SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Implant, Intragastric for Morbid Obesity

Device Trade Name: Spatz3 Adjustable Balloon System

Device Procode: LTI

Applicant's Name and Address: Spatz FGIA, Inc
1801 S Perimeter Rd, Suite 130
Fort Lauderdale, FL 33309

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P190012

Date of FDA Notice of Approval: October 15, 2021

II. INDICATIONS FOR USE

The Spatz3 Adjustable Balloon System is indicated for temporary use for weight loss in adults with obesity Body Mass Index (BMI) of 35.0-40.0 kg/m^2 or a BMI of 30.0 to 34.9 kg/m^2 with one or more major obesity-related comorbid conditions who have failed to achieve and maintain weight-loss with a supervised weight control program. The Spatz3 Adjustable Balloon System is to be used in conjunction with a long-term supervised diet and behavior modification program designed to increase the possibility of long-term weight-loss maintenance. The maximum placement period for Spatz3 Adjustable Balloon System is 8 months.

III. CONTRAINDICATIONS

1. Prior gastrointestinal surgery with sequelae, i.e. recurrent abdominal pain, bowel obstruction, episodes of transient bowel obstruction, adhesive peritonitis or known abdominal adhesions; prior intestinal resection; or prior multiple lower abdominal or pelvic surgeries.
2. Prior open or laparoscopic bariatric surgery.
3. Prior surgery of any kind on the esophagus, stomach, duodenum or any type of hiatal hernia surgery.
4. Any inflammatory disease of the gastrointestinal tract including esophagitis, Barrett's esophagus, gastric ulceration, duodenal ulceration, or specific inflammation such as Crohn's disease, or cancer or other diseases of the bowel system.

5. Potential upper gastrointestinal bleeding conditions such as esophageal or gastric varices, congenital or acquired intestinal telangiectasis, or other congenital anomalies of the gastrointestinal tract such as atresias or stenoses.
6. A gastric mass.
7. A hiatal hernia > 2 cm or severe or intractable gastro-esophageal reflux symptoms.
8. Acid reflux symptoms to any degree that require more than one medication for symptom control.
9. A structural abnormality in the esophagus or pharynx such as a stricture or diverticulum that could impede passage of the balloon alongside the endoscope.
10. Achalasia or any other severe esophageal motility disorder that may pose a safety risk during the removal of the device.
11. Severe coagulopathy.
12. Insulin-dependent diabetes (either Type 1 or Type 2) or a significant likelihood of requiring insulin treatment in the following 12 months.
13. Subjects with any serious health condition unrelated to their weight that would increase the risk of endoscopy.
14. Chronic abdominal pain.
15. Motility disorders of the gastrointestinal tract such as gross esophageal motility disorders, gastroparesis or intractable constipation.
16. Hepatic insufficiency or cirrhosis.
17. Serious or uncontrolled psychiatric illness or disorder that could compromise patient understanding of or compliance with follow up visits and removal of the device after 8 months.
18. Alcoholism or drug addiction.
19. Patients receiving daily prescribed treatment with aspirin > 100 mg, anti-inflammatory agents, anticoagulants or other gastric irritants.
20. Patients who are unable or unwilling to take prescribed proton pump inhibitor medication for the duration of the device implant.
21. Patients who are known to have, or suspected to have, an allergic reaction to materials contained in the system.
22. Patients who have BOTH -ever developed a serotonin syndrome AND are currently taking any drug known to affect the levels of serotonin in the body [e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs)] should not undergo placement of the device.
23. Patients who are pregnant or breast-feeding.

24. Patients with Severe cardiopulmonary disease or other serious organic disease which might include known history of coronary artery disease, myocardial infarction within the past 6 months, poorly controlled hypertension, required use of NSAIDs.
25. Patients who are currently positive for H. Pylori.
26. Patients taking medications on specified hourly intervals that may be affected by changes to gastric emptying, such as anti-seizure or anti-arrhythmic medications.
27. Patients who are taking corticosteroids, immunosuppressants, or narcotics.
28. Symptomatic congestive heart failure, cardiac arrhythmia or unstable coronary artery disease.
29. Pre-existing respiratory disease such as chronic obstructive pulmonary disease (COPD) or pneumonia.
30. Pre-existing cancer undergoing chemotherapy or radiation therapy.
31. Diagnosis of autoimmune connective tissue disorder (e.g. lupus, erythematous, scleroderma) or immunocompromised.
32. Life expectancy less than 1 year or severe renal, hepatic, pulmonary or cardiac condition.
33. Specifically diagnosed genetic or hormonal cause for obesity such as Prader Willi syndrome or untreated hypothyroidism.
34. Eating disorders including night eating syndrome (NES), bulimia, binge eating disorder, or compulsive overeating.
35. Untreated endocrine disorders affecting weight.
36. The presence of more than one intragastric balloon at the same time

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Spatz3 Adjustable Balloon System labeling.

V. DEVICE DESCRIPTION

The Spatz3 Adjustable Balloon System is a silicone sphere filled with saline that is placed in the stomach for up to 8 months taking up stomach volume and delaying stomach emptying.

Insertion of the balloon into the patient's stomach begins with an endoscopy under conscious sedation to inspect the upper gastrointestinal tract, and to rule out any contraindicating circumstances. The balloon is then inflated with 400-550 ml of sterile saline with the addition of 1% methylene blue, and is left in place for up to 8 months. The balloon volume (range from 300-850 ml) can be adjusted via endoscopy during the time period in which it remains in the patient's stomach to alleviate intolerance (down-adjustment) or to increase the balloon effect (up adjustment). At the conclusion of the

implant period, the balloon is extracted endoscopically under conscious sedation using the snare provided in the extraction kit.

A. Device Components

The Spatz3 Adjustable Balloon System includes the following components:

- Spatz3 Adjustable Balloon
- Extension tube
- Insertion Facilitator (Remora)
- Cap Assembly
- Syringe (in its original packaging, cleared via K112057)
- Spatz3 Adjustable Balloon System Adjustment/Extraction Kit

Spatz3 Adjustable Balloon

The Spatz3 Adjustable Balloon consists of a balloon positioned around a curved catheter inside the balloon, and whose catheter continues and exits outside of the balloon. The external catheter houses the stretchable inflation tubing, which allows the balloon to have its volume adjusted after initial insertion, while the balloon remains in the stomach. At the proximal end of the inflation tube there is a silicone funnel with a luer-lock valve. Figure 1 illustrates the Spatz3 Adjustable Balloon.

Figure 1: Spatz3 Adjustable Balloon in the folder pre-insertion state (left) and fully inflated (right)

Extension Tube

The device is supplied with an extension tube that is connected to the valve on its distal end, with a 3-way stopcock on its proximal end for inflation/deflation (Figure 2). A 50 ml syringe is used to inflate the balloon with sterile saline with the addition of 1% methylene blue solution at a concentration of 2 ml per 500 ml of saline via the 3-way stopcock at the proximal end of the extension tube. Following inflation, the extension tube is pulled out of the mouth (by stretching the inflation tube), and disconnected from the valve and then replaced by the cap.

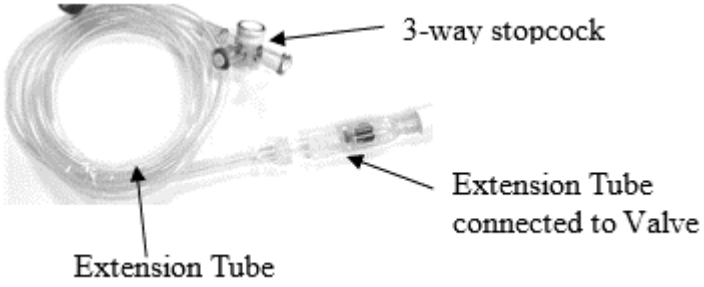

Figure 2: Extension Tube

Insertion Facilitator (Remora)

The Insertion Facilitator, otherwise known as the Remora, is used during the implant procedure (Figure 3).

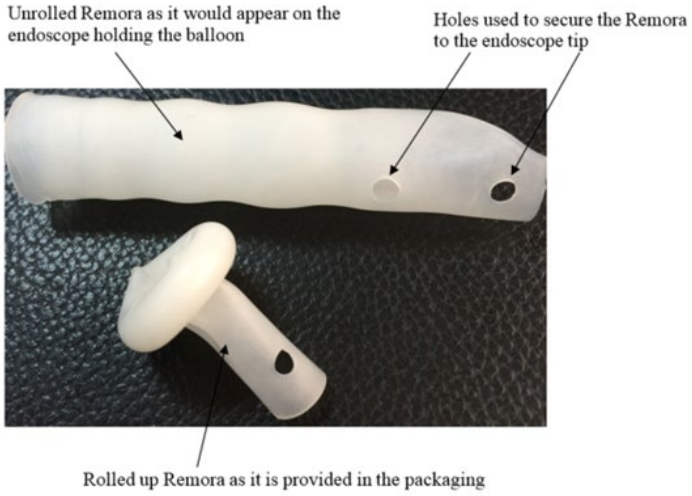

Figure 1: Insertion Facilitator (Remora)

Cap Assembly

The Cap Assembly (Figure 4) is attached to the end of the filling valve. A stainless-steel metal cylinder is bonded within a well in the cap. The cylinder is hollow and contains the nylon suture loop. The loop is knotted and fits into the cylinder in one direction, but the lumen of the cylinder narrows and does not allow the knot to pass through the hole in the cylinder.. The metal cylinder with the loop are called “easy extract.” The easy extract assembly (within the cap assembly) provides a means for the endoscopist to grasp the valve for removal during adjustment or extraction procedures. A standard grasping forceps is used to grasp the nylon loop, which is then pulled out of the mouth (the inflation tube stretches), which is then attached to the extension tube for the adjustment of the balloon volume or the complete deflation of the balloon prior to extraction.

