	**167 (50.9%)**	**373**	**173 (54.9%)**
Abdominal Pain	494	244 (72.6%)	Mild: 83.8% Moderate: 16.0% Severe: 0.2%	4 (1.2%)	211	192 (57.1%)	128	112 (34.1%)	154	117 (37.1%)
Nausea	311	188 (56.0%)	Mild: 83.9% Moderate: 16.1% Severe: 0.0%	2 (0.6%)	138	135 (40.2%)	79	70 (21.3%)	94	71 (22.5%)

Device Related Adverse Event	Safety Population (n= 336)				1st Balloon (n=336)		2nd Balloon (n=328)		3rd Balloon (n=315)	
	Events*	Subjects* (%)	Severity of Events % of Events	Subjects w/ Early Removal (%)	Events	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)
Vomiting	71	58 (17.3%)	Mild: 78.9% Moderate: 21.1% Severe: 0.0%	4 (1.2%)	29	27 (8.0%)	19	17 (5.2%)	23	21 (6.7%)
Indigestion/ Heartburn	69	57 (16.9%)	Mild: 69.6% Moderate: 30.4% Severe: 0.0%	0 (0.0%)	18	18 (5.4%)	20	17 (5.2%)	30	29 (9.2%)
Bloating	54	49 (14.6%)	Mild: 90.7% Moderate: 9.3% Severe: 0.0%	0 (0.0%)	14	14 (4.2%)	19	19 (5.8%)	21	21 (6.7%)
Burping/ Belching	37	31 (9.2%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	10	10 (3.0%)	9	9 (2.7%)	18	18 (5.7%)
Diarrhea	30	28 (8.3%)	Mild: 96.7% Moderate: 3.3% Severe: 0.0%	0 (0.0%)	9	9 (2.7%)	5	5 (1.5%)	15	14 (4.4%)

Device Related Adverse Event	Safety Population (n= 336)				1st Balloon (n=336)		2nd Balloon (n=328)		3rd Balloon (n=315)	
	Events*	Subjects* (%)	Severity of Events % of Events	Subjects w/ Early Removal (%)	Events	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)
Gastric Irritation**	25	24 (7.1%)	Mild: 48.0% Moderate: 48.0% Severe: 4.0%	0 (0.0%)	N/A	N/A	N/A	N/A	N/A	N/A
Constipation	10	9 (2.7%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	1	1 (0.3%)	5	5 (1.5%)	4	4 (1.3%)
Difficulty in Sleeping	9	9 (2.7%)	Mild: 66.7% Moderate: 33.3% Severe: 0.0%	0 (0.0%)	3	3 (0.9%)	1	1 (0.3%)	5	5 (1.6%)
Excessive Gas	8	8 (2.4%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	3	3 (0.9%)	0	0 (0.0%)	5	5 (1.6%)
Esophagitis**	6	6 (1.8%)	Mild: 33.3% Moderate: 66.7% Severe: 0.0%	0 (0.0%)	N/A	N/A	N/A	N/A	N/A	N/A

Device Related Adverse Event	Safety Population (n= 336)				1st Balloon (n=336)		2nd Balloon (n=328)		3rd Balloon (n=315)	
	Events*	Subjects* (%)	Severity of Events % of Events	Subjects w/ Early Removal (%)	Events	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)
Hypersalivation	4	3 (0.9%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	1	1 (0.3%)	2	1 (0.3%)	1	1 (0.3%)
Chest Pain	3	3 (0.9%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	1	1 (0.3%)	1	1 (0.3%)	1	1 (0.3%)
Gastric Ulcer**	3	3 (0.9%)	Mild: 0.0% Moderate: 66.7% Severe: 33.3%	1 (3.3%)	N/A	N/A	N/A	N/A	N/A	N/A
Device Intolerance	2	2 (0.6%)	Mild: 0.0% Moderate: 50.0% Severe: 50.0%	0 (0.0%)	0	0 (0.0%)	1	1 (0.3%)	1	1 (0.3%)
Hiccups	2	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	0	0 (0.0%)	1	1 (0.3%)	1	1 (0.3%)

