SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Weight Loss Therapy System

Device Trade Name: AspireAssist®

Device Procode: OYF

Applicant's Name and Address: Aspire Bariatrics Inc.
3200 Horizon Drive
Suite 100
King of Prussia, Pa 19406

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P150024

Date of FDA Notice of Approval: June 14, 2016

II. INDICATIONS FOR USE

The AspireAssist® is intended to assist in weight reduction of obese patients. It is indicated for use in adults aged 22 or older with a Body Mass Index (BMI) of 35.0-55.0 kg/m^2 who have failed to achieve and maintain weight loss with non-surgical weight loss therapy. The AspireAssist is intended for a long-term duration of use in conjunction with lifestyle therapy and continuous medical monitoring.

III. CONTRAINDICATIONS

- Previous abdominal surgery that significantly increases the medical risks of gastrostomy tube placement
- Esophageal stricture, pseudo-obstruction, severe gastroparesis or gastric outlet obstruction, inflammatory bowel disease
- History of refractory gastric ulcers
- Ulcers, bleeding lesions, or tumors discovered during endoscopic examination
- Uncontrolled hypertension (blood pressure>160/100)
- History or evidence of serious pulmonary or cardiovascular disease, including acute coronary syndrome, heart failure requiring medications, or NYHA (New York Heart Association) class III[1] or IV[2] heart failure

[1]Class III: Patients with marked limitation of activity and who are comfortable only at rest
[2]Class IV: Patients who should be at complete rest, are confined to bed or chair, and who have discomfort with any physical activity

- Coagulation disorders (platelets < 50,000, PT > 2 seconds above control or INR > 1.5)
- Anemia (hemoglobin <8.0 g/dL in women and <10.0 g/dL in men)
- Pregnant or lactating
- Diagnosed Bulimia or diagnosed Binge Eating Disorder (using DSM criteria)
- Night Eating Syndrome
- Chronic abdominal pain that would potentially complicate the management of the device
- Physical or mental disability, or psychological illness that could interfere with compliance with the therapy
- At high risk of having a medical complication from the endoscopic procedure or the AspireAssist weight loss program for any reason, including poor general health or severe organ dysfunction such as cirrhosis or renal dysfunction (GFR <60 mL/min/1.73 m^2, including Stage II or more severe chronic kidney disease)

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the AspireAssist labeling.

V. DEVICE DESCRIPTION

The AspireAssist is a device designed to facilitate weight loss in obese patients by (i) enabling removal of a portion of stomach contents through a gastrostomy tube, and (ii) requiring thorough chewing in order for stomach contents to enter the 6mm diameter tube. The device is used in conjunction with lifestyle therapy to help patients develop healthier eating habits and reduce caloric intake.

The device consists of the A-Tube™ and a "gravity" flow director system through which patients aspirate (drain) gastric contents about 20 to 30 minutes after consumption of a meal directly into the toilet. The AspireAssist is used after the three (3) major meals each day, takes about 5-10 minutes to complete, and typically removes about 30% of the calories consumed. Accordingly, this approach aids in portion control, a key principle of weight management therapy. Additionally, all food must be thoroughly chewed to fit through the tube, promoting slower consumption and reduced caloric intake.

A. Device Components

The AspireAssist system consists of the implanted A-tube and multiple external parts: the Skin-Port, Connector, Companion, Tubing Set, Reservoir, and Lanyard. These are shown in **Figures 1 and 2** and are described further below.

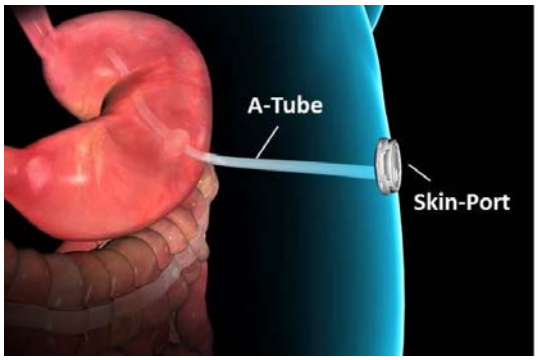


Figure 1. Implanted A-tube with Skin-Port

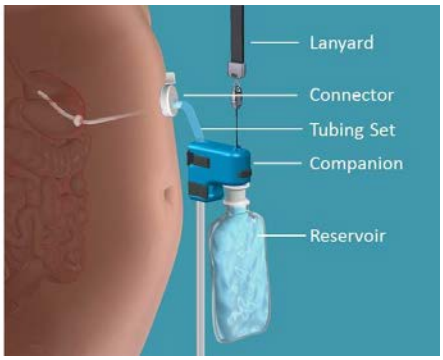


Figure 2. Implanted A-tube with Assembled System

A-tube

The A-Tube (**Figure 3**) is a silicone tube, similar to a percutaneous endoscopic gastrostomy (PEG) tube, with an intragastric portion with aspiration holes and a bumper, and an extragastric tubing portion with graduated markings. The A-tube is implanted endoscopically similarly to a standard PEG tube for gastric feeding. Once the gastrocutaneous fistula is partially healed, about 7 days after A-Tube placement, the external portion of the A-Tube is cut to a length so that it is almost flush with the abdominal skin.

As a patient loses weight (and abdominal thickness decreases), the length of the A-tube is shortened to keep the proximal end of the A-tube and Skin-Port (described below) approximately flush with the abdominal skin. This procedure can be done by a nurse or trained healthcare professional and involves removal of the Skin-Port, cutting the proximal end of the A-tube, and re-attachment of the Skin-Port. The AspireAssist Skin-Port installation tool kit facilitates the procedure.

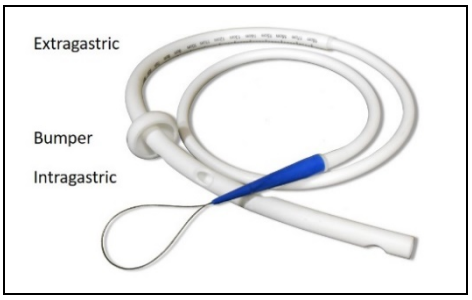


Figure 3. A-tube

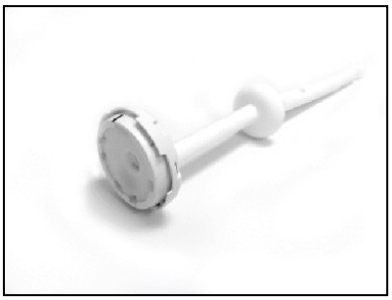


Figure 4. Skin-Port with A-Tube

Skin Port

The Skin-Port™ connects to the proximal end of the A-Tube, holds it in place at the skin level, and prevents the tube from migrating into the stomach. The Skin-Port contains a valve that is normally closed to prevent gastric leakage, and is opened when the patient aspirates after a meal. **Figure 4** (above) shows the Skin-Port when connected to the A-Tube.

The Skin-Port protrudes approximately 1 cm above the skin and was designed with a low profile to be as unobtrusive as possible and to minimize the chances of snagging on clothing or other objects.

Skin Port Installation Tool Kit

The AspireAssist Skin-Port Installation Tool Kit is provided to facilitate Skin Port placement and removal. The tool kit is comprised of five (5) main components or tools: Clamp Tray, Tube Cutter, Sleeve Tool, Valve Opening Tool, and Valve Removal Tool. The Connector (described below) mates to the Skin-Port and allows coupling between the A-Tube and the Companion. Engagement of the Connector to the Skin-Port opens the Skin-Port valve. Disengagement of the Connector to the Skin-Port closes the Skin-Port valve.

Connector

The Connector (**Figure 5**) mates with the Skin-Port and allows coupling between the A-tube and the Companion (aspiration device, described below). Engagement of the Connector to the Skin-Port opens the Skin-Port to allow aspiration; disengagement of the Connector closes the valve.

The Connector contains a "counter" that tracks the number of times the Connector engages to the Skin-Port. When the count reaches 115 cycles (which occurs, typically, after about 5 - 6 weeks of therapy), the Connector will no longer engage with the Skin-Port. To continue therapy the patient must return to the clinic to obtain a new Connector. This was designed as a safety feature to assure that the AspireAssist is used under the care of a physician.