The valve has within it a silicone piece that prevents fluid escape even when the cap is off.

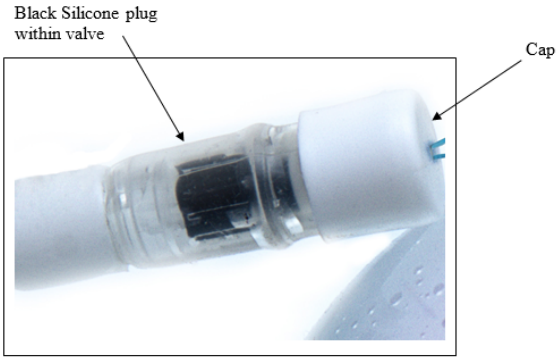

Figure 2: Cap Assembly

Spatz3 Adjustable Balloon System Adjustment/Extraction Kit

The Spatz3 Adjustable Balloon System Adjustment/Extraction Kit includes 3 extension tubes (and associated 3-way stopcocks) and 3 copies of the instructions for use. The extension tubes (and associated 3-way stopcocks) that are included in the Adjustment/Extraction Kit are identical to those components provided in the Spatz3 Adjustable Balloon System and are provided as a means for adjusting the balloon volume after the initial procedure.

B. Principle of Operation

Spatz3 Adjustable Balloon insertion, volume adjustment, and removal from the patient's stomach is accomplished via endoscopy under conscious sedation.

At the time of insertion, the balloon is inflated with 400-550 ml of sterile saline with 1% methylene blue.

Spatz3 Adjustable Balloon volume down adjustment is recommended for patients who are intolerant to the balloon. Patients may try dietary changes and medications prior to making the decision to have the Spatz3 Adjustable Balloon volume decreased.

Spatz3 Adjustable Balloon volume up adjustments are recommended for patients between weeks 14-24 of therapy, who have diminished balloon effect, and who are asymptomatic, with BMI above 25 kg/m^2, and without any evidence of gastric ulcer, erosive gastritis, esophagitis (any grade).

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives to achieve weight-loss for individuals with obesity (BMI > 30 kg/m^2), which can be divided into six categories: non-surgical treatments, gastric banding, gastric emptying therapy, bariatric surgery, and other intragastric balloons. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his or her physician to select the method that best meets expectations and lifestyle.

Non-Surgical Treatments

Non-surgical treatments for obesity include:

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

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.

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. One device has received FDA approval, the AspireAssist. The device allows patients to remove approximately 30% of the food from the stomach at each meal before it is absorbed.

Bariatric Surgery

Bariatric surgery is typically recommended for patients with a BMI of 30 kg/m^2 – 35 kg/m^2 with one or more obesity-related comorbid conditions or for patients with a BMI of 40 kg/m^2 or more. The most common types of bariatric surgery are described below.

a. Roux-en-Y Gastric Bypass

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.

b. Vertical Sleeve Gastrectomy

Vertical sleeve gastrectomy is a procedure that reduces the size of the stomach by surgical stapling of the stomach with removal of a large portion of the stomach. The size of the stomach is permanently reduced without bypassing the intestines.

c. Biliopancreatic Diversion Duodenal Switch

The biliopancreatic diversion with duodenal switch is a procedure in which the greater curve of the stomach is removed, 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.

Intragastric Balloons
Intragastric balloons are indicated for weight loss when used in conjunction with diet and exercise in 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 not achieved sufficient weight loss with diet and exercise alone.

VII. MARKETING HISTORY

The Spatz3 Adjustable Balloon System received CE Mark on August 30, 2012. The Spatz3 Adjustable Balloon System has regulatory approvals in the European Union, Australia, Brazil, Canada, Mexico, Israel, Turkey, Colombia, New Zealand, Argentina, Malaysia, Vietnam, Egypt, Saudi Arabia, Ecuador, Peru, Thailand, Singapore, Panama, Costa Rica and El Salvador. There are several smaller countries that do not have a regulatory system in place where doctors and hospitals accept the CE Mark and the Spatz3 Adjustable Balloon System is distributed.

The Spatz3 Adjustable Balloon System was voluntarily and temporarily withdrawn from the Israeli market in September 2019 following deaths in 2 patients; however, a causal link was not determined.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential risks associated with upper endoscopic procedures include but are not limited to abdominal cramping and discomfort from the air used to distend the stomach, sore or irritated throat, bleeding, infection, tearing of the esophagus or stomach, and aspiration pneumonia. Some of these risks may lead to death. The risk increases if additional procedures are performed. The most common complications involve a temporary decrease in the rate of breathing or heart rate, which can be corrected by giving extra oxygen or by reversing the effect of the sedative medications. Patients with heart, lung, kidney, liver, or other chronic diseases are at higher risk for complications.

Adverse events that may result from the Spatz3 Adjustable 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 (i.e., complications) associated with the use of the device.

- Gastric outlet obstruction. A partially-filled balloon or a leaking balloon could lead to gastric outlet obstruction, requiring balloon removal. It is also possible for a fully inflated balloon to lodge itself in the gastric outlet causing a pyloric obstruction which can produce a mechanical impediment to gastric emptying. Gastric outlet obstruction may require surgical removal.
- Bacterial growth in the fluid which fills the balloon. Rapid release of this fluid into the intestine could cause infection, fever, cramps and diarrhea.

- Gastric atony resulting in gastric food accumulation that can lead to rotting of food, which becomes infected with spillage into the intestines and diarrhea – a bacterial overgrowth type situation
- Balloon deflation and subsequent replacement.
- Intestinal obstruction by the balloon. An insufficiently filled balloon or a leaking balloon that has lost sufficient volume may be able to pass from the stomach into the small bowel. It may pass all the way into the colon and be passed with stool. However, if there is a narrow area in the bowel, as may occur after prior surgery on the bowel or adhesion formation, the balloon may not pass and then may cause a bowel obstruction. If this occurs, surgery or endoscopic removal could be required.
- Esophageal obstruction. Once the balloon is being filled in the stomach, the balloon could be inadvertently pulled back into the esophagus. If this occurs, surgery or endoscopic removal could be required.
- Gastric distention with retained food and fluid due to severely delayed gastric emptying with or without outlet obstruction from displacement of the balloon into the antrum.
- Injury to the digestive tract during placement of the balloon in an improper location such as in the esophagus or duodenum. This could cause bleeding and perforation, which could require a surgical or endoscopic correction for control.
- Insufficient or no weight loss.
- Adverse health consequences resulting from weight loss such as gallstones, dehydration, loss of muscle mass, mood changes, electrolyte abnormalities, menstrual changes and nutritional deficiencies.
- Gastric discomfort, feelings of nausea and vomiting following balloon placement as the digestive system adjusts to the presence of the balloon.
- Continuing nausea and vomiting. This could result from direct irritation of the lining of the stomach, delayed gastric emptying and/or the balloon blocking the outlet of the stomach. It is even theoretically possible that the balloon could prevent vomiting (not nausea or retching) by blocking the inlet to the stomach from the esophagus.
- A feeling of heaviness in the abdomen.
- Abdominal or back pain, either steady or cyclic.
- Gastroesophageal reflux.
- Injury to the lining of the digestive tract as a result of direct contact with the endoscope, the balloon, grasping forceps or as a result of increased acid production by the stomach. This could lead to ulcer formation with pain, bleeding or even perforation. Surgery could be necessary to correct this condition.
- Death due to adverse events related to intestinal obstruction, gastroesophageal perforation, and/or pulmonary aspiration is possible

- Acute pancreatitis characterized by nausea, vomiting, abdominal pain, dehydration. The severity can range from mild to severe and may require balloon down adjustment, or removal. This may result in hospitalization, surgery or death in severe cases.
- Spontaneous hyperinflation due to gas production within the balloon. Spontaneous hyperinflation can cause abdominal pain, nausea and vomiting, and in severe cases it can lead to ulceration, and rarely it can cause gastric perforation and death.

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

The integrity and performance of the Spatz3 Adjustable Balloon System was evaluated with the testing summarized in Table 1.