Device Related Adverse Event	Safety Population (n= 336)				1st Balloon (n=336)		2nd Balloon (n=328)		3rd Balloon (n=315)	
	Events*	Subjects* (%)	Severity of Events % of Events	Subjects w/ Early Removal (%)	Events	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)
Sore Throat	2	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	2	1 (0.3%)	0	0 (0.0%)	0	0 (0.0%)
Dry Heaving	1	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	1	1 (0.3%)	0	0 (0.0%)	0	0 (0.0%)
Food Passage Difficulty	1	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	0	0 (0.0%)	1	1 (0.3%)	0	0 (0.0%)
Fullness	1	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	0	0 (0.0%)	1	1 (0.3%)	0	0 (0.0%)
Retaining Food & Fluid**	1	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	N/A	N/A	N/A	N/A	N/A	N/A

Device Related Adverse Event	Safety Population (n= 336)				1st Balloon (n=336)		2nd Balloon (n=328)		3rd Balloon (n=315)	
	Events*	Subjects* (%)	Severity of Events % of Events	Subjects w/ Early Removal (%)	Events	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)
Syncope	1	1 (0.3%)	Mild: 0.0% Moderate: 100.0% Severe: 0.0%	0 (0.0%)	1	1 (0.3%)	0	0 (0.0%)	0	0 (0.0%)
Upper Body Injury/ Pain	1	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	0	0 (0.0%)	1	1 (0.3%)	0	0 (0.0%)
ALL Metabolic/ Nutritional Events	**9**	**8 (2.4%)**	**Mild: 66.7% Moderate: 33.0% Severe: 0.0%**	**0 (0.0%)**	**5**	**5 (1.5%)**	**2**	**2 (0.6%)**	**2**	**2 (0.6%)**
Headache/ Migraines	7	6 (1.8%)	Mild: 71.4% Moderate: 28.6% Severe: 0.0%	0 (0.0%)	4	4 (1.2%)	2	2 (0.6%)	1	1 (0.3%)
Dizziness	1	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	1	1 (0.3%)	0	0 (0.0%)	0	0 (0.0%)

Device Related Adverse Event	Safety Population (n= 336)				1st Balloon (n=336)		2nd Balloon (n=328)		3rd Balloon (n=315)	
	Events*	Subjects* (%)	Severity of Events % of Events	Subjects w/ Early Removal (%)	Events	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)
Fatigue	1	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	1	1 (0.3%)
ALL Respiratory Events	**3**	**3 (0.9%)**	**Mild: 66.7% Moderate: 33.3% Severe: 0.0%**	**0 (0.0%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**	**3**	**3 (0.9%)**
Shortness of Breath	2	2 (0.6%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	2	2 (0.6%)
Asthma	1	1 (0.3%)	Mild: 0.0% Moderate: 100.0% Severe: 0.0%	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	1	1 (0.3%)
ALL Other Events	**1**	**1 (0.3%)**	**Mild: 100.0% Moderate: 0.0% Severe: 0.0%**	**0 (0.0%)**	**1**	**1 (0.3%)**	**0**	**0 (0.0%)**	**0**	**0 (0.0%)**

Device Related Adverse Event	Safety Population (n= 336)				1st Balloon (n=336)		2nd Balloon (n=328)		3rd Balloon (n=315)	
	Events*	Subjects* (%)	Severity of Events % of Events	Subjects w/ Early Removal (%)	Events	Subjects (%)	Events	Subjects (%)	Events	Subjects (%)
Allergic Reaction	1	1 (0.3%)	Mild: 100.0% Moderate: 0.0% Severe: 0.0%	0 (0.0%)	1	1 (0.3%)	0	0 (0.0%)	0	0 (0.0%)
ALL	**1,159**	**300 (89.3%)**	**Mild: 82.6% Moderate: 17.1% Severe: 0.3%**	**11 (3.3%)**	**448**	**256 (76.2%)**	**295**	**167 (50.9%)**	**378**	**175 (55.6%)**

*Total Events/%Subjects include 1st, 2nd, 3rd balloon placements as well as those identified at removal.
**ADE onset date is not known.