Figure 5. Connector

Companion

The Companion™ is the aspiration device. The Companion is reusable and operated by the patient. When connected to the Skin-Port (via the Connector Tube and Connector), it allows the patient to alternately drain stomach contents and rinse both the stomach and A-Tube with potable water. A manual latch on the Companion allows for the patient to control the flow of food aspirated. When the latch is open, food will flow from the stomach into the A-tube, enter the tubing set, and flow directly down into a toilet. When the clamp is closed, water can be squeezed into the stomach from the reservoir to help loosen food particles. The Companion is an entirely passive device; drainage occurs through gravity without mechanical suction.

Tubing Set
The Tubing Set is comprised of three main components, the T-Fitting, the Connector Tube, and the Drain Tube. The Tubing Set is attached to the Connector and Companion and provides a conduit for directing food to a toilet or waste container.

Reservoir
The Reservoir is a flexible water bottle which is filled with potable water and connects to the Companion for the purpose of providing water for infusion into the stomach.

Lanyard
The Lanyard is constructed of black polyester webbing, which forms the neck strap. Prior to use the patient places the Lanyard around their neck to support the weight of the Companion, Tubing Set, and Reservoir.

Emergency Clamp
The Emergency Clamp is an accessory to the AspireAssist. The Emergency Clamp is similar in design to a hemostat with a locking mechanism that maintains a positive hold once closed. The Emergency Clamp is used in the event the Skin-Port becomes disconnected from the A-tube at any time to prevent leakage of stomach contents.

B. Principles of Operation

To use the AspireAssist, the patient assembles the device by inserting the Tubing Set into the Companion, inserting the filled Reservoir into the Companion, and placing the lanyard around his/her neck as shown in **Figure 6**. While standing in the upright position, the patient attaches the Connector to the Skin-Port. During aspiration the patient opens the drain clamp on the Companion, and the stomach contents flow from the Connector Tube, through the T-Fitting, and down the Drain Tube to a toilet. During the flushing step, the patient closes the clamp on the Companion and squeezes the Reservoir to infuse the stomach with water. The water travels from the reservoir to the Companion, through the T-fitting to the Connector Tube and into the stomach through the A-tube. The drain clamp is then opened to aspirate additional stomach contents. The infusion of water and aspiration can be repeated until no food particles are observed in the evacuated fluid.

Once aspiration is complete, the patient detaches the Connector from the Skin Port and rinses the aspiration device and tubing to be clear of all food particles. The aspiration process typically takes between 5-10 minutes.

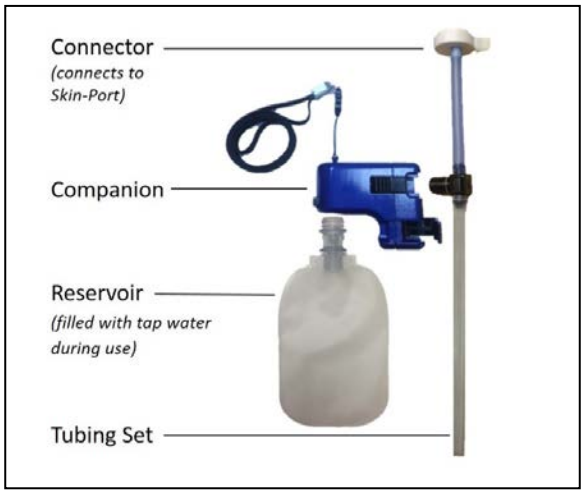


Figure 6. Assembled System

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for 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, intragastric balloons, 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 his/her 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 modification programs; 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 five (5) years.

D. Intragastric Balloons

Intragastric balloons are indicated for weight reduction when used in conjunction with diet and exercise in obese patients with a BMI of 30 to 40 kg/m^2 with or without one or more obesity related comorbidities depending on the specific device. Intragastric balloons are indicated for use in adult patients who have failed weight reduction with diet and exercise alone.

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 AspireAssist has been CE Marked in the European Union since October 2011.

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

Most potential adverse effects associated with the AspireAssist include events associated with any conventional gastrostomy tube placement including those related to the placement procedure and stoma related care. Other potential effects that are unique to the

AspireAssist are associated with the therapy itself including electrolyte abnormalities, eating behaviors, and concomitant medications.

The risks of endoscopic placement of the A-Tube are the same as endoscopic placement of a standard Percutaneous Endoscopic Gastrostomy (PEG) tube and includes sedation complications, discomfort, sore throat, pain, abdominal bloating, indigestion, bleeding, infection, nausea, vomiting, hypoventilation, peritonitis, aspiration pneumonia, perforation, and death.

Risks related to the stoma include: abdominal discomfort/pain, peristomal skin irritation/ inflammation, erythema and granulation tissue, peristomal leakage and/or bleeding, stoma site infection, buried bumper syndrome, persistent fistula after tube removal, and skin induration.

Risks related to the aspiration process (e.g., the process of removing a portion of each meal) include occasional indigestion, nausea, vomiting, constipation, and diarrhea.

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

The integrity and performance of the AspireAssist was evaluated through the testing summarized in **Table 1**.

Table 1. Non-Clinical Performance Testing

Device Components	Test Description	Acceptance Criteria	Test Result
AspireAssist System	Counter Accuracy and Function Test to verify accuracy of Connector counter feature and end of count lock-out function.	Connector counter feature is pre-set to 115 and designed to decrease by 1 count every time it opens Skin-Port valve. Connector must meet these functional requirements when maximum number of uses is reached: • Counter accuracy must be +/- 10%. • Counting feature shall not be resettable. • Prevent user from opening Skin-Port valve.	Pass

Device Components	Test Description	Acceptance Criteria	Test Result
AspireAssist System	System Reliability Test to verify function of AspireAssist System and components over specified useful life.	System must meet following pre-specified performance criteria after 1,096 uses (1 year equivalent simulated use), with Skin-Port replaced after 548 connections (6 month equivalent simulated use), Reservoir replaced after 274 uses (3 month equivalent simulated use), and Connector replaced after 115 connections (maximum number of uses) to Skin-port: • No leaks in System, with Drain Tube occluded by Companion and A-Tube clamped off on segment that resides in stomach, when subjected to hydrostatic pressure of 2.0psi for 5 minutes. • No leaks in System, with Skin-Port closed and A-Tube clamped off on segment that resides in stomach, when subjected to hydrostatic pressure of 2.0psi for 5 minutes. • Fluid flow from Reservoir to patient ≥ 5.0 ounces per minute with an input pressure of 1.25 psi at Reservoir (test performed with water). • < 0.5 ml of fluid leakage when connecting/disconnecting Connector to Skin-Port. • Torque required to open and close Skin-Port valve: ≥ 3 in-oz and ≤ 42 in-oz. • Companion shall be able to support weight of full Reservoir, infuse water, and perform rinse functions.	Pass
AspireAssist System	Mechanical Integrity Testing to verify integrity connection points.	Connections between system components must meet following pre-specified minimum tensile strengths: • Connector to Skin-Port: > 14 lbs • Skin-Port to A-Tube: > 8 lbs	Pass
AspireAssist System	Interconnect Function Testing to verify function of Connector to Skin-Port interconnect.	Torque required to open and close Skin-Port valve when connected to Connector or disconnected from Connector must be ≥ 3 in-oz and ≤ 42 in-oz.	Pass

Device Components	Test Description	Acceptance Criteria	Test Result
AspireAssist System	Aspiration Flow Rate Test to verify flow through AspireAssist System.	System shall allow an aspiration flow ≥ 75 fluid ounces per minute when fully assembled and tested using water.	Pass
AspireAssist System	Shipping Test Verify function of AspireAssist non-sterile components after being subjected to simulated shipping.	System must meet following pre-specified requirements after having been tested in accordance to ISTA Test Protocol 3A guidelines • Counter feature accuracy must be +/- 10%. • No leaks in System, with Drain Tube occluded by Companion and A-Tube clamped off on segment that resides in stomach, when subjected to hydrostatic pressure of 2.0psi for 5 minutes. • No leaks in System, with Skin-Port closed and A-Tube clamped off on segment that resides in stomach, when subjected to hydrostatic pressure of 2.0psi for 5 minutes. • Fluid flow from Reservoir to patient ≥ 5.0 ounces per minute with an input pressure of 1.25 psi at Reservoir (test performed with water). • < 0.5 ml of fluid leakage when connecting/disconnecting Connector to Skin-Port. • Torque required to open and close Skin-Port valve: ≥ 3 in-oz and ≤ 42 in-oz.	Pass
A-Tube	Mechanical Integrity Testing to verify bond strengths of A-Tube assembly.	Assembly must meet following pre-specified tensile strength requirements after sterilization, after full duration of product shelf life, and after shipping test: • Guide Wire loop to Dilator: > 30 lbs • Dilator to Leader Tube: >18 lbs • Leader Tube to A-Tube Proximal Segment: > 18 lbs • A-Tube Proximal Segment to A-Tube Distal Segment: > 18 lbs • Bumper shall not pull through 12.7mm hole at < 12 lbs	Pass
A-Tube	Radiopacity Test to verify A-Tube is visible under x-ray.	A-Tube shall be visible under x-ray when tested in accordance to ASTM F640 Radiopacity Test.	Pass