Table 1: Summary of nonclinical studies

Test	Purpose	Acceptance Criteria	Results
Nonclinical Performance Testing			
Dimensional and Visual Inspection	Verify that the Spatz3 Adjustable Balloon System complies with all the specified visual and dimensional requirements.	100% pass of visual and dimensional inspection, with 95% confidence and 95% reliability.	Pass
Balloon Inflation and Deflation Time	Verify the time required to inflate the Spatz3 Adjustable Balloon to the maximum volume and to then deflate the balloon.	Balloon inflation time: Balloon inflation time is less than 10 min with 95% confidence and 95% reliability. Balloon deflation time: Balloon deflation time is less than 12 min, with 95% confidence and 95% reliability.	Pass
Burst Test	Verify the ability of the Spatz3 Adjustable Balloon to withstand rupture under a worst-case scenario of 2.5 times the maximum rated volume (2500 ml)	No balloon bursts at inflation volume of 2500±50 ml, with 95% confidence and 95% reliability.	Pass
Bond Strength	Verify the strength of the bonds between the Spatz3 Adjustable Balloon	The force until assembly failure should be greater than 3 kgf, with 95%	Pass

	assembly and the inflation tube assembly	reliability and 95% confidence.	
Valve Connection Integrity Test	Verify the integrity of the valve-funnel connection and valve-inflator connection of the device under conditions of blocked fluid flow	The valve-luer connection can withstand a pressure to up to 3 atmospheres for 30 sec (No Leak) as per ISO 594-02 clause 5.2, with 95% confidence and 95% reliability. The valve-inflator connection can withstand a pressure to up to 3 atmospheres for 30 sec (No Leak) as per ISO 594-02 clause 5.2, with 95% confidence and 95% reliability	Pass
Inflation System Strength	Verify the ability of the inflation system to withstand elongation to 70 cm, and to demonstrate that the failure point is greater than double the forces experienced in a worst-case clinical scenario	The device should not exhibit tears, cracks or any signs of stress after 70 cm elongation. Failure force of the inflation system under tensile testing should be > 1.5 kgf (2 times pull force measured at 50 cm elongation) with 95% reliability and 95% confidence.	Pass
Cap Assembly	Verify that the inflation tube cap does not separate from the inflation valve under expected conditions of use and that the suture used to extract the cap assembly does not fail.	The cap assembly is able to withstand a peak pulling force of at least 1.5 kgf (2 times pull force measured at 50 cm elongation) with 95% confidence and 95% reliability.	Pass
Balloon Insertion	Simulate the implantation procedures in a model of the esophagus and verify the ability of the Spatz3 Adjustable Balloon to pass through the model and be successfully released.	The balloon passes through an anatomical model while it is mounted on the endoscope using the remora and is released from the endoscope at the end of the procedure, with 95% confidence and 95% reliability.	Pass
Balloon and Inflation Tube Dimension Inspection	Verify that the Spatz3 Adjustable Balloon System thickness complies with dimensional requirements.	100% pass of visual and dimensional inspection, with 95% confidence and 95% reliability.	Pass

Simulated Gastric Environment	Verify the ability of the Spatz3 Adjustable Balloon to withstand gastric acidity levels and simulated gastric motion while maintaining integrity and functionality.	No leakage or bursting during the 112 days of acid bath immersion - no change in the color of the acid bath. No leakage or bursting during the weekly fatigue test. Balloon weight prior to acid bath and after 112 days of accelerated aging conditions that mimic 9 months will not differ by more than 2%. Balloon inflation system functions after 112 days of accelerated aging conditions that mimic 9 months - the balloon can be inflated and deflated in less than 12 min. No tear/failure during repetitive stretching (10 stretches) of the Inflation System to 70 cm with successful return of the inflation tube to its place after 112 days of accelerated aging conditions that mimic 9 months. Balloon can be extracted successfully from model without breaking after 112 days of accelerated aging conditions that mimic 9 months. Inflation System force at 70 cm point should be <2X=1.5 kgf, which is the force measured during elongation of the inflation tube to 50 cm 112 days of accelerated aging conditions that mimic 9 months. Cap Assembly should hold force of 2X=1.5 kgf without failure after 112 days of	Pass*

		accelerated aging conditions that mimic 9 months. Valve examination after 112 days of accelerated aging conditions that mimic 9 months: • Visual inspection of the valve for any damage/ break. • No leak from the funnel or valve: (from the funnel body or from the valve itself) while the funnel is kinked, and the valve is injected with a pressure of 3 atm for 30 sec. • No leak from the valve while trying to inject in 0.5 atm through the inflation tube (silicone seal is working) for 20 seconds. No leak /burst after 112 days of accelerated aging conditions that mimic 9 months, the ability to withstand balloon inflation of 2500±50 ml. Biochemical analysis of the acid bath liquid at 0, 56 & 112 days for the presence of methylene blue.	
Microbiology testing	Determine device total bioburden and assess for specific enteric and pathogenic microbes to confirm acceptable bioburden. Routine environmental monitoring is performed yearly, quarterly or monthly, depending upon the test.	The bioburden method was validated, and testing was completed in conformance with ISO 11737-1:2018. In addition, bioburden will be tested every 3 months.	Bioburden is acceptable

	Routine microbiological monitoring includes: periodic environmental monitoring, monitoring of air handling systems and monitoring of employee hands and gowning areas.		
Magnetic resonance (MR) compatibility	To evaluate the MRI safety and compatibility and support the MR compatibility labeling.	• Magnetically induced displacement force shall be less than worst-case force due to the earth's gravity evaluated according to ASTM F2052; • Magnetically induced torque shall be less than worst-case torque due to the earth's gravity evaluated according to ASTM F2213; • Radio frequency heating of the device during a continuous MRI procedure 15 minutes in duration shall be less than 2°C evaluated according to ASTM F2182 • Image artifact assessed for characterization only	Testing results are acceptable and support MR conditions for safe use
Packaging and 24-month Shelf Life Testing			
Package integrity (accelerated aging, simulated distribution and shipping followed by associated package integrity testing)	Validate packaging in environmental conditions.	Samples were subjected to accelerated aging equivalent to 24 months of shelf life according to ASTM F1980 (2016) and conditioned according to ASTM D4169. Packaging integrity was evaluated according to ASTM F1886/F1886M.	Results support packaging integrity and shelf life.
Maintenance of device functionality (accelerated aging, simulated distribution and shipping followed by functional testing)	Verify product specifications are met throughout the shelf life.	Meet product specifications.	Results support shelf life.

* Per the testing method and data provided, FDA could not conclude that there was not a change in the color of the acid bath. However, the interpretation of the result is minimal in the overall device risk analysis.

B. Additional Studies

Biocompatibility

The Spatz3 Adjustable Balloon with Cap Assembly is classified as a permanent implant in contact with mucosal membrane during clinical use (>30 days). In accordance with FDA CDRH's Biocompatibility guidance, "Use of International Standard ISO 10993-1, Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process", the following biocompatibility endpoints were assessed for the Spatz3 Adjustable Balloon implant:

- Cytotoxicity
- Irritation
- Sensitization
- Acute systemic toxicity
- Subacute systemic toxicity
- Material-mediated pyrogen
- Genotoxicity
- Intramuscular implantation
- Chronic systemic toxicity (chemical extractable study with toxicological risk assessment)

The Spatz3 Adjustable Balloon System Extension Tube, Insertion Facilitator (remora), and Adjustment/Extraction kit are considered to have limited contact with mucosal membrane (<24 hrs). In accordance with FDA CDRH's Biocompatibility guidance, the following biocompatibility endpoints were assessed for these device components:

- Cytotoxicity
- Irritation
- Sensitization

Results from the biocompatibility analyses support the biocompatibility of the Spatz3 Adjustable Balloon System.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study (Spatz3 US Pivotal Study) to establish a reasonable assurance of safety and effectiveness of the Spatz3 Adjustable Balloon System for temporary use for weight loss in adults with obesity (BMI ≥ 30 kg/m^2 and < 40 kg/m^2) who have failed to achieve and maintain weight-loss with a supervised weight control program in the US under IDE #G160061. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The purpose of the US Pivotal study was to evaluate the safety and effectiveness of the Spatz3 Adjustable Balloon in subjects with a BMI ≥30 kg/m^2 and <40 kg/m^2 who failed to achieve and maintain weight-loss with a weight control program. Subjects were studied in a randomized, controlled, multi-center study. The control group

received dietary/exercise counselling for 32 weeks. The treatment group received dietary/exercise counselling plus the Spatz3 Adjustable Balloon for 32 weeks, followed by a 6-month follow up period.

Subjects and investigators were not blinded. Only clinical staff taking weight measurements were blinded. All treatment group subjects underwent upper endoscopy and those without endoscopic contraindications were implanted with the Spatz3 Adjustable Balloon for 32 weeks. All subjects were instructed to follow a 1000-1200 kcal/day-deficit diet during their participation in the study; however, compliance was not evaluated.

The treatment group were asked to remain in the 6-month follow-up phase regardless of when their balloon was extracted.