Table 13. Device-Related Adverse Events Identified at Removal – Procedure Related

Device Related Adverse Event	Safety Population (n=336)				
	Events	Subjects (%)	Mild	Moderate	Severe
Gastric Bleeding/ Abrasion	17	17 (5.1%)	15 (88.2%)	1 (5.9%)	1 (5.9%)
Esophageal Bleeding/ Abrasion	14	14 (4.2%)	11 (78.6%)	3 (21.4%)	0 (0.0%)
Esophagastric Bleeding/ Abrasion	12	12 (3.6%)	9 (75.0%)	3 (25.0%)	0 (0.0%)
Oxygen Desaturation	4	4 (1.2%)	2 (50.0%)	2 (50.0%)	0 (0.0%)
Vocal Chord Spasm	2	2 (0.6%)	0 (0.0%)	2 (100.0%)	0 (0.0%)
Hypertension	1	1 (0.3%)	0 (0.0%)	1 (100.0%)	0 (0.0%)
Coughing	1	1 (0.3%)	1 (100.0%)	0 (0.0%)	0 (0.0%)
Sore Throat	1	1 (0.3%)	1 (100.0%)	0 (0.0%)	0 (0.0%)
Swollen Lips	1	1 (0.3%)	1 (100.0%)	0 (0.0%)	0 (0.0%)

Table 14. Total Number of Device-Related Adverse Events With Severity (Safety Population, n=336)

	Events	Subjects (%) (n=336)	Severity of Events
Device-Related ADEs	1,159	300 (89.3%)	Mild: 82.6% Moderate: 17.1% Severe: 0.3%
Removal Procedure Related ADEs	53	45 (13.4%)	Mild: 75.5% Moderate: 22.6% Severe: 1.9%
Combined	**1,212**	**305 (90.8%)**	**Mild: 82.3%** **Moderate: 17.3%** **Severe: 0.4%**

Table 15. Subjects with Less Than 3 Balloons (Safety Population, n=336)

Reason	No 2nd Balloon	No 3rd Balloon	Combined
Device Failed Effectiveness*	5 (1.5%)	5 (1.5%)	**10 (3.0%)**
Device Intolerance**	2 (0.6%)	4 (1.2%)	**6 (1.8%)**
ALL	**7 (2.1%)**	**9 (2.7%)**	**16 (4.8%)**

*Device Failed Effectiveness: Unwilling or unable to swallow additional balloons.
**Device Intolerance: Abdominal Pain or Nausea

c. Device Failures and Replacements

A total of 985 balloons were administered in the Study Population (n=336). These 985 balloons were administered in the 198 Treatment Group subjects and 138 Control Group subjects who opted to have the Obalon Balloon System after completing the Week 24 follow-up visit.

The swallowing procedure had a high degree of success, with only 8.3% (18/216) and 6.9% (14/203) swallow failures in the Treatment and Control Groups, respectively. A summary of the swallow failures for all three administration procedures is shown in Table 16.

Table 16. Subjects Unable to Swallow 1st, 2nd, and 3rd Balloons

Device Number	Treatment Group Subjects Unable to Swallow Balloon (%)	Control Group Subjects Unable to Swallow Sham (%)	Total Subjects Unable to Swallow Balloon or Sham Device (%)
1st	18/216 (8.3%)	14/203 (6.9%)	32/419 (7.6%)
2nd*	1/195 (0.5%)	1/188 (0.5%)	2/383 (0.5%)
3rd*	1/185 (0.5%)	1/182 (0.5%)	2/367 (0.5%)

*The denominator represents those subjects that attempted placement of a device (balloon/sham). A 2nd and 3rd device attempt was conducted on only those subjects eligible for placement (e.g., had not exited the study or did not have an on-going adverse event that the investigator felt could be worsened by placement of another device).

There were a total of five (5) product performance issues. Out of the 985 balloons administered, four (4) catheters were bit by patients and could not be used (4/985, 0.4%). Additionally, one balloon deflation was noted during the removal procedure (1/981, 0.1%). No balloons, including the one deflation, migrated out of the stomach at any time during the study.

2. Effectiveness Results

a. Primary Endpoint Outcome

The analysis of effectiveness was based on the 189 subjects on the Modified Intent-to-Treat (mITT) Treatment subjects at 24 weeks. Key effectiveness outcomes are presented in Table 17 and Table 18.

The SMART Pivotal Trial met its first co-primary effectiveness endpoint. The mITT mean %TBL was 6.6% for Treatment subjects and 3.42% for Control subjects, giving a mean difference of 3.18 %TBL. The p-value was 0.0354 for a 2.1 %TBL super-superiority margin. This result demonstrates that the Obalon Balloon-treated subjects had a weight loss significantly greater than Control subjects plus a 2.1 %TBL superiority margin, as seen in Table 17. The Per Protocol Data is also shown in this table.