Device Components	Test Description	Acceptance Criteria	Test Result
A-Tube with Skin-Port	MRI Safe Test to verify A-Tube with Skin-Port attached is MRI safe.	A-Tube with Skin-Port attached is confirmed to be MRI safe when tested in accordance to ASTM F-2119-07 Standard Test Method for Evaluation of MR Image Artifacts from Passive Implants.	Pass
Skin-Port Installation Tool Kit	Functional Tests Tests to verify function of Skin-Port Installation Tool Kit.	Components provided in Skin-Port Installation Tool Kit must demonstrate they are capable of performing these functions: • Separate Skin-Port Valve from Skin-Port Flange without damage to components. • Prevent flow of fluid from A-Tube during Skin-Port removal, A-Tube shortening, and Skin-Port attachment. • Cut A-Tube to proper length. • Attach and seal Skin-Port to A-Tube along length of proximal segment of A-Tube as close to 3.0cm from bumper.	Pass
Companion	Drop Test Test to verify function of Companion after drop on hard surface.	Companion must meet following pre-specified requirements after having been dropped from 1 meter onto hardwood board lying flat on concrete surface, dropped on all six sides: • No leaks in System, with Drain Tube occluded by Companion and A-Tube clamped off on segment that resides in stomach, when subjected to hydrostatic pressure of 2.0psi for 5 minutes. • Fluid flow from Reservoir to patient is ≥ 5.0 fluid ounces per minute with an input pressure of 1.25 psi at Reservoir (tested with water).	Pass
Companion	Mechanical Integrity Test to verify mechanical integrity of neck strap and hanging feature.	Both Neck Strap and Companion hanging feature must withstand 5 lbs for 15 minutes without cracking or breaking.	Pass

B. Additional Studies

Biocompatibility

The AspireAssist patient contacting device components were subjected to biocompatibility testing in accordance with the requirements of ISO 10993-1:2009. Patient contacting components include the A-tube, Skin-Port, Introducer, and the

Flow Path (Reservoir, Companion, and Tubing set). All biocompatibility testing was conducted in compliance with GLP Regulations per 21 CFR Part 58.

The A-tube component is categorized as an implant (tissue contact) device with permanent exposure (> 30 days). The results of biocompatibility testing for the A-tube are summarized in **Table 2**.

Table 2. AspireAssist A-Tube Biocompatibility Testing

Biocompatibility Test	Acceptance Criteria	Test Results
Evaluation and Testing Within a Risk Management Process	Must comply with test requirements according to ISO 10993-1	Pass
Cytotoxicity Study using the ISO Elution Method	Must meet pre-specified criteria according to ISO 10993-5	Pass
ISO Maximization Sensitization Study – Extract	Must meet pre-specified criteria according to ISO 10993-10	Pass
ISO Intracutaneous Study Reactivity– Extract	Must meet pre-specified criteria according to ISO 10993-10	Pass
ISO Acute Systemic Toxicity Study – Extract	Must meet pre-specified criteria according to ISO 10993-11	Pass
13 Week Systemic Toxicity Study in Rats Following Subcutaneous Implant	Must meet pre-specified criteria according to ISO 10993-11	Pass
Genotoxicity: Bacterial Reverse Mutation Study	Must meet pre-specified criteria according to ISO 10993-3	Pass
Genotoxicity: Mouse Lymphoma Assay	Must meet pre-specified criteria according to ISO 10993-3	Pass
Genotoxicity: Mouse Peripheral Blood Micronucleus Study	Must meet pre-specified criteria according to ISO 10993-3	Pass
ISO Muscle Implantation Study – 4 week, 13 week	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

Biocompatibility Test	Acceptance Criteria	Test Results
Chemical Characterization of Materials	Must meet pre-specified criteria according to ISO 10993-18	Pass

A toxicological risk assessment based on the leachables/extractables compounds identified from chemical characterization for the A-tube 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 risks of toxicological concern to patients.

The flow path components of the device are categorized as an indirect contact (mucosal membrane) device for long term cumulative use in patients. The results of biocompatibility testing for the flow path components are summarized in **Table 3**.

Table 3. AspireAssist Flow Path Biocompatibility Testing

Biocompatibility Test	Acceptance Criteria	Test Results
Evaluation and Testing Within a Risk Management Process	Must comply with test requirements according to ISO 10993-1	Pass
Cytotoxicity Study using the ISO Elution Method	Must meet pre-specified criteria according to ISO 10993-5	Pass
ISO Maximization Sensitization Study – Extract	Must meet pre-specified criteria according to ISO 10993-10	Pass
ISO Intracutaneous Reactivity Study – Extract	Must meet pre-specified criteria according to ISO 10993-10	Pass
ISO Acute Systemic Toxicity Study – Extract	Must meet pre-specified criteria according to ISO 10993-11	Pass
Genotoxicity: Bacterial Reverse Mutation Study	Must meet pre-specified criteria according to ISO 10993-3	Pass
Genotoxicity: Mouse Lymphoma Assay	Must meet pre-specified criteria according to ISO 10993-3	Pass
Genotoxicity: Mouse Peripheral Blood Micronucleus Study	Must meet pre-specified criteria according to ISO 10993-3	Pass

Biocompatibility Test	Acceptance Criteria	Test Results
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 leachables/extractables compounds identified from chemical characterization for the flow-path device components 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 risks of toxicological concern to patients.

The Skin-Port component is categorized as a skin-contacting device with permanent exposure (> 30 days). The results of biocompatibility testing for the Skin-Port are summarized in **Table 4**.

Table 4. AspireAssist Skin-Port Biocompatibility Testing

Biocompatibility Test	Acceptance Criteria	Test Results
Evaluation and Testing Within a Risk Management Process	Must comply with test requirements according to ISO 10993-1	Pass
Cytotoxicity Study using the ISO Elution Method	Must meet pre-specified criteria according to ISO 10993-5	Pass
ISO Maximization Sensitization Study – Extract	Must meet pre-specified criteria according to ISO 10993-10	Pass
ISO Intracutaneous Reactivity Study – Extract	Must meet pre-specified criteria according to ISO 10993-10	Pass
ISO Acute Systemic Toxicity Study – Extract	Must meet pre-specified criteria according to ISO 10993-11	Pass
Genotoxicity: Bacterial Reverse Mutation Study	Must meet pre-specified criteria according to ISO 10993-3	Pass
Genotoxicity: Mouse Lymphoma Assay	Must meet pre-specified criteria according to ISO 10993-3	Pass

Biocompatibility Test	Acceptance Criteria	Test Results
Genotoxicity: Mouse Peripheral Blood Micronucleus Study	Must meet pre-specified criteria according to ISO 10993-3	Pass

Sterilization, Packaging, and Shelf Life

The AspireAssist A-tube is provided sterile and are intended for single use. Sterilization validation testing was performed in accordance with the guidelines of ISO 11135-1:2014, *Sterilization of Health Care Products – Ethylene Oxide*. Validation was conducted to demonstrate a sterility assurance level (SAL) of 10^{-6} sterilization. Testing for the A-tube is summarized in **Table 5**.

Table 5. Summary of Sterility Testing

Sterility Test	Acceptance Criteria	Test Results
A-Tube EtO Sterilization Validation by Adoption	Must meet pre-specified criteria according to AAMI TIR 28 & ANSI/AAMI/ISO 11135	Pass
Ethylene oxide sterilization residuals	Must meet pre-specified criteria according to ISO 10993-7	Pass
Bacterial Endotoxins Test, or *Limulus* Amebocyte Lysate (LAL) test	Must meet pre-specified criteria according to ANSI/AAMI ST72 USP <161> & USP <85>	Pass
Bioburden Testing	Must meet pre-specified criteria according to ANSI/AAMI/ISO 11737-1	Pass
Shelf Life Testing (expiration dating 1 year) accelerated aging	Must meet pre-specified criteria according to ASTM F 1980-07	Pass
Shelf Life Testing (expiration dating 3 year) accelerated aging	Must meet pre-specified criteria according to ASTM F 1980-07	Pass

Packaging validation testing was performed in accordance with the requirements of ISO 11607-1:2009, *Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems and packaging systems*.