The Spatz3 Adjustable Balloon was initially inflated according to the following criteria:

- Initial balloon volume for subjects with height < 64 inches:
    - 450 ml (without history of gastroesophageal reflux)
    - 400 ml (with history of gastroesophageal reflux)

- Initial balloon volume for subjects with height ≥ 64 inches;
    - 550 ml (without history of gastroesophageal reflux)
    - 500 ml (with history of gastroesophageal reflux)

All treatment group subjects received the following oral medications:

- Aprepitant (Emend - implantation procedure only) 125 mg immediately prior to or 1 hour after the procedure, 80 mg the morning after the procedure and another 80 mg two mornings after the procedure.
- Ondansetron 8 mg taken every 6 hours starting 1 hour after the implant and upward adjustment procedures for 12 tablets (3-4 days).
- Hyoscyamine 0.125 mg prn for abdominal pain or spasm 1-2 tablets every 4 hours sublingually (maximum 12 tablets/ 24 hours) after the implant and upward adjustment procedures.
- Percocet 10 mg was provided for subjects who had abdominal pain that was not relieved by Hyoscyamine.
- A PPI (proton pump inhibitor such as Nexium 20 mg, Protonix 40 mg or Prevacid 30 mg) was taken daily for the entire 8 months to reduce acid in the stomach.
- Probiotic, Acidophilus, 8-10 Billion CFU was taken once daily for the 8-month period.

An independent Data Safety Monitoring Board (DSMB) served as an autonomous advisory group for Spatz FGIA, Inc., the sponsor of this trial. The DSMB was responsible for safeguarding the interests of trial participants, assessing the safety and efficacy of the interventions during the trial, adjudication of adverse events, evaluating any device deficiencies, and for monitoring the overall conduct of the clinical trial.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the Spatz3 US Pivotal study was limited to patients who met the following inclusion criteria:

   a. Age 22 – 65 years
   b. BMI ≥ 30 and <40 kg/m^2
   c. Willingness to comply with the substantial lifelong dietary restrictions required by the procedure
   d. History of obesity (BMI ≥ 30 kg/m^2) for at least 2 years
   e. History of failure with non-surgical weight loss methods
   f. Willingness to follow protocol requirements, including signed informed consent, routine follow-up schedule, completing laboratory tests, completing diet counseling
   g. Residing within a reasonable distance from the investigator's office and able to travel to the investigator to complete all routine follow-up visits
   h. Ability to give informed consent
   i. Women of childbearing potential (i.e., not post-menopausal or surgically sterilized) must agree to use adequate birth control methods

   Patients were not permitted to enroll in the Spatz3 US Pivotal study if they met any of the following exclusion criteria:

   a. Prior gastrointestinal surgery with sequelae, i.e. obstruction, and/or adhesive peritonitis or known abdominal adhesions
   b. Prior open or laparoscopic bariatric surgery
   c. Prior surgery of any kind on the esophagus, stomach or any type of hiatal hernia surgery
   d. Any inflammatory disease of the gastrointestinal tract including esophagitis, Barrett's esophagus, gastric ulceration, duodenal ulceration, cancer or specific inflammation such as Crohn's disease
   e. Potential upper gastrointestinal bleeding conditions such as esophageal or gastric varices, congenital or acquired intestinal telangiectasis, or other congenital anomalies of the gastrointestinal tract such as atresias or stenoses
   f. A gastric mass
   g. A hiatal hernia > 2 cm or severe or intractable gastro-esophageal reflux symptoms
   h. Acid reflux symptoms to any degree that require more than one medication for symptom control
   i. A structural abnormality in the esophagus or pharynx such as a stricture or diverticulum that could impede passage of the balloon alongside the endoscope
   j. Achalasia or any other severe esophageal motility disorder that may pose a safety risk during the removal of the device
   k. Severe coagulopathy

l. Insulin-dependent diabetes (either Type 1 or Type 2) or a significant likelihood of requiring insulin treatment in the following 12 months
m. Subjects with any serious health condition unrelated to their weight that would increase the risk of endoscopy
n. Chronic abdominal pain
o. Motility disorders of the GI tract such as gross esophageal motility disorders, gastroparesis or intractable constipation
p. Hepatic insufficiency or cirrhosis
q. Serious or uncontrolled psychiatric illness or disorder that could compromise patient understanding of or compliance with follow up visits and removal of the device after 8 months
r. Alcoholism or drug addiction
s. Patients unwilling to participate in an established medically-supervised diet and behavior modification program, with routine medical follow-up
t. Patients receiving daily prescribed treatment with aspirin, anti-inflammatory agents, anticoagulants or other gastric irritants
u. Patients who were unable or unwilling to take prescribed proton pump inhibitor medication for the duration of the device implant
v. Patients who are known to have, or suspected to have, an allergic reaction to materials contained in the system
w. Patients who had ever developed a serotonin syndrome and are currently taking any drug known to affect the levels of serotonin in the body [e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs)] should not undergo placement of the device
x. Patients who were pregnant or breast-feeding
y. Subjects with severe cardiopulmonary disease or other serious organic disease which might include known history of coronary artery disease, myocardial infarction within the past 6 months, poorly-controlled hypertension, required use of NSAIDs
z. Subjects who had tested positive for H. Pylori
aa. Subjects taking medications on specified hourly intervals that may be affected by changes to gastric emptying, such as anti-seizure or anti-arrhythmic medications
bb. Subjects who were taking corticosteroids, immunosuppressants, and narcotics
cc. Subjects who were taking diet pills
dd. Use of an intragastric device prior to this study due to the potential increase in risk associated with implantation of a balloon in a previously instrumented and possibly scarred stomach
ee. Participation in any clinical study that could affect weight loss within the past 6 months due to the potential to confound findings
ff. Symptomatic congestive heart failure, cardiac arrhythmia or unstable coronary artery disease
gg. Pre-existing respiratory disease such as chronic obstructive pulmonary disease (COPD), pneumonia or cancer

hh. Diagnosis of autoimmune connective tissue disorder (e.g. lupus, erythematous, scleroderma) or immunocompromised
ii. Life expectancy less than 1 year or severe renal, hepatic, pulmonary or other medical condition, in the opinion of the investigator because of an increased risk profile
jj. Specific diagnosed genetic or hormonal cause for obesity such as hypothyroidism or Prader Willi syndrome
kk. Eating disorders including night eating syndrome (NES), bulimia, binge eating disorder, or compulsive overeating
ll. Known history of endocrine disorders affecting weight

2. Follow-up Schedule

Follow-up visits for treatment and control subjects occurred according to the following schedule: visits at 1 week after implant/randomization, 2 weeks, and 4 weeks (± 3 days), and thereafter every 4 weeks (±2 weeks) until primary endpoint assessment at 32 weeks.

A summary of required visits and procedures is shown in Table 2.

Table 2: Required visits and procedures

	Screening assessments	7 days prior to implant	Implantation	Adjustment	Explantation	Follow-up assessment Weeks 1-32	Post-explant assessment Weeks 36-56
Informed Consent	X						
Date of Birth/Gender	X						
Body Weight	X	X[6]	X	X	X	X	X
Body Height	X						
BMI	X	X	X			Week 32 only	X [4]
Ideal Weight/ Excess Weight	X				X	Week 32 only	X [4]
Medical History	X						
Physical Exam[1]	X			X	X		Week 36 [5]
Blood Pressure	x		X	X	X	X	Week 36 [5]
CBC and Coagulation[2]	X						Week 36 [5]
H. Pylori Serology	X						
Chemistry Panel[3]	X						Week 36 [5]
HgbA1C2 (patients with diabetes)	X						Week 36 [5]

	Screening assessments	7 days prior to implant	Implantation	Adjustment	Explantation	Follow-up assessment Weeks 1-32	Post-explant assessment Weeks 36-56
EKG(Only for those >40 y/o)	X						
Psychological Evaluation	X						
Inclusion and Exclusion Criteria	X						
Develop/Review Dietary Plan	X						
Satiety and Dietary Assessment						X	X [4]
Investigator or Nurse Follow-Up				X	X	X	X [4]
Medications List	X	X				X	Week 36 [5]
Urine Pregnancy Test (Only for women of child bearing potential)	X	X					
Adverse Events/Device Complications			X	X	X	X	X
Verify Birth Control for Females[7]	X						

[1]Investigator or co-investigator performed the physical exam.
[2]CBC (complete blood count) includes: hemoglobin (Hgb), hematocrit (Hct), white blood cells (WBC), mean corpuscular volume (MCV), platelets. Coagulation includes: Prothrombin Time or International Normalized Ratio (INR), Partial Thromboplastin Time (PTT). Was done at screening only.
[3]Chemistry panel includes: sodium, potassium, chloride, CO_2, BUN, creatinine, glucose, SGOT/AST, SGPT/ALT, alkaline phosphatase, total bilirubin, total protein, albumin, total cholesterol, Fe/TIBC, B12, Folic Acid, 25-Hydroxy Vitamin D, TSH.
[4]Week 56, or 24 weeks after extraction.
[5]Or 4 weeks after extraction.
[6]This is the baseline weight that was used for the endpoint assessments.
[7]Acceptable birth control methods were verified at every visit.

At 18 weeks ± 4 weeks, treatment group subjects were evaluated, and those that met the criteria in Table 3 were eligible to undergo an adjustment procedure wherein the Spatz3 Adjustable Balloon volume was increased with the expectation that this would result in enhanced weight loss. The Spatz3 Adjustable Balloon adjustment was done with an endoscopic procedure.