Table 17. Co-Primary Effectiveness Endpoint at 24 Weeks – Mean % TBL Difference from Sham

Main Analysis of 6-Month %TBL	Least Square Mean		Difference in LS Means (Treatment – Control)			
	Treatment	Control	Estimate	95% LCL	95% UCL	p-value
Per Protocol Cohort Treatment=185 Control=181	-6.86	-3.59	-3.28	-4.32	-2.24	**0.0261**
Modified Intent to Treat (mITT) Treatment=198 Control=189	-6.60	-3.42	-3.18	-4.19	-2.17	**0.0354**

The SMART Pivotal Trial also met its second co-primary effectiveness endpoint. The mITT Treatment subjects who achieved a 5% TBL or greater weight loss at 24 weeks was an estimated 62.1% with a lower confidence bound of 59.2%. This was significantly greater than the responder rate of 35%, as seen in Table 18.

Table 18. Co-Primary Effectiveness Endpoint at 24 Weeks – % Responder Rate (% of Subjects with 5% TBL or more)

Criteria (≤)	Per Protocol Cohort (n=185)		Modified Intent to Treat (n=198)	
	Estimate	95% Confidence Interval	Estimate	95% Confidence Interval
-5% TBL	**120 (64.9%)**	**(57.5 %, 71.7%)**	**123 (62.1%)**	**(59.2%, 73.2 %)**
-6% TBL	98 (53.0%)	(45.5 %, 60.3%)	101 (51.0%)	(47.1%, 61.9%)
-7% TBL	81 (43.8%)	(36.5 %, 51.3%)	83 (41.9%)	(37.6%, 52.3%)
-8% TBL	68 (36.8%)	(29.8 %, 44.1%)	69 (34.8%)	(30.3%, 44.7%)
-9% TBL	55 (29.7%)	(23.2 %, 36.9%)	56 (28.3%)	(23.7%, 37.4 %)
-10% TBL	49 (26.5%)	(20.3 %, 33.5%)	49 (24.7%)	(20.3%, 33.5%)

b. **Observational Analyses**

Additional weight loss parameters were evaluated at Week 48 for maintenance of weight loss. 171 of the mITT Treatment subjects measured a weight loss at Week 24 and were evaluated for weight loss maintenance at Week 48. These additional weight loss parameters are presented in Table 19.

Table 19. Weight Loss Parameters at 24 and 48 Weeks by Treatment Group

	Treatment					Control				
Cohort	**n**	**% TBL** Mean SD (Median) Min, Max	**% EWL** Mean SD (Median) Min, Max	**Pounds** Mean SD (Median) Min, Max	**BMI Change** Mean SD (Median) Min, Max	**n**	**% TBL** Mean SD (Median) Min, Max	**% EWL** Mean SD (Median) Min, Max	**Pounds** Mean SD (Median) Min, Max	**BMI Change** Mean SD (Median) Min, Max
mITT at 24 weeks	198	-6.6 ± 5.1 (-6.1) [-19.3, 9.5]	-24.1 ± 19.2 (-21.8) [-80.7, 28.8]	-14.4 ± 11.7 (-12.6) [-49.7, 21.1]	-2.3 ± 1.8 (-2.1) [-7.1, 3.6]	189	-3.4 ± 5.0 (-2.8) [-18.7, 9.6]	-12.2 ± 18.8 (-10.2) [-104, 30.4]	-7.4 ± 11.2 (-5.8) [-52.4, 21.8]	-1.2 ± 1.8 (-1.0) [-7.1, 3.5]