After accelerated aging equivalent to 36 months of shelf life and simulated shipping conditioning, the packaging for the components was evaluated to ensure that package integrity was maintained over the shelf life. The devices were also evaluated to determine whether the device functionality was maintained. The shelf life and packaging testing demonstrated that the packaging protects the device and the device maintains performance for a 36-month shelf life.

The remaining device components are provided non-sterile. Shelf-life testing was conducted under accelerated aging conditions to support device functionality for a 6-month shelf-life.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed clinical studies to establish a reasonable assurance of safety and effectiveness of the AspireAssist device for weight loss in the US. Clinical data supporting the safety and effectiveness of the AspireAssist are available from two (2) clinical studies, the IDE feasibility study and the IDE pivotal study. The feasibility study was conducted under G080134. The data obtained from the pivotal study, conducted under IDE G120045, constitutes the main dataset to support safety and effectiveness of the AspireAssist device and were the basis for the PMA approval decision. A summary of the studies are presented below.

Feasibility Study

This study was a randomized, controlled, open-label, 12-month trial conducted at a single study site within the US. Subjects were randomized to treatment with either the AspireAssist, which includes the AspireAssist plus lifestyle therapy (AT Group) or to lifestyle therapy alone (behavior education, diet and exercise) (Control Group) in a 2:1 ratio, respectively. Eighteen (18) obese subjects, 11 in the AT group (BMI: 42.6 ± 4.7 kg/m^2) and seven (7) in the control group (BMI: 43.4 ± 5.3 kg/m^2), were enrolled in the study. A-Tube placement was successful in all AT subjects. One (1) subject withdrew from the study after four (4) weeks of therapy because of abdominal discomfort.

No serious adverse events were reported during the feasibility study. Minor adverse events in the AT Group included discomfort at the A-Tube site during the first week after implantation and abdominal discomfort after the first week (successfully treated with medication). The most common adverse events include constipation, bloating, nausea, peristomal skin irritation, peristomal bleeding, and sore throat post A-tube placement. Plasma electrolytes, renal function tests, liver biochemistries, and specific nutritional markers (serum vitamin B12, vitamin D concentration, and prothrombin time) were stable throughout the study. No adverse psychological effects or adverse effects on eating behavior associated in the AT Group were detected.

At 52 weeks of therapy, the mean %EWL[3] was 49.0%±24.4% (45.3 ± 17.2 lbs) in the AT group (n=10) and 14.9%±24.6% (13.6 ± 23.3 lbs) in the control group (n=4). Successful weight loss (≥ 25% EWL) was achieved in 100% of the AT group. Seven (7) of the subjects in the AT group elected to continue in the study past the 52-week time point.

PATHWAY Pivotal Study

A. Study Design

The PATHWAY Pivotal Trial, was a prospective, randomized, multi-center, controlled, open-label, 52-week clinical study. Patients were enrolled between 11/13/2012 and 6/13/2014. The database for this PMA reflected data collected through 6/24/2015 and included 111 treatment and 60 control patients. There were ten (10) investigational sites.

Screened subjects who met inclusion and exclusion criteria, were randomized in a 2:1 ratio to the AT Treatment Group (use of the AspireAssist plus Lifestyle Therapy) or to a Control Group (Lifestyle Therapy). Lifestyle therapy was a program provided to all subjects which consisted of behavior education, diet, and exercise with 10 visits over the 52-week period.

The primary effectiveness endpoint assessments occurred at 52-weeks. At each annual visit AspireAssist (AT) subjects were given the option to continue in the study for an additional year up to a total of 5 years if a minimum of 10% total body weight loss (TBL) was maintained. AT subjects who achieved 5 to 9.9% TBL were considered for study continuation if they enrolled in an enhanced coaching sub-study. AT subjects who did not meet these criteria underwent device removal and were followed for 6 months (3 visits) to assess adverse events (AEs), fistula tract closure, weight maintenance, and concomitant medications. Control subjects exited the study at 52-weeks.

The study was a randomized 52-week comparison of treatment and control conditions, comparing the AT Treatment Group mean percent excess weight loss (%EWL) to the Control Group. The AT Treatment Group responder rate dichotomized at 25% EWL was also assessed.

The analyses for safety and effectiveness were based on a comparison of the all enrolled and treated subjects that were randomized to the AT Treatment Group or the Control Group (modified Intent-to-Treat or "mITT" population). Treated subjects in the AT Treatment Group include subjects that received the device and started Lifestyle Therapy and treated subjects in the Control Group include those that started Lifestyle Therapy. Subjects who were randomized but withdrew before treatment are not included in the primary analysis population.

[3] %EWL is calculated using ideal weight corresponding to a BMI=25.

1. Clinical Inclusion and Exclusion Criteria

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

   - Measured BMI of 35.0-55.0 kg/m^2 at time of screening.
   - 21- 65 years of age (inclusive) at time of screening.
   - Failed attempt for a duration equal to 3-months at weight loss by alternative approaches (e.g. supervised or unsupervised diets, exercise, behavioral modification programs).
   - Stable weight (<3% change in self-reported weight) over the previous 3 months at time of screening).
   - Women of childbearing potential must agree to use at least one form of birth control (prescription hormonal contraceptives, diaphragm, IUD, condoms with or without spermicide, or voluntary abstinence) from time of study enrollment through study exit.
   - Willing and able to provide informed consent in English and comply with the protocol.

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

   - Previous abdominal surgery that significantly increases the medical risks of gastrostomy tube placement.
   - Esophageal stricture, pseudo-obstruction, severe gastroparesis or gastric outlet obstruction, inflammatory bowel disease.
   - History of refractory gastric ulcers.
   - Ulcers, bleeding lesions, or tumors discovered during endoscopic examination.
   - History of radiation therapy to the chest or abdomen.
   - Uncontrolled hypertension (blood pressure >160/100).
   - Diabetes treated with insulin or sulfonylurea medications.
   - Any change in diabetes medication in previous 3 months.
   - Hemoglobin A1C >9.5%.
   - History or evidence of serious pulmonary or cardiovascular disease, including acute coronary syndrome, heart failure requiring medications, or NYHA (New York Heart Association) class III or IV heart failure (defined below):
     - Class III: patients with marked limitation of activity and who are comfortable only at rest
     - Class IV: patients who should be at complete rest, confined to bed or chair and who have discomfort with any physical activity
   - Coagulation disorders (platelets < 100,000, PT > 2 seconds above control or INR > 1.5).
   - Anemia (Hemoglobin <11.0 g/dL in women and <12.5 g/dL in men).
   - Liver enzymes (ALT and AST) ≥3.0 times the upper limit of normal.

- Thyroid Stimulating Hormone (TSH) >1.5 x upper limit of normal at screening.
- Osteoporosis (DEXA T-Score ≤ -2.5 standard deviations below normal peak values).
- History of fragility fractures (fractures resulting from a fall from a standing height or less, or presenting in the absence of obvious trauma).
- Pregnant or lactating.
- Diagnosed Bulimia or diagnosed Binge Eating Disorder (using DSM IV criteria).
- Night Eating Syndrome (diagnosed by Eating Disorder Examination (EDE)).
- Serum potassium < 3.8 mEq/L.
- Chronic abdominal pain that would potentially complicate the management of the device.
- Taking a GLP-1 agonist < 6 months.
- Taking prescription or over-the-counter medications for weight loss in the last 3 months before screening, or planning to participate in a commercial weight loss program in the next 24 months. This includes taking medications for an unrelated medical condition which have been shown to result in weight loss such as Topiramate or Bupropion.
- Taking medication once or more per week that causes weight gain (e.g., atypical antipsychotics, monoamine oxidase inhibitors, lithium, selected anticonvulsants, tamoxifen, glucocorticoids).
- Self- reported history of substance abuse in last 3 years.
- Malignancy in the last 5 years (except for non-melanoma skin cancer).
- Physical or mental disability or psychological illness that could interfere with compliance with the therapy.
- At high risk of having a medical complication from the endoscopic procedure or AspireAssist therapy weight loss program for any reason, including poor general health or severe organ dysfunction, such as cirrhosis or renal dysfunction (GFR <60 mL/min/1.73 m^2 at screening, calculated by using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation).