Table 3: Week 18 balloon adjustment algorithm

Subject Status	Week 18 Upward Balloon Adjustment
Reached goal weight (calculated by maximum BMI of 25 kg/m^2) without any symptoms of gastroesophageal reflux or symptoms suggestive of gastritis or gastric ulcer	No adjustment (No Week 18 endoscopy performed)
Gastric ulcer identified by a prior unscheduled endoscopy	No adjustment (No additional endoscopy besides the follow-up endoscopies to confirm healing, per the protocol)
Gastric ulceration or esophagitis found at Week 18 endoscopy	No adjustment (investigator decided if balloon required extraction)
No gastric ulceration, esophagitis, or erosive gastritis found at Week 18 endoscopy (non-erosive gastritis permitted)	• No addition if gastroesophageal reflux was not controlled by medication • 200 ml if subject was previously down adjusted for intolerance but was asymptomatic at Week 18 • 200 ml for any height patient with gastroesophageal reflux controlled by medication • 250 ml for patient with height <64 inches without gastroesophageal reflux • 300 ml for patient with height ≥64 inches without gastroesophageal reflux Maximum final volume did not exceed 850 ml

The principle investigator could make an adjustment to the balloon volume at any time if the patient had symptoms of continued nausea, vomiting, uncontrolled gastroesophageal reflux or abdominal pain.

An additional 250 ml could be added to the balloon for patients without any balloon effect from days 4-14 after the implantation, defined as lacking all of the following symptoms: nausea, vomiting, abdominal pressure, post prandial fullness, abdominal pain, heartburn, and eructation.

1-2 weeks after the adjustment procedure subjects had a follow-up appointment with the principle investigator or nurse practitioner. Each follow-up visit included:

1. Clinical assessment by the principle investigator, a nurse practitioner, or a physician's assistant for both the treatment group and control group.
2. Satiety and dietary assessment for both the treatment group and control group.
3. Record of adverse events, device complications, and concomitant medication.

4. Weight measurement done by blinded staff. The subject was not permitted to speak with the weighing personnel and was not to disclose if they were on the control group or the treatment group.

At Week 32, control group subjects exited the study and treatment group subjects with the Spatz3 Adjustable Balloon still implanted underwent device extraction. Treatment group subjects were followed for an additional 6 months after device extraction, with follow-up visits occurring 4 weeks ± 3 days after extraction and every 4 weeks ± 2 weeks thereafter. These follow-up visits for the treatment group included:

1. Clinical assessment at the visit 4 weeks after extraction.
2. Satiety and dietary assessment.

An unscheduled endoscopy could have been performed at any time, at the discretion of the principle investigator. Table 4 details the follow-up procedure for findings of unscheduled or the scheduled Week 18 endoscopy.

Table 4: Follow-up procedure for findings of unscheduled or scheduled Week 18 endoscopy

Endoscopic Findings	Follow-up procedure
Ulcer with smallest dimension ≥2 cm or any stigmata of increased risk of bleeding (*e.g.*, visible vessels or clots)	• Balloon extracted • Biopsy for H.pylori performed and treatment prescribed if positive • Subject treated with medication • Endoscopic evaluation after 3 months post-finding to confirm healing
Ulcer with smallest dimension ≥ 1 cm and <2 cm	• Balloon volume decreased by 150 ml (or 100 ml if starting volume is 400 ml) • Biopsy for H.pylori performed and treatment prescribed if positive • Subject treated with medication • Endoscopic follow-up at 8 weeks and if not healed at 8 weeks - additional endoscopy at 16 weeks to confirm healing • At the 8-week follow-up, if signs of healing defined by a 25% reduction in either length or width are not observed, then the balloon should be extracted • At the 16-week follow-up, if signs of healing defined by a 50% reduction from baseline in either length or width are not observed, then balloon extraction, and healing confirmed at follow up endoscopy 2-3 months after extraction • Subject not to undergo adjustment at 18±4 weeks

Ulcer with largest diameter ≥1 cm and smallest diameter <1 cm	• Balloon volume decreased by 150 ml (or 100 ml if starting volume is 400 ml) • Biopsy for H. pylori performed and treatment prescribed if positive • Subject treated with medication • Endoscopic follow-up at 12 weeks and if not healed at 12 weeks, an additional endoscopy at 20 weeks to confirm healing • At the 12-week follow-up, if signs of healing defined by a 25% reduction in either length or width are not observed, then balloon extraction • At the 20-week follow-up, if signs of healing defined by a 50% reduction from baseline in either length or width are not observed, then balloon extracted • Subject not to undergo adjustment at 18±4 weeks
Ulcer <1 cm in all directions (<0.5 cm was not considered an ulcer) and erosive gastritis	• Biopsy for H. pylori performed and treatment prescribed if positive • Subject treated with medication • Balloon volume decreased at the discretion of the principle investigator • Endoscopic follow-up prior to the 8-month extraction not needed if asymptomatic • Subject not to undergo adjustment at 18±4 weeks
Non-erosive gastritis	• Biopsy for H. pylori performed and treatment prescribed if positive • Subject treated with medication • Endoscopic follow-up and healing confirmation deferred until the adjustment endoscopy at week 18±4 weeks or extraction endoscopy at 8 months, whichever comes first at least 2 months after this unscheduled endoscopy), unless symptomatic.
Grade 3 or 4 esophagitis	• Balloon extracted • Subject treated with medication • Endoscopic evaluation conducted after 3 months to confirm healing

Grade 1 or 2 esophagitis	• Balloon not extracted if asymptomatic • Subject treated with medication • Endoscopic follow-up deferred until extraction endoscopy at 8 months, unless symptomatic • Subject not to undergo adjustment at 18±4 weeks

Blood hemoglobin was monitored during scheduled or unscheduled endoscopies in patients who had ulcers or reported signs of upper gastrointestinal bleeding (hematemesis or melena).

Patients were monitored for symptoms of pancreatitis, and if appropriate, checking of pancreas enzymes (amylase and lipase) should have been done. If pancreas enzymes (amylase and lipase) were found to be > 3X upper limit of normal for institution:

- In a systemically ill patient with evidence of moderately severe or severe acute pancreatitis, the balloon was to be removed and close clinical follow-up of these severely ill patients.
- In a patient who does not meet the criteria of severe pancreatitis, balloon volume adjustment was required with removal of 150 ml (or 100 ml for a 400 ml balloon) and repeat pancreas enzymes 48 hours after adjustment with clinical follow-up.

If pancreas enzymes were found to be < 3X upper limit of normal for institution:

- In a systemically ill patient with evidence of moderately severe or severe acute pancreatitis, the balloon was to be removed and close clinical follow-up of these severely ill patients.
- If typical pain persists for > 48-72 hours, balloon volume adjustment was required with removal of 150 ml (or 100 ml for a 400 ml balloon) and repeat pancreas enzymes 48 hours after adjustment with clinical follow-up
- If pain resolves and within 48-72 hours -- no further action was required except clinical follow-up.

3. Clinical Endpoints

With regards to safety, the incidence, frequency, and severity of adverse events related to treatment with the device were reported. There was no pre-specified criteria for the safety endpoint.

With regards to effectiveness, the Spatz3 US Pivotal Study had two co-primary effectiveness endpoints:

- Percent change in total body weight (%TBL) at 32 weeks; and

- Clinical response, where a responder is defined as a subject with at least a 5% TBL at 32 weeks.

Both primary endpoints must be met for the study to be considered a success. The primary analyses are based on the intent-to-treat (ITT) population.

The following secondary endpoints were pre-specified in the clinical protocol and an observational analysis was provided for each:

- Maintenance of 40% of the total body weight loss with the balloon six months after the balloon is removed.

- Clinical response, where a responder is defined as a subject with at least a 25% loss in excess body weight at 32 weeks.

The ITT population included the 288 subjects randomized, while the Per-Protocol population (PPP) included 202 subjects (132 treatment and 70 control) who were not excluded for one of the following reasons:

- Did not meet the inclusion criterion of baseline BMI $\geq 30 kg/m^2$ and < 40 kg/m^2.
- Did not receive the treatment he/she was randomized to.
- Early balloon removal or early discontinuation from control group.
- More than three missed or significantly out of window visits before week 32.
- Non-compliance with the volume addition/removal requirements.

The co-primary hypotheses based on the ITT population were as follows:

- The mean %TBL in the Spatz3 Adjustable Balloon group exceeds that in the control group by 4.5%: H_O: $\mu_S - \mu_C \leq 4.5\%$ versus H_A: $\mu_S - \mu_C > 4.5\%$, where μ_S and μ_C are the population mean %TBL for the Spatz3 Adjustable Balloon and control groups, respectively.

- The response rate in the Spatz3 Adjustable Balloon group is superior to a performance goal of 50%, where a responder is defined as a ≥5% TBL at 32 weeks: H_O: $\pi \leq 50\%$ versus H_A: $\pi > 50\%$, where π is the population response rate in the Spatz3 Adjustable Balloon group.