	Treatment					Control				
Cohort	**n**	**% TBL Mean SD (Median) Min, Max**	**% EWL Mean SD (Median) Min, Max**	**Pounds Mean SD (Median) Min, Max**	**BMI Change Mean SD (Median) Min, Max**	**n**	**% TBL Mean SD (Median) Min, Max**	**% EWL Mean SD (Median) Min, Max**	**Pounds Mean SD (Median) Min, Max**	**BMI Change Mean SD (Median) Min, Max**
Per Protocol at 24 weeks	185	-6.9 ± 5.0 (-6.2) [-19.3, 9.5]	-25.2 ± 19.2 (-22.7) [-80.7, 28.8]	-15.0 ± 11.7 (-13.2) [-49.7, 21.1]	-2.4 ± 1.8 (-2.2) [-7.1, 3.6]	181	-3.6 ± 5.0 (-3.1) [-18.7, 9.6]	-12.8 ± 18.9 (-11.2) [-104, 30.4]	-7.8 ± 11.3 (-6.2) [-52.4, 21.8]	-1.3 ± 1.8 (-1.0) [-7.1, 3.5]
mITT Week 48 – Week 24* Weight Change	171	0.9 ± 4.1 (1.1) [-14.4, 12.0]	3.2 ± 14.9 (3.6) [-46.4, 43.2]	1.8 ± 9.3 (2.6) [-41.6, 27.8]	0.3 ± 1.4 (0.4) [-5.2, 4.2]	N/A	N/A	N/A	N/A	N/A
Per Protocol Week 48 – Week 24* Weight Change	168	0.9 ± 4.1 (1.2) [-14.4, 12.0]	3.3 ± 15.0 (3.7) [-46.4, 43.2]	1.9 ± 9.4 (2.6) [-41.6, 27.8]	0.3 ± 1.5 (0.4) [-5.2, 4.2]	N/A	N/A	N/A	N/A	N/A

*171 out of the 198 mITT Subjects had a measured negative %TBL at Week 24 and were evaluated for weight change at Week 48.

**168 out of the 185 Per Protocol Treatment subjects had a measured negative %TBL at Week 24 and were evaluated for weight change at Week 48.

N/A: Control Group weight loss was not evaluated.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR Part 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 15 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

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

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology-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.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The SMART pivotal study had two (2) co-primary effectiveness endpoints, both of which were met. These endpoints demonstrated that the Obalon Balloon System was more effective than a medically supervised diet and exercise program alone for 24 weeks.

The first co-primary endpoint specified that the Treatment Group would achieve a mean percent total body loss (% TBL) that was significantly greater than the Control Group by a superiority margin of 2.1 at 24 weeks when the device was removed. The average weight loss was 6.6% TBL for the Treatment Group and 3.42 %TBL for the Control Group. This resulted in a mean difference between the Treatment and Control Groups of 3.18% TBL (95% CI: [2.17, 4.19]).

The second co-primary effectiveness endpoint specified that significantly greater than 35% of subjects in the Treatment Group would achieve greater than 5% TBL at 24 weeks when the device was removed. The results demonstrated that 62.1% of subjects in the Treatment Group achieved a 5% TBL (95% CI: [55.0, 68.9%]).

The study did not have any pre-specified secondary endpoints. There were several observational analyses, including a weight maintenance period 24 weeks after the device was removed. On average, the mITT group regained approximately 0.9% TBL (1.8 lbs) of the weight loss at 48 weeks.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies, as well as data collected in clinical studies conducted to support PMA approval as described above.

The SMART pivotal study did not have a pre-specified safety endpoint. The safety assessment of the Obalon Balloon System included a complete review of reported serious adverse events (SAEs) and adverse events, as well as device and procedure-relatedness of adverse events.

There was one device-related SAE reported in one subject, resulting in a device or procedure-related SAE rate of 0.3% (1/336). A significant percentage of subjects experienced adverse device effects (ADEs) such as abdominal pain, nausea, and vomiting. Most of these ADEs were mild in nature and resolved within 14 days. Ten (10) subjects required early balloon removals due to non-serious ADEs (10/336, 3.0%).

The most significant concerns with the Obalon Balloon System are related to reports from previous clinical studies and commercial use outside the United States. Previous clinical studies demonstrated that balloon deflations and bowel obstructions can occur in rare circumstances. However, the balloon was redesigned after these previous clinical studies. There was one balloon deflation out of 981 balloons implanted in the SMART pivotal study and this did not cause a bowel obstruction.

A balloon inflation in the esophagus that caused a perforation, sepsis, and subsequent death was reported outside the United States. This risk is mitigated by the use of radiographic confirmation of the balloon's location in the stomach and the pre-pulse verification.