2. Follow-up Schedule

All study subjects were required to participate in Lifestyle Therapy approximately once per month for the first 12 months of the study. This therapy consisted of individual Lifestyle Therapy sessions lasting 20-30 minutes and group sessions lasting about 60 minutes. Topics include includes nutritional, physical activity, and behavioral education topics. Subjects were taught to follow a structured eating plan, which involved eating 3 meals a day, eating slowly and chewing food well, drinking plenty of fluids with each meal, and limiting snacking between meals. Physical activity topics included the health benefits of physical activity and strategies for increasing lifestyle activity. The behavioral program emphasized strategies of self-monitoring and goal-setting, and included problem-solving, dealing with high-risk situations/cues for unhealthy eating, and stress management.

Tables 6 and 7 summarize the scheduled visits and assessments for the AT Treatment Group and Control Group, respectively.

Table 6. AspireAssist Treatment Schedule

Screening	Implantation	Skin-Port Placement (Week 0, 14 +/- 4 days after implant)	Follow-up Visits (Weeks 2, 6, 10, 14, 20, 24, 28, 32, 36, 40, 44, 48, 52 weeks +/- 7 days)
• Informed Consent • Screening Interview (Inclusion/ Exclusion Assessment) • Medical History & Physical Exam • EKG • Psychological Assessments & Subject Questionnaires (IWQOL, QEWP, EDE) • Body Weight • Height • Urine (Pregnancy, Protein) • Clinical Lab Assessment (CMP + Magnesium, CBC, PT/PTT, TSH, Lipid Panel, Iron, Vitamin D, Hemoglobin A1C, Hemoglobin) • DEXA (Hip, Spine)	• Body Weight • Device Implantation	• Skin Port placement, AspireAssist Training • Medical Visit (weight, vital signs, concomitant medications, AE's) • Lifestyle Therapy • Urine Protein	• Psychological Assessments & Subject Questionnaires (IWQOL, QEWP, EDE) (weeks 14, 28 and 52) • Medical Visit (weight, vital signs, concomitant medications, AE's) • Lifestyle Therapy • Urine Protein • Electrolyte Panel, Magnesium, Calcium • CMP + Magnesium, Lipid Panel (weeks 28 and 52) • CBC, Vit D, DEXA (52 weeks) • Hemoglobin and Hematocrit (weeks 14 and 28) • Iron, Hemoglobin A1C (weeks 14, 28 and 52)

Table 7. Lifestyle Therapy Treatment Schedule

Screening	Initiation	Week 2 Visit (14 +/- 2 days)	Follow-up Visits (Week 6, 10, 14, 20, 24, 28, 32, 36, 40, 44, 48, 52 weeks +/- 7 days)
• Informed Consent • Screening Interview (Inclusion/Exclusion Assessment) • Medical History & Physical Exam • EKG • Psychological Assessments & Subject Questionnaires (IWQOL, QEWP, EDE) • Body Weight • Height • Urine (Pregnancy, Protein) • Clinical Lab Assessment (CMP + Magnesium, CBC, PT/PTT, TSH, Lipid Panel, Iron, Vitamin D, Hemoglobin A1C, Hemoglobin) • DEXA (Hip, Spine)	• Medical Visit (weight, vital signs, concomitant medications, AE's) • Lifestyle Therapy	• Medical Visit (weight, vital signs, concomitant medications, AE's) • Lifestyle Therapy	• Psychological Assessments & Subject Questionnaires (IWQOL, QEWP, EDE) (weeks 28 and 52) • Medical Visit (weight, vital signs, concomitant medications, AE's) • Lifestyle Therapy • Urine Protein • Electrolyte Panel, Magnesium, Calcium • CMP + Magnesium, Lipid Panel (weeks 28 and 52) • CBC (52 weeks) • Hemoglobin and Hematocrit (weeks 14 and 28) • Hemoglobin A1C (weeks 14, 28 and 52)

The key timepoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

With regards to safety, the PATHWAY study included a complete review of the incidence of procedure-related, device-related, and therapy-related adverse events, as well as the incidence of device related, or unrelated, serious adverse events, including unanticipated adverse device effects. In addition, the development of

adverse eating behaviors has been assessed. There was no pre-specified primary safety endpoint for the PATHWAY Pivotal Study.

With regards to effectiveness, the PATHWAY Pivotal Trial had two (2) co-primary effectiveness endpoints, consisting of

- To demonstrate a mean difference of at least 10% EWL (measured by the BMI method) between the AT Treatment Group and the Control Group (super-superiority) at 52 weeks of therapy.
- To demonstrate at least a 50% responder rate in the AT Treatment Group, as defined by %EWL of at least 25% (measured by the BMI method) at 52 weeks.

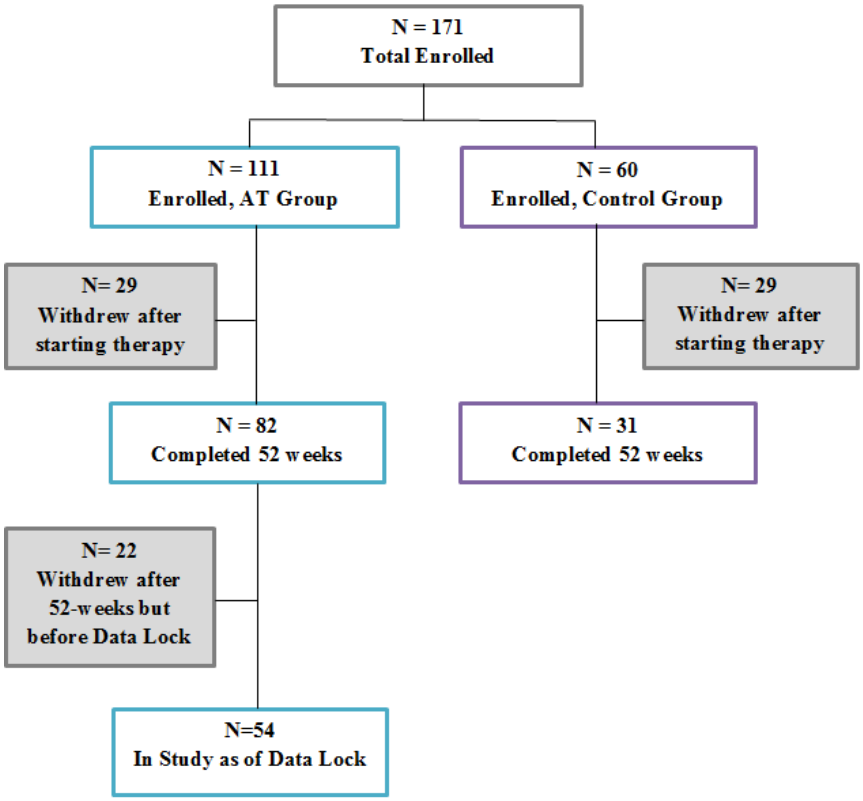
With regard to success/failure criteria, both primary effectiveness endpoints must be met for the study to be considered a success.

B. Accountability of PMA Cohort

Two hundred eighty-two (282) subjects were screened and 75 failed to meet study criteria. The remaining 137 subjects were randomized to the AT Treatment Group and 70 subjects were randomized to the Control Group. Prior to study enrollment (treatment) 26 AT and 10 control subjects dropped out; therefore, the study enrolled a total of 171 (111 AT and 60 control) subjects (mITT population). Twenty-nine (29) subjects withdrew from each group prior to 52 weeks. Therefore, at the time of the database lock a total of 82 (73.9%) AT and 31 (51.7%) Control subjects completed the 52-week study. Twenty-two (22) subjects withdrew after 52-weeks; 20 of these subjects did not meet the criteria to continue in the study and two (2) subjects declined to participate further. Therefore, 60 subjects continued to participate in the study and provided safety and effectiveness data after 52-weeks. However, at the time of data lock only 54 subjects remained in the study.

A subject accountability flowchart is presented in **Figure 7**.

Figure 7. Subject Accountability Chart



Of the 111 AspireAssist subjects who enrolled in the study, 29 withdrew from the study prior to 52-weeks. Of these 29 subjects, five (5) subjects moved out of the area, one (1) subject had unrelated health issues, 22 subjects withdrew due to subject decision (e.g., lack of time to aspirate, no motivation, nausea or discomfort, lack of efficacy, and intimacy issues), and one (1) subject withdrew due to an adverse event (abdominal discomfort).