To compare the Week 32 %TBL between the Spatz3 Adjustable Balloon (treatment) and control groups, a linear model was fit. This model had terms for the treatment group, site, baseline BMI, and sex, and was run on three datasets of Week 32 blinded weights:

- an ITT population dataset in which missing Week 32 weights were imputed through a multiple imputation procedure;

- an ITT population dataset in which missing Week 32 weights were imputed through a last observation carried forward (LOCF) procedure; and

- the PPP dataset.

B. Accountability of PMA Cohort

The Spatz3 US Pivotal Study subject cohort consisted of 288 subjects at 7 investigational sites in the US who were randomized 2:1 to treatment (Spatz3 Adjustable Balloon) and control. 187 subjects received the balloon (treatment) and 101 subjects served as control.

Of the 187 subjects who received a balloon, 156 (83% (156/187)) completed Week 32 and 31 subjects (17% (31/187)) needed an early balloon removal, most of them due to adverse events (15% (29/187)). Of the 101 subjects who were randomized to the control group, 75 (75% (75/101)) completed Week 32 and 26 (26% (26/101)) withdrew early.

The 187 treatment group subjects were asked to remain in the 6-month follow-up phase regardless of when their balloon was extracted. Of those, 37 (20% (37/187)) dropped out early, and 150 (80% (150/187)) completed 6-month follow-up.

Figure 5 shows the study accountability tree.

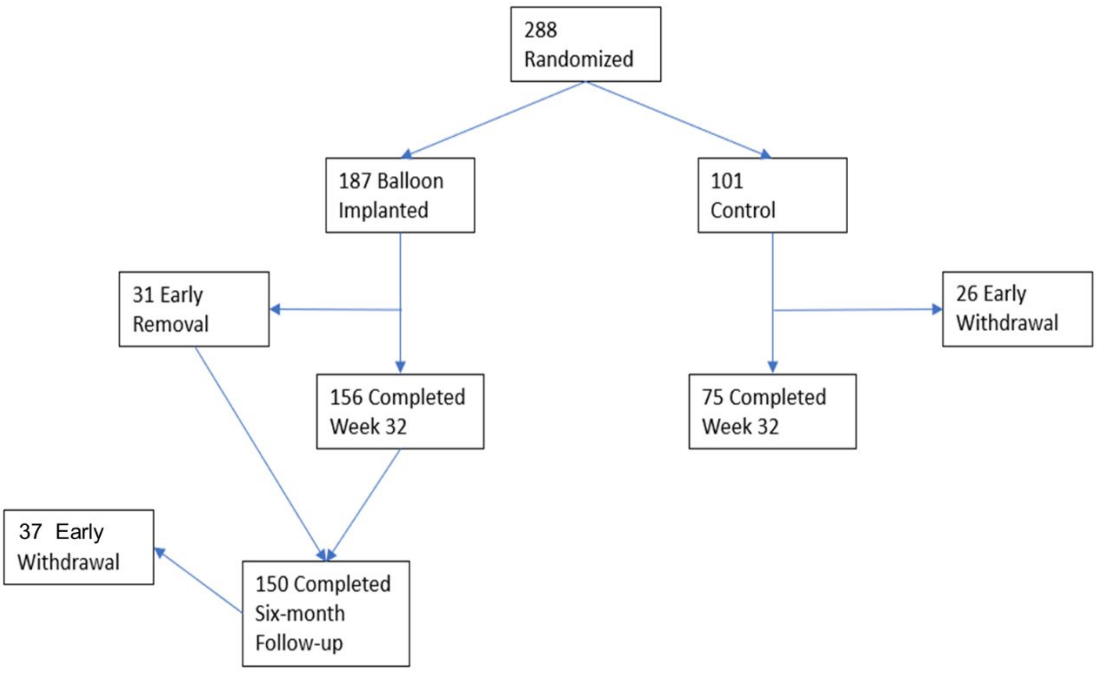

Figure 5: Study accountability tree

C. Study Population Demographics and Baseline Parameters

Baseline demographics were similar between the Spatz3 Adjustable Balloon and the control groups. Subjects had a mean age of 44 years, mean weight of 216 lbs., and a mean BMI of 35.8 kg/m^2. Females accounted for 87% of subjects in the Spatz3 Adjustable Balloon group and 89% in the control group. Black or African Americans made up 26% of subjects in the Spatz3 Adjustable Balloon group and 26% in the control group. Study subjects in the treatment group had comparable medical histories to those in the control group.

Key demographics and baseline physical characteristics are presented in Table 5.

Table 5: Baseline sex, ethnicity, race, and medical history

Characteristic	ITT Population		
	Control	Balloon Implanted	All Subjects
Age (years) – Mean (range)	44.0 (24.0-64.0)	44.4 (22.0-64.0)	44.3 (22.0-64.0)
Weight (lb.) – Mean (range)	216.4 (161-300)	216.3 (161-297)	216.4 (161-300)
Height (in) – Mean (range)	65.1 (59.0-73.0)	65.1 (58.5-73.0)	65.1 (58.5-73.0)
BMI (kg/m^2)	35.8 (30.3-40.9)	35.8 (30.2-40.3)	35.8 (30.2-40.9)
Sex – n (%)			
Female	90 (89%)	162 (87%)	252 (88%)
Male	11 (11%)	25 (13%)	36 (13%)
Race – n (%)			
White	72 (71%)	132 (71%)	204 (71%)
Black or African American	26 (26%)	49 (26%)	75 (26%)
Asian	1 (1%)	1 (1%)	2 (1%)
Native Hawaiian or Pacific Islander		1 (1%)	1 (0%)
None of the above	1 (1%)	3 (2%)	4 (1%)
Unknown	1 (1%)	1 (1%)	2 (1%)
Ethnicity – n (%)			
Hispanic or Latino	8 (8%)	10 (5%)	18 (6%)
Not Hispanic or Latino	92 (91%)	173 (93%)	265 (92%)
Unknown	1 (1%)	4 (2%)	5 (2%)
Medical History			
Hypertension – n (%)	32 (32%)	41 (22%)	73 (25%)
Diabetes – n (%)	4 (4%)	13 (7%)	17 (6%)
Sleep Apnea – n (%)	1 (1%)	1 (1%)	2 (1%)
Elevated Lipids – n (%)	23 (23%)	41 (22%)	64 (22%)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on all 288 randomized subjects: 187 treated subjects and 101 control subjects. The data include adverse events for treatment group subjects for the full duration of the study, which includes 32 weeks (8 months) of treatment and 6-months of follow-up. The data includes adverse events for control subjects for the full 32 weeks of dietary/exercise counseling.

The safety assessment of the Spatz Adjustable Balloon System included a complete review of reported serious adverse events (SAEs) and adverse events (AEs), as well as device and procedure-relatedness of AEs. Adverse effects are reported in Table 6 and Table 7.

Adverse effects that occurred in the PMA clinical study:

a. Serious Adverse Events

Ten (5.3%) treatment group subjects experienced 29 SAEs, while one control subject (1%) experienced one SAE. There were 24 device-related SAEs in 7 out of 187 treatment group subjects. The incidence of device-related SAEs was 3.7% (7/187, 95% C.I. 1.5%, 7.8%). An incidence of esophageal mucosal tear was related to the device placement procedure. Out of the 7 subjects with SAEs, 4 subjects had an early balloon removal. The most frequent SAEs were nausea, vomiting, and abdominal pain. Additional details are provided in Table 6.

Table 6: Device-related serious adverse events

Event	Device or Procedure Related*	Subjects with SAE** (% of All Treatment Subjects)	Events	Onset (Days to Event)	% of Subjects with SAE that had Balloon Removed
Nausea	Device	6/187 (3.2%)	7	Mean = 84.6 days Median = 131 days Range = 0-150 days	2/6 (33%)
Vomiting	Device	5/187 (2.7%)	5	Mean = 90.4 days Median = 131 days Range = 1-150 days	2/5 (40%)
Abdominal pain	Device	4/187 (2.1%)	4	Mean = 9.8 days Median = 1 days Range = 0-37 days	2/4 (50%)

Event	Device or Procedure Related*	Subjects with SAE** (% of All Treatment Subjects)	Events	Onset (Days to Event)	% of Subjects with SAE that had Balloon Removed
Dehydration	Device	3/187 (1.6%)	3	Mean = 92.7 days Median = 131 days Range = 7-140 days	1/3 (33%)
Diarrhea	Device	2/187 (1.1%)	2	Mean = 75.5 days Median = 76 days Range = 1-150 days	0/2 (0%)
Gastroesophageal reflux disease	Device	1/187 (0.5%)	1	Mean = 37.0 days Median = 37 days Range = 37-37 days	1/1 (100%)
Failure to thrive***	Device	1/187 (0.5%)	1	Mean = 7.0 days Median = 7 days Range = 7-7 days	1/1 (100%)
Hypokalemia	Device	1/187 (0.5%)	1	Mean = 150.0 days Median = 150 days Range = 150-150 days	0/1 (0%)
Esophageal Mucosal Tear	Device and Procedure	1/187 (0.5%)	1	Mean = 0 days Median = 0 days Range = 0-0 days	1/1(100%)

* A device-related adverse event was a result of device use; whereas a procedure-related adverse event was a result of the endoscopic procedure. An adverse event can be related to the device, procedure, both, or neither.