C. Benefit-Risk Determination

The probable benefits of the device are based on the data collected in clinical studies conducted to support PMA approval as described above. The benefits of the Obalon Balloon System are moderate weight loss and some level of weight loss maintenance in some subjects who lost weight with the device 24 weeks after the device was removed. While the weight loss was moderate with a small superiority margin versus control patients, the safety profile demonstrated one device or procedure-related SAE. There are risks for patients developing adverse events related to the device. Most commonly, patients experienced abdominal pain, nausea, and vomiting. However, most of these adverse events were mild in nature and resolved within 14 days. Only a small percentage of subjects within the SMART pivotal study required early balloon explantation due to adverse events. The most worrisome risks are rare procedural errors and the risk of bowel obstruction from deflated balloons.

1. Patient Perspectives

   This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data supports the intended use of the Obalon Balloon System for the treatment of obesity and that the probable benefits outweigh the probable risks.

D. 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 primary effectiveness endpoints demonstrated a mean %TBL of 6.6% in the Treatment Group as compared to 3.42% in the Control Group. Additionally, the responder analysis demonstrating that 62.1% of patients lost at least 5% TBL supports that the device is likely to be clinically effective in a significant portion of patients. Finally, the safety profile for the Obalon Balloon System is reasonable, with one SAE reported in 336 subjects in the SMART Pivotal Trial.

In conclusion, the benefit-risk model profile favors the approval of this device.

XIII. CDRH DECISION

CDRH issued an approval order on September 8, 2016. The final conditions of approval cited in the approval order are described below.

OSB Lead PMA Post-Approval Study – Obalon Balloon System Post-Approval Study: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval.

The Obalon Balloon System Post-Approval Study is a prospective, open-label, single-arm study of the safety and effectiveness of the Obalon 6-month Balloon System, as an adjunct to weight loss for obese adults 22 years of age and older with a Body Mass Index (BMI) of 30 kg/m^2 to 40 kg/m^2. This is a 12-month follow-up study in which subjects will be treated during the first 6 months with placement (via swallow) of up to three (3) Obalon Balloons in conjunction with a moderate intensity weight loss and behavioral modification program standardized throughout the sites, followed by observational evaluation for an additional 6 months after device removal. A total of 200 subjects will be enrolled at 10 to 15 sites in the United States; 180 evaluable subjects will be available at 6 months.

The primary endpoint is to evaluate the safety of Obalon by assessing the rate of device- or procedure-related Serious Adverse Event(s) (SAEs) (composite safety endpoint). Where the SAE is defined as any AE that results in death or persistent/significant disability and/or incapacity, which may include emergency room visits, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, or requires medical/surgical intervention to prevent any of the above, through 6 months of treatment with the Obalon 6-month Balloon System. The observed rate will be compared to a performance goal of 10% at 6 months assuming an expected 4.5% device or procedure related SAE rate. The secondary effectiveness endpoint is comprised of (1) the mean % Total Body Loss (%TBL) and (2) the proportion of subjects achieving at least -5% TBL through the first 6 months after the device is implanted.

Additional endpoints include observational safety and effectiveness analyses including the percentage of subjects and frequency of individual Adverse Events (AEs) that are device- or procedure-related, frequency and cause of early explantations, rates of gastric ulceration, esophageal tear, balloon deflation, means of other weight loss metrics such as % Excess Weight Loss (EWL), Weight Loss (WL) in pounds, and BMI change, percentage of subjects with at least 6%, 7%, 8%, 9%, and 10% TBL, percentage of subjects with at least 25% EWL, patient-reported outcomes assessing tolerability of device and/or quality of life, weight loss metrics by number of balloons placed, weight loss metrics by frequency of weight loss and behavioral modification program counseling.

Follow-up assessments will be in office visits at Day 0, monthly during the first 6 months and at 12 months after initial implant. The Obalon 6-month Balloon System requires removal of all 3 balloons at the end of the 6-month period. Subjects will be followed for an additional 6 month period to ensure there are no Adverse Events as a result of balloon removal or residual events due to balloon use. Subjects with gastric ulcerations at the time of device explant will be followed with endoscopic evaluation every 8 weeks until the ulcer has visually resolved.

The applicant's manufacturing facilities have been 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

[1] Jensen, Michael D., et al. "2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society." *Journal of the American College of Cardiology* 63.25_PA (2014).