Of the 60 Control subjects who enrolled in the study, 29 withdrew prior to 52-weeks. The primary reasons were lack of time for study visits, unhappy with group assignment, and unrelated health issues.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an obesity pivotal study performed in the US.

Review of demographic data showed a high degree of comparability between Treatment (AT) and Control subjects in regards to BMI distribution, physical, race, and ethnicity parameters as shown by **Tables 8 to 10**.

Table 8. BMI Distribution for Each Treatment Group

Treatment Group	BMI (kg/m^2)	Number Enrolled (% of group)
AT	35.0 -39.9	45 (40.5)
AT	≥ 40	66 (59.5)
Control	35.0 -39.9	30 (50.0)
Control	≥ 40	30 (50.0)

Table 9. Baseline Information for Enrolled Subjects

Description	Mean±Std Dev (AT)	Mean±Std Dev (Control)
N	111	n=60
Sex (M/F)	15 (13.5%)/96 (86.5%)	7 (11.7%)/53 (88.3%)
Age (years)	42.4±10.0	46.8±11.6
Height (cm)	166.3±8.2	165.7±8.0
Baseline Weight (kg)	116.9±21.2	112.8±16.1
Baseline BMI (kg/m^2)	42.0± 5.1	40.9 ± 3.9

Table 10. Demographic Information for Enrolled Subjects

		n (%) (AT)	n (%) (Control)
Race	Caucasian	74 (66.7%)	42 (70.0%)
	African American	33 (29.%7)	17 (28.3%)
	Other	4 (3.6%)	1 (1.7%)
Ethnicity	Hispanic	11 (10.0%)	11 (18.3%)
	Not Hispanic	100 (90.0%)	49 (81.7%)

D. Safety and Effectiveness Results

1. Safety Results

Safety assessment of the AspireAssist included a complete review of the incidence of procedure-related, device-related, and therapy-related adverse events, as well as the incidence of device related, or unrelated, serious adverse events, including unanticipated adverse device effects. In addition, the development of adverse eating behaviors has been assessed. There was no pre-specified primary safety endpoint for the PATHWAY Pivotal Study. The analysis of safety was based on the 111 Treatment Subjects randomized to receive the device.

The key safety outcomes for this study are presented below in **Tables 11 to 14**.

a. Serious Adverse Events

Within the first 52 weeks, there were five (5) Serious Adverse Events (SAEs) related to the device or procedure, involving four (4) out of 111 AspireAssist subjects, yielding a related-SAE rate of 3.6% (95% CI: 0.1%-7.1%).

None of the SAEs resulted in death or permanent injury to the subject and were either of short-duration or, if the event lasted more than 3 days, had minimal impact on the subject's quality of life. Each of these five (5) SAEs are described in **Table 11** below.

Of the subjects that experienced a device or procedure-related SAE, all had a BMI at less than 40 kg/m^2 at the time of the reported event.

Table 11. Summary of all SAEs

Adverse Event	n (%) Subjects	N Events
SAEs Related to the Device		
A-Tube Replaced	1 (0.9%)	1
SAEs Related to the Procedure		
Peritonitis (mild pneumo-peritoneum without abscess)	1 (0.9%)	1
Abdominal pain post procedure	1 (0.9%)	2
Non-bleeding pre-pyloric ulceration	1 (0.9%)	1*

*Event recorded at week 53

There was one (1) SAE after the 52-week study period which involved one (1) subject who experienced a small opening in the tissue just superior to the A-Tube stoma site.

b. Adverse Events

Table 12 describes a summary of the most common device and procedure-related adverse events (AEs) which occurred in ≥ 5% of AspireAssist subjects over the 52 week study period. The most common adverse events were similar in nature to those with standard PEG tube placement, and include peristomal granulation tissue, pain, abdominal discomfort, and nausea/vomiting. As shown in **Table 12**, the majority of events, with the exception of granulation tissue, were acute and resolved within the first 7 days. These events were also generally mild in severity with only two events described by the subject as severe.

Table 12: Most Common Adverse Events Related To the Device or Procedure

AE Category	N (%) N=111	Onset	Duration				Severity** Number of events total/N (%)	Number of events occurring within 7 days total/N (%)
		Mean Median Range (days)	Mean Median Range (days)	N (%) Onset ≤7 days	N (%) >14 days	N (%) >30 days	Mild Moderate Severe	Mild Moderate Severe
Peristomal Granulation Tissue	45 (40.5)	118.3 79 19-380	312.5 131 0-787	0 0 0	45/45 (100.0)	40/45 (88.9)	41/45 (91.1) 3/45 (6.7) 1/45 (2.2)	0 0 0
Pain, abdominal ≤ 4 weeks after A-Tube placement	42* (37.8)	0.26 0 0-3	19.3 13 1-160	42/42 (100.0)	12/42 (28.6)	4/42 (9.5)	18/42 (42.8) 24/42 (57.1) 1/42 (2.4)	17/42 (40.5) 24/42 (57.1) 1/42 (2.4)
Peristomal bleeding, discharge, inflammation, irritation	34 (30.6)	101 52.5 0-383	68.1 31 3-503	10/34 (34.5)	0/34 (0)	0/34 (0)	29/34 (85.3) 5/34 (14.7) 0	9/34 (26.5) 1/34 (2.9) 0
Nausea/ Vomiting	21 (18.9)	45.2 0 0-366	10.1 3 0-108	15/21 (71.4)	1/21 (4.8)	1/21 (4.8)	11/21 (52.4) 10/21 (47.6) 0	8/21 (38.1) 7/21 (33.3) 0
Abdominal discomfort, intermittent	21 (18.9)	20.1 1 0-147	44.1 13 3-297	16/21 (76.2)	5/21 (23.8)	4/21 (19.0)	15/21 (71.4) 6/21 (28.6) 0	11/21 (52.4) 5/21 (23.8) 0
Other, Peristomal bacterial infection/ possible infection	16 (14.4)	4.2 4 1-7	12.6 10 7-45	13/16 (81.3)	2/16 (12.5)	1/16 (6.3)	15/16 (93.8) 1/16 (6.3) 0	12/16 (75.0) 1/16 (5.3) 0
Pain, abdominal > 4 weeks after A-Tube placement	9 (8.1)	163 94 32-376	49.4 28 1-136	0 0 0	9/9 (100.0)	9/9 (100.0)	3/9 (33.3) 6/9 (66.7) 0	0 0 0
Change in bowel habits	5 (4.5)	1.3 0.5 0-4	121.3 11 4-459	4/5 (80.0)	1/5 (20.0)	1/5 (20.0)	5/5 (100.0) 0 0	4/5 (80.0) 0 0

*One subject reported two (2) AEs for pain.

**Severity: *Mild*: symptoms tolerated with some difficulty; *Moderate*: interference with normal daily activities; *Severe*: requires hospitalization

A total of 228 related adverse events were reported by 93 subjects during study year one. As shown in **Table 13**, a total of 228 related adverse events (including the 5 SAEs described in **Table 11**), have been reported by 93 (83.8%), AT subjects. On average, each AT subject experienced 2.5 related adverse events within the first 52-weeks.

Table 13. Adverse Events ≤ 52weeks

Event description	# of events	# of subjects	% of subjects (N=111)
Peristomal granulation tissue	45	45	40.5%
Pain, abdominal ≤ 4 weeks after A-Tube placement	43	42	37.8%
Abdominal discomfort, intermittent	21	18	16.2%
Nausea/vomiting	21	20	18.0%
Peristomal irritation	21	19	17.1%
Other: Peristomal bacterial infection confirmed/Possible infection (symptoms not confirmed by culture, antibiotic prescribed in most cases)	16	15	13.5%
Hypokalemia	9	4	3.6%
Pain, abdominal >4 weeks after A-Tube placement	9	9	8.1%
Other: dyspepsia (acid reflux, heartburn, hiccups, belching)	7	7	6.3%
Peristomal inflammation	6	6	5.4%
Peristomal discharge	5	5	4.5%
Change in bowel habits (Constipation/diarrhea/loose stools)	5	5	4.5%
Accidental A-Tube dislodgement or trauma	3	3	2.7%
Peristomal bleeding	2	2	1.8%
Fungal infection, peristomal	2	2	1.8%
Miscellaneous single events*	13	13	0.9%
TOTAL related AEs/AADEs (for 111 AT subjects)	**228**	**93****	**83.8%**

*Others: (1) A-Tube Replacement, (1) broken front tooth veneer, (1) buried bumper, (1) ecchymosis, (1) fever, (1) free-air in abdomen (anticipated after tube placement), (1) peristomal ulceration, (1) persistent fistula, (1) worsening bilateral leg edema, (1) pain (hand), (1) pain (substernal discomfort), (1) peritonitis, (1) stomach spasm. Each event occurred once in one subject, so the % of subjects experiencing each event is 0.9%.