** An SAE is defined as an untoward event that: results in death; is life-threatening; requires inpatient hospitalization or prolongation of an existing hospitalization; results in persistent or significant disability or incapacity; is associated with a congenital anomaly or birth defect; or qualifies as "other" medically significant event.

***Failure to thrive defined as overall weakness and resulted from the following AEs: Nausea, Vomiting, Dehydration, Abdominal pain

b. Adverse Events

A total of 2,522 device-related AEs were reported. The majority of events were mild in severity (71.1%, 1,561/2,522). There were 446 moderate severity events (20.3%) and 179 severe events (8.1%).

Almost all treatment group subjects (183/187, 98%) experienced gastrointestinal AEs, with nausea, dyspepsia and vomiting being the most frequent (90% (169/187), 74% (137/187), and 72% (134/187) of subjects, respectively). Ten of

the 187 treatment group subjects (5.3%) required intravenous fluid infusion or intramuscular injections of Phenergan for severe nausea and vomiting.

In other system organ classes headache (44/187, 24%), hiccups (63/187, 34%), dizziness (40/187 21%), and dehydration (38/187, 20%) were the most frequent AEs. Though not associated with an AE, one balloon deflation was observed at the time of balloon removal (1/187, 0.5%). The suspected reason for the deflation was the presence of a fungus biofilm on the surface of the balloon.

Table 7: Device and procedure-related gastrointestinal adverse events occurring in >10% of the Spatz3 Adjustable Balloon -treatment subjects

Device- or Procedure-Related Adverse Event	Subjects (% of Treatment Subjects) N=187	Day of Onset Median (Mean) Range	Duration (days) Median (Mean) Range	Severity n/N (%) Mild Moderate Severe	Subjects with Onset </= 3 Days Post-Implantation		
					Any Duration (% of Treatment Subjects)	Duration 14-30 Days (% of </= 3 Days)	Duration >30 Days (% of </= 3 Days)
Nausea	169 (90.4%)	19 (62.7) 0-381	6 (17.7) 0-217	66/169 (39.1%) 62/169 (36.7%) 41/169 (24.3%)	152 (89.9%)	7 (4.6%)	13 (8.6%)
Dyspepsia	137 (73.3%)	18 (68.8) 0-385	14 (28.3) 0-247	64/137 (46.7%) 52/137 (38.0%) 21/137 (15.3%)	106 (77.4%}	16 (15.1%)	10 (9.4%)
Vomiting	134 (71.7%)	28 (68.1) 0-381	3 (12.8) 0-154	67/134 (50.0%) 37/134 (27.6%) 30/134 (22.4%)	79 (59.0%}	4 (5.1%)	5 (6.3%)

Device- or Procedure-Related Adverse Event	Subjects (% of Treatment Subjects) N=187	Day of Onset Median (Mean) Range	Duration (days) Median (Mean) Range	Severity n/N (%) Mild Moderate Severe	Subjects with Onset </= 3 Days Post-Implantation		
					Any Duration (% of Treatment Subjects)	Duration 14-30 Days (% of </= 3 Days)	Duration >30 Days (% of </= 3 Days)
Eructation	121 (64.7%)	23 (55.0) 0-385	40 (60.9) 0-291	95/121 (78.5%) 19/121 (15.7%) 5/121 (4.1%)	79 (65.3%}	12 (15.2%)	32 (40.5%)
Abdominal pain	113 (60.4%)	10 (58.3) 0-384	8 (20.4) 0-366	49/113 (43.4%) 44/113 (38.9%) 20/113 (17.7%)	92 (81.4%}	12 (13.0%)	14 (15.2%)
Constipation	95 (50.8%)	27 (71.8) 0-398	24 (34.1) 0-239	79/95 (83.2%) 12/95 (12.6%) 3/95 (3.2%)	42 (44.2%}	6 (14.3%)	11 (26.2%)
Diarrhea	73 (39.0%)	43 (81.8) 0-349	5 (16.7) 0-147	44/73 (60.3%) 23/73 (31.5%) 6/73 (8.2%)	18 (24.7%}	4 (22.2%)	1 (5.6%)
Breath odor	61 (32.6%)	29 (69.3) 0-314	27 (45.1) 0-275	57/61 (93.4%) 2/61 (3.3%) 1/61 (1.6%)	28 (45.9%}	5 (17.9%)	10 (35.7%)
Abdominal rigidity	38 (20.3%)	0 (51.6) 0-231	7 (13.3) 0-123	24/38 (63.2%) 13/38 (34.2%) 1/38 (2.6%)	34 (89.5%}	2 (5.9%)	4 (11.8%)

Device- or Procedure-Related Adverse Event	Subjects (% of Treatment Subjects) N=187	Day of Onset Median (Mean) Range	Duration (days) Median (Mean) Range	Severity n/N (%) Mild Moderate Severe	Subjects with Onset </= 3 Days Post-Implantation		
					Any Duration (% of Treatment Subjects)	Duration 14-30 Days (% of </= 3 Days)	Duration >30 Days (% of </= 3 Days)
Abdominal distension	29 (15.5%)	11 (50.9) 0-331	29 (66.5) 1-300	23/29 (79.3%) 4/29 (13.8%) 2/29 (6.9%)	13 (44.8%}	4 (30.8%)	6 (46.2%)
Gastro-esophageal reflux disease	19 (10.2%)	43 (70.8) 0-274	21 (31.0) 0-96	10/19 (52.6%) 5/19 (26.3%) 4/19 (21.1%)	4 (21.1%}	0 (0%)	1 (25.0%)

Twenty-eight treatment group subjects (28/187, 15%) received downward adjustments as a result of AEs. The proportion of subjects who had downward adjustments increased depending on the initial balloon volume (from 0% with 400 ml initial volume to 20% with 550 ml initial volume). The mean time between implantation and downward adjustment across initial volume subgroups was 98 to 106 days (Table 8). Nausea, vomiting, and dyspepsia were the most frequent AEs that triggered adjustments.

Table 8: Summary of downward volume adjustments due to adverse events by initial balloon volume

Initial Volume (ml)	All Subjects N (% of 187)	Down-Adjusted Subjects N (% of # at initial volume)	Days After Implant Mean ± SD Median (Min-Max)	Volume Decreased (ml) Mean ± SD Median (Min-Max)	Subjects with Adverse Events with Action = 'Decreased Volume' N (% of down adjusted subjects)
400	14 (7%)	0 (0.0%)	n/a	n/a	n/a

Initial Volume (ml)	All Subjects N (% of 187)	Down-Adjusted Subjects N (% of # at initial volume)	Days After Implant Mean ± SD Median (Min-Max)	Volume Decreased (ml) Mean ± SD Median (Min-Max)	Subjects with Adverse Events with Action = 'Decreased Volume' N (% of down adjusted subjects)
450	44 (24%)	5 (11.4%)	101±74 134 (21-175)	165±49 150 (125-250)	Nausea: 4 (80%) Vomiting: 4 (80%) Dyspepsia: 3 (60%) Abdominal pain: 2 (40%) Concentrated urine*: 1 (20%) Constipation: 1 (20%) Diarrhea: 1 (20%) Fatigue: 1 (20%)
500	32 (17%)	4 (12.5%)	106±65 137 (9-142)	150±0 150 (150-150)	Dehydration: 1 (25%) Dyspepsia: 1 (25%) Nausea: 1 (25%) Vomiting: 1 (25%)
550	97 (52%)	19 (19.6%)	98±52 119 (8-168)	166±50 150 (100-300)	Vomiting: 13 (68%) Nausea: 12 (63%) Dyspepsia: 7 (37%) Eructation: 6 (32%) Abdominal pain: 5 (26%) Breath odor: 3 (16%) Abdominal distension: 2 (11%) Hiccups: 2 (11%) Constipation: 1 (5%) Dehydration: 1 (5%) Diarrhea: 1 (5%) Dizziness: 1 (5%) Headache: 1 (5%)

Initial Volume (ml)	All Subjects N (% of 187)	Down-Adjusted Subjects N (% of # at initial volume)	Days After Implant Mean ± SD Median (Min-Max)	Volume Decreased (ml) Mean ± SD Median (Min-Max)	Subjects with Adverse Events with Action = 'Decreased Volume' N (% of down adjusted subjects)
All	187 (100%)	28 (15.0%)	100±56 127 (8-175)	163±45 150 (100-300)	Vomiting: 18 (64%) Nausea: 17 (61%) Dyspepsia: 11 (39%) Abdominal pain: 7 (25%) Eructation: 6 (21%) Breath odor: 3 (11%) Abdominal distension: 2 (7%) Constipation: 2 (7%) Dehydration: 2 (7%) Diarrhea: 2 (7%) Hiccups: 2 (7%) Concentrated urine*: 1 (4%) Dizziness: 1 (4%) Fatigue: 1 (4%) Headache: 1 (4%)

There were 50 treatment group subjects (50/187, 27%) who had AEs and requested balloon removal. Twenty-eight of them (28/50, 56%) had a downward volume adjustment to see if this would allow therapy to continue (Table 9). Of these 28 subjects who had downward adjustments, 21 completed the 8-month balloon implantation procedure and thus avoided an early explant. Of the 31 subjects who had an early explant, 29 were due to AEs, 1 to pregnancy, and 1 to relocation.