**Totals do not add as some subjects had more than one adverse event

Table 14 describes adverse events which occurred after 52 weeks and are generally similar in nature to the adverse events prior to 52 weeks. The last three (3) events include one (1) subject who felt that she was overeating in the evening, one (1) subject with a mild ulceration which did not require treatment, and the persistent fistula is reported above as the post 52 week SAE where there was a small tissue opening which developed above the stoma site.

Table 14. Related AEs >52-weeks

Event description	Number of events	Number of subjects (%) N=60*
Peristomal granulation tissue	3	3 (2.7)
Pain, abdominal >4 weeks after A-Tube	3	3 (2.7)
Peristomal irritation	1	1 (0.9)
Abdominal discomfort, intermittent	1	1 (0.9)
Bacterial infection, peristomal	1	1 (0.9)
Hypokalemia	1	1 (0.9)
Other: eating disorder NOS	1	1 (0.9)
Other: gastric ulcer	1	1 (0.9)
Persistent fistula	1	1 (0.9)
Total	**13**	13 (21.7)

*data is calculated based on the n=60 who continued therapy after 52 weeks

During the study one (1) AT subject was suspected of developing an eating disorder, but did not meet the EDE criteria compared to one (1) Control Subject who met the EDE criteria for binge eating and withdrew from the study. Therefore, no AT subjects developed binge eating, bulimia, or night-eating disorder as measured by the Eating Disorder Examination within 52-weeks.

2. Effectiveness Results

The analysis of effectiveness was based on the 111 Treatment Subjects randomized to receive the device.

a. Primary Endpoint Outcome

The analysis of effectiveness was based on the 111 AT Treatment Group and 60 Control Group subjects in the modified Intent-to-Treat (mITT) population at 52 weeks with multiple imputations for missing values (subjects that withdrew prior to 52 weeks). Key effectiveness outcomes are presented in **Tables 15 and 16**.

The PATHWAY Pivotal Trial met its first co-primary effectiveness endpoint. The intent-to-treat mean %EWL for AT Treatment Subjects was 31.5% and 9.8% for Control Subjects at 52 weeks, giving a mean difference in %EWL of 21.7% (95% CI, 15.3% to 28.1%). The p-value for the superiority test for a 10.0% superiority margin was 0.0083, demonstrating that the treatment subjects had a weight loss significantly greater than that for Control Subjects plus a superiority margin of 10.0 % EWL, as seen in **Table 15**.

Table 15. Summary of Primary Effectiveness Endpoint #1

Method	N (AT)	N (Control)	Mean %EWL (AT)	Mean %EWL (Control)	Difference in Mean %EWL (95% CI)	P value (10% Delta)
Modified Intent-to-Treat	111	59*	31.5	9.8	21.7 (15.3, 28.1)	0.0083

*One Control subject withdrew after the first visit and therefore lacks sufficient data for multiple imputations.

The second co-primary effectiveness endpoint for the PATHWAY study was not met. The mITT-treated subjects who achieved a 25% EWL or greater weight loss at 52 weeks was 56.8% (95% CI, 49.0% to 64.5%), with a lower confidence bound of 49.0%, which was not significantly greater than the required responder rate of 50% ($p < 0.0001$), as seen in **Table 16**. Note: In the Control Group, 15.3% (95% CI, 8.2% to 25.1%) were responders.

Table 16. Summary of Co-Primary Effectiveness Endpoint #2

	Number of subjects	Number of Responders	Responder Rate	P value 50% Responder Rate
AT	111	63	56.8% (49.0, 64.5)	.0754
Control	60	13	22.0% (12.1, 29.9)	1.0000

3. Additional Analyses

Tables 17 to 19 below include additional effectiveness analyses in the per-protocol study population. This population includes all treated subjects who completed the scheduled follow-up visits up to and including 52-weeks. The study showed that the per-protocol AT Treatment Group achieved 37.2% EWL as compared to 13.0% EWL in the Control Group. Additionally, 68.3% of the per-protocol AT Treatment Group achieved a 25% EWL or greater weight loss at 52 weeks.

Table 17. Co-Primary Efficacy Endpoint #1 (Per-Protocol Population)

Analysis Population	N (Control)	N (AspireAssist)	Mean %EWL (Control)	Mean %EWL (AspireAssist)	Difference in Mean %EWL (95% CI)	P value (10% Delta)
Per-Protocol	31	82	13.0	37.2	24.2 (15.5, 32.9)	0.0038

Table 18. Co-Primary Efficacy Endpoint #2 (Per-Protocol Population)

Analysis Population	Group	Number of subjects	Number of Responders	Responder Rate (95% CI)	P value (50% Responder Rate)
Per-Protocol	AspireAssist	82	56	68.3% (58.8, 76.7)	0.0002
	Control	31	8	25.8% (13.5, 41.8)	0.9990

Secondary effectiveness outcomes for the study at 52 weeks were: 1) Mean percent absolute weight loss in the AT Treatment Group compared to the Control Group, 2) proportion of subjects who achieve ≥10% absolute weight loss in the AT Treatment Group compared to the Control Group, 3) mean percent change serum lipids (triglyceride, HDL-cholesterol and LDL-cholesterol concentration) in the AT Treatment Group compared to the Control Group; 4) mean percent change in systolic and diastolic blood pressures in the AT Treatment Group compared to the Control Group; 5) "Impact of Weight on Quality of Life" (IWQOL) questionnaire; 6) change in mean hemoglobin A1C (only subjects with Type 2 diabetes at baseline), 7) percent procedural success (defined as successful endoscopic placement of the A-Tube) in all subjects undergoing endoscopy; and 8) mean percent change in medications.

The outcomes for the secondary endpoints 1 and 2 are included in **Table 19** below:

Table 19. Summary of Secondary Efficacy Weight Loss Endpoints 1 and 2 (mITT)

Parameter	Unit of Measure	Control	AspireAssist	Difference (AspireAssist – Control)	Difference (95% CI)
% TBL	Mean Percent TBL	3.6	12.1	8.6	6.2, 10.9
≥10% TBL	Percent of Subjects	22.1	58.6	36.5	24.84, 48.21

The study was not powered for assessment of changes and did not include a pre-determined endpoint for factors associated with health improvements; however, data were collected to measure changes in comorbid conditions and quality of life (secondary endpoints 3 to 6). Results suggest that there were small, but not statistically significant, improvements in comorbid parameters for diabetes, hypertension, hyperlipidemia, and quality of life from baseline to 52 weeks in the AT Treatment and Control Groups. These small improvements were likely attributable to factors shared by the AT Treatment Group and the Control Group, such as Lifestyle Therapy.

For secondary endpoint 7, out of 114 endoscopies attempted in 112 subjects, there were 111 successful A-Tube placements. Excluding the two (2) aborted procedures in subjects who had contraindications for A-Tube placement, there were 111 successful A-Tube placements in 112 endoscopy attempts, yielding a procedure success rate of 99%. In one subject, adequate transillumination could not be obtained initially and the procedure was aborted; however, in a subsequent procedure transillumination was successfully obtained by repositioning this subject.

The 8th secondary endpoint is the mean change in medications from baseline. The total number of medications taken at baseline for the three (3) comorbidities identified as secondary endpoints: hypertension, dyslipidemia, and Type 2 diabetes for subjects that have completed 52 weeks were evaluated. Over the course of therapy, both the AT Treatment Group and the Control Group saw a decrease in the total number of medications and the average number of medications per subject. There were also several subjects who stopped all medication for a specific comorbidity.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 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 10 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 and Urology Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The PATHWAY pivotal study had two (2) co-primary effectiveness endpoints, only one (1) which was met. However, these endpoints demonstrated that the AspireAssist treatment was more effective than a lifestyle therapy behavior modification program alone for 52 weeks.

The first co-primary endpoint specified that AspireAssist (AT) Treatment Group would achieve a mean percent excess weight loss (%EWL) that was significantly greater than the Control Group by a superiority margin of 10.0 at 52 weeks. The average %EWL at 52 weeks was 31.5% for the AT Treatment Group and 9.8% for the Control Group, resulting in an average difference between the AT Treatment Group and Control Group of 21.7% (95% CI: [15.3, 28.1%]).

The second co-primary endpoint specified that significantly greater than 50% of subjects in the AT Treatment Group would achieve greater than 25% EWL at 52 weeks. This endpoint was not met. The study demonstrated that 56.8% (95% CI: [49.0, 64.5%]) of subjects in the AT Treatment Group had achieved 25% EWL.

The study was not powered for assessment of changes and did not include a pre-determined endpoint for factors associated with health improvements; however, data were collected to measure changes in comorbid conditions and quality of life. Results suggest that there were small, but not statistically significant, improvements in comorbid parameters for diabetes, hypertension, hyperlipidemia, and quality of life from baseline to 52 weeks in the treatment and control groups. Additionally, over the course of therapy both the AT Treatment Group and the Control Group saw a decrease in the number of medications per subject. These small improvements were likely attributable to factors shared by the AT Treatment Group and the Control Group, such as Lifestyle Therapy.

B. Safety Conclusions

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

The PATHWAY pivotal study did not have a pre-specified safety endpoint. The safety assessment of the AspireAssist included a complete review of the incidence of procedure-related, device-related, and therapy-related adverse events, as well as the incidence of device related, or unrelated, serious adverse events, including unanticipated adverse device effects. In addition, the development of adverse eating behaviors has been assessed.

There were no unanticipated adverse device effects and no deaths that occurred in the pivotal study. The procedural risk was consistent with traditional gastrostomy tube placements.

There were five (5) Serious Adverse Events (SAEs) related to the device or procedure, involving 4 out of 111 AspireAssist subjects, yielding a related-SAE rate of 3.6% (95% CI: 0.1%-7.1%) within 52-weeks. There was one SAE after the 52 week study period which involved one subject who experienced a small opening in the tissue just superior to the A-Tube stoma site.

None of the SAEs resulted in death or permanent injury to the subject and were either of short-duration or, if the event lasted more than three days, had minimal impact on the subject's quality of life.

The most common AEs were related to the skin site stoma and included: peristomal granulation tissue, peristomal bleeding/irritation, and peristomal infection. There is no difference in the incidence of stomal issues for the A-tube as compared to traditional gastrostomy tubes. Other common AEs include, pain, nausea/vomiting, abdominal discomfort, and change in bowel habits.

The pivotal study reported that no AT Treatment Group subjects developed binge eating, bulimia, or night-eating disorder, as measured by the EDE within the first 52-weeks due to use of the AspireAssist device.

C. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in clinical studies conducted to support PMA approval as described above and is based on a demonstration of significant weight loss with the device compared to the behavior modification lifestyle therapy program. Specifically, there was 31.5% EWL and 12.1 %TBL in the AT Treatment Group compared to 9.8% EWL and 3.6% TBL in the Control Group at 52-weeks.

There are risks for patients developing adverse events related to the device. The most common AEs were related to the skin site stoma and included: peristomal granulation tissue, peristomal bleeding/irritation, and peristomal infection. However, there is no difference in the incidence of stomal issues for the A-tube as compared to traditional gastrostomy tubes. Other common AEs include: pain, nausea/vomiting, abdominal discomfort, and change in bowel habits. Most adverse events resolved within 30 days with the exception of peristomal granulation tissue.

Additional factors to be considered in determining probable risks and benefits for the AspireAssist device included the options currently available for the treatment of obesity. The effectiveness for the AspireAssist is less than what would be expected with gastric banding or other surgical interventions; however, the effectiveness is better than what would be expected with diet and exercise or pharmacologic therapy. Additionally, the benefit-risk of the AspireAssist device is favorable compared to other endoscopically placed obesity devices.

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 support that for the assistance in weight reduction of obese patient (i.e., in adults aged 22 or older with a Body Mass Index of 35.0-55.0 kg/mg^2 who have failed to achieve and maintain

weight loss with non-surgical weight loss therapy) 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 an overall mean %EWL of 31.5% in the AT Treatment Group as compared to 9.8% in the Control Group. Additionally, the finding that 56.8% of subjects in the AT Treatment Group achieved at least 25% EWL supports that the device is likely to be clinically effective in a significant portion of patients. Finally, the AspireAssist device has an acceptable safety profile.

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

XIII. CDRH DECISION

CDRH issued an approval order on June 14, 2016. The final conditions of approval cited in the approval order are described below.

1. *ODE Lead PMA Post-Approval Study - Extended Follow-up of the Premarket Cohort (PATHWAY Clinical Trial):* The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The Extended Follow-Up Study is a multicenter, single-arm prospective, active surveillance study designed to gather long-term data on the incidence, duration, and severity of adverse events, weight loss, compliance with AspireAssist therapy, impact of AspireAssist therapy on eating behavior and the effectiveness and safety outcomes after device removal. This study will continue to follow patients from the PATHWAY pivotal study for up to five years post implantation who maintain ≥ 10 % absolute weight loss (relative to baseline) at each annual visit. Any subject that has the device explanted will be followed for two years post device explantation. A total of 46 subjects are available for the extended follow-up study and will be invited to participate in the extended follow-up PAS.

   There are no pre-defined safety and efficacy endpoints for this active surveillance study. While the device is implanted, the safety of the device will be evaluated by: 1) the incidence of device-related, procedure-related, and therapy-related adverse events; 2) the incidence of device-related or unrelated serious adverse events, including unanticipated adverse device effects; and 3) development of adverse eating behaviors as measured by the Eating Disorder Examination (EDE) and the Questionnaire on Eating and Weight Patterns – Revised (QEWP-R). The efficacy of the device while implanted will be assessed by percent excess weight loss (%EWL) and total body loss (%TBL). Other efficacy study endpoints while the device is implanted include the change in obesity-related comorbidities (blood pressure, lipid levels, triglycerides, HbA1c) and change in medication. After the device is removed, patients will be followed for two years. During the first six months patients will be monitored for fistula closure, weight loss,

and adverse events and subjects with diabetes will be monitored for HbA1c, blood glucose, and diabetes medications. For six to 24 months after device removal subjects will be followed for weight loss, adverse events, psychological assessment, lipids and HbA1C.

2. *OSB Lead PMA Post-Approval Study- AspireAssist Post Approval Study*: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. This study will be conducted as per protocol provided interactively on March 23, 2016, Version P016-001V Revision B**.**

   The purpose of this post-approval study is to assess the safety and effectiveness of the AspireAssist device with regard to: compliance with AspireAssist therapy and transient weight-loss following the therapy, impact of AspireAssist therapy on eating behavior, incidence, duration and severity of adverse events (in particular, infection and stoma-related issues) and the effectiveness and safety outcomes after device explant. This is a new enrollment study that will include subjects who are 22 years of age or older, with a body mass index (BMI) of 35.0-55.0kg/m^2, who meet the inclusion and exclusion criteria per approved protocol, and who agree to participate in the study. Study subjects will be followed for five (5) years post-implant. Additionally, subjects who have the device removed will be followed for two (2) years post-explant.

   An exact binomial test will be used to assess if the serious adverse event rate at 5 years is less than 7%. A total of 323 subjects will be consecutively enrolled, from 15 sites (15-35 subjects per site). Five years data will be available on 259 subjects, which should provide 80% power to reject the null hypothesis of the study, assuming a serious adverse event (SAE) rate of 3% (observed in premarket studies).

   The primary safety endpoint of this post-approval study assesses the hypothesis that the five-year serious adverse event (as defined by the Safety Adjudication Committee) rate is less than 7%.

   The study will also assess the following secondary effectiveness endpoints:
   1. Compliance with appropriate use of the AspireAssist system (Weight loss % Excess Weight Loss (EWL) and % Total Body Loss (TBL), and connector counts will be assessed). Excess weight will be determined from ideal body weights based on a BMI = 25kg/m^2
   2. Percentage of patients achieving a 25% EWL
   3. Percentage of patients who have a positive or negative change in medications related to comorbidities (hypertension, diabetes, and dyslipidemia)

   And the following secondary safety endpoints:
   1. Percentage of patients with AEs related to eating disorders
   2. Five-year rate of incidence, duration and severity of AEs related to stoma issues including infection (bacterial or fungal) and granulation tissue

Continuous outcomes will be provided through descriptive statistics with 95% confidence intervals, and all rates will be calculated and presented with exact 95% confidence intervals.

Interim reports will be provided every six months for the first two years of the study, and annually thereafter.

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.