Table 9: Early explants by reason and downward volume adjustment

Reason for requested explant	Number pf patients requested explant	Number of patients who had down adjustment	Early explants conducted	Early explants avoided
Adverse events	50/187 (27%)	28/50 (15%)	29/50 (58%)	21/50 (42%)
Pregnancy	1/187 (0.5%)	0/187 (0%)	1/1 (100%)	0/1 (0%)
Relocation	1/187 (0.5%)	0/187 (0%)	1/1 (100%)	0/1 (0%)
Total	52/187 (28%)	28/187 (15%)	31/52 (60%)	21/52 (40%)

Table 10 provides a summary of early explants by initial balloon volume. Eleven of the 31 early explanted-subjects had abnormal endoscopic findings in the esophagus and 6 in the stomach. There wasn't a clear trend towards a higher proportion of early explants or a higher incidence of endoscopic findings with increasing initial balloon volume.

Table 10: Summary of early explants by initial balloon volume

Initial Volume (ml)	All Subjects N (% of 187)	Early Explanted Subjects N (% of #at initial volume)	Days After Implant Mean ± SD Median (Min-Max)	Reasons for Removal	Total # of Endoscopic findings at early explant
400	14 (7%)	1 (7.1%)	7±0 7 (7-7)	Adverse event: 1	None
450	44 (24%)	6 (13.6%)	132±46 146 (40-165)	Adverse event: 5 Subject's decision: 1	Esophagus abnormal: 4 Esophagitis grade 1 or 2: 1 Esophagitis grade 3 or 4: 2 Barrett's esophagus: 1 Stomach abnormal: 1 Erosive Gastritis: 1
500	32 (17%)	8 (25.0%)	71±73 46 (2-203)	Adverse event: 6 Relocation: 1 Subject's decision: 1	Esophagus abnormal: 1 Esophagitis grade 1 or 2: 1
550	97 (52%)	16 (16.5%)	64±64 34 (1-168)	Adverse event: 14 Pregnancy: 1 Subject's decision: 1	Esophagus abnormal: 6 Esophagitis grade 1 or 2: 2 Esophagitis grade 3 or 4: 2 Stomach abnormal: 5 Non-erosive gastritis: 4 Gastric ulcer: 1 Pyloric ulcer: 1
All	187 (100%)	31 (16.6%)	77±67 54 (1-203)	Adverse event: 26 Pregnancy: 1 Relocation: 1 Subject's decision: 3	Esophagus abnormal: 11 Esophagitis grade 1 or 2: 4 Esophagitis grade 3 or 4: 4 Barrett's esophagus: 1 Stomach abnormal: 6 Erosive Gastritis: 1 Non-erosive gastritis: 4 Gastric ulcer: 1 Pyloric ulcer: 1

2. Effectiveness Results

The analysis of effectiveness was based on the ITT cohort, which included 187 treatment and 101 control subjects. Key effectiveness outcomes are presented in Table 11, Table 12, and Table 13.

Primary Effectiveness Endpoints

Both co-primary endpoints were met.

Total Body Weight Loss

The Spatz3 US Pivotal Study met its first co-primary endpoint for all prespecified datasets (Table 11). At Week 32 the difference between the treatment group and control group arm mean %TBLs predicted by the linear model from the multiply-imputed ITT population dataset was 11.7% TBL, and its 97.5% lower confidence bound was 9.9% TBL. As this exceeds the pre-specified super-superiority margin of 4.5% TBL, the combination of Spatz3 Adjustable Balloon and dietary/exercise counseling is deemed to have super-superiority over dietary/exercise counseling alone.

Additional pre-specified analysis results are:

- LOCF-imputed ITT (ITT-LOCF) population dataset: difference between predicted means = 10.7% TBL with LCB 9.0% TBL; and
- PPP dataset: difference between predicted means = 11.1% TBL with LCB 9.2% TBL.

Table 11: Total body loss (%TBL) at Week 32

	Treatment	**Control[1]**	**Treatment – Control Difference**			
	Mean (SD, min-max)	**Mean (SD, min-max)**	**ΔMeans**	**ΔLSMeans[2]**	**97.5% LCB[3]**	**p**
%TBL – ITT - Multiple Imputation	15.0% (7.7%, -1.9%-34.7%)	3.3% (6.7%, -19.0%-21.7%)	11.7%	11.7%	9.9%	<0.0001
%TBL – ITT - LOCF	13.8% (7.5%, -0.5%-32.8%)	3.1% (5.5%, -6.7%-21.7%)	10.7%	10.7%	9.0%	<0.0001
%TBL - PPP – No Imputation	15.2% (6.9%, 1.4%-32.8%)	4.1% (5.9% -6.7%-21.7%)	11.1%	11.1%	9.2%	<0.0001

[1] 100 control subjects are included in the analysis though 101 in total were enrolled because information was not collected from 1 patient that was necessary to fit the statistical analysis model.

[2] Difference between means predicted by a statistical model with factors for treatment, site, sex, and baseline BMI.

[3] 97.5% lower confidence bound (LCB) for the difference between the model-predicted means.

Responder Analysis
The Spatz3 Adjustable Balloon Study also met its second co-primary effectiveness endpoint. The three datasets mentioned above were used to calculate the proportion of responders, i.e., treatment group subjects whose Week 32 %TBL exceeded 5% TBL, and an exact 97.5% lower confidence bound for that proportion. These proportions (91.7%, 87.7%, and 96.2% from the multiply-imputed ITT population, ITT-LOCF population, and PPP datasets, respectively) and their lower confidence bounds (87.2%, 82.1%, and 91.4%) were above the pre-specified performance goal of 50% (Table 12).

Table 12: Response rate (%TBL≥5%) in treatment group at Week 32

	All Treatment Subjects		Responders (%TBL≥5%)		
	N	Mean %TBL	N	Proportion	97.5% LCB
ITT - Multiple Imputation	187	15.0%	171.4[1]	91.7%	87.2%
ITT - LOCF	187	13.8%	164	87.7%	82.1%
PPP – No Imputation	132	15.2%	127	96.2%	91.4%

[1] Mean of the five counts from the five multiply-imputed datasets

Secondary Effectiveness Endpoints

The study had two prespecified secondary endpoints.

Maintenance of Weight Loss
The first secondary endpoint was the proportion of treatment group subjects who, by the end of the 6-month post-removal follow-up, had maintained ≥40% of the weight loss they had achieved by the balloon extraction date. This analysis was conducted on treatment group subjects who completed Week 56 regardless of their protocol compliance (150 treated subjects completed week 56 of the study). Subjects who had an early balloon removal were included (if they completed the 6-month follow-up) and two analyses were performed:

- using the actual post-extraction weight on the extraction day,
- and using their imputed week 32 weight (the mean of the 5 imputed week 32 weights").

The proportion calculated from the non-imputed ITT population dataset was 74.0% excluding subjects with missing weight measurements. The proportion from the multiply-imputed ITT population dataset was 73.3%" (Table 13).

Table 13: Weight loss maintenance 6 months post balloon removal – ITT population

	Responders (Preserved ≥40% of weight loss)	
	N	**Proportion**
Post-extraction weight on the extraction day	111	74.0% (111/150)
Multiply-imputed Week 32 visit weight	110	73.3% (110/150)

Excess Weight Loss

The second secondary endpoint was proportion of balloon group subjects that achieved percent excess weight loss (%EWL) ≥ 25% at 32 weeks. Excess Body Weight Loss (EWL), which assumes an ideal BMI of 25 kg/m^2 and uses height (h) measured in inches, was calculated as follows:

$$Ideal\ Weight\ (lb) = \frac{25\ x\ h^2}{703}$$

$$Excess\ Weight\ (lb) = Day\ 0\ weight\ (lb) - Ideal\ Weight\ (lb)$$

$$\%EWL = \frac{TBL\ (lb)}{Excess\ Weight\ (lb)}\ x\ 100\%$$

The proportion of subjects with EWL ≥ 25% was calculated from the multiply-imputed ITT population dataset (Table 14).

Table 14: Response rate (EWL ≥ 25%) at Week 32 – ITT population

	All Treatment Subjects		Responders (EWL≥25%)	
	N	**Mean %EWL**	**N**	**Proportion**
Multiple Imputation	187	53.6%	157	84.0%

3. Subgroup Analyses
   No pre-procedure characteristics were evaluated for potential association with outcomes.

4. Pediatric Extrapolation
   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

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 7 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. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

FDA has alerted health care providers about potential risks with liquid-filled intragastric balloons.[1] Specific risks include, but may not be limited to: spontaneous hyperinflation, acute pancreatitis, esophageal perforation, gastric perforation, aspiration, and death. As such, FDA considered the Spatz3 Adjustable Balloon System global product complaint data when making the benefit-risk assessment for the Spatz3 Adjustable Balloon System.

Table 15 includes Spatz3 Adjustable Balloon System AE complaints reported through OUS clinical product surveillance between August 30, 2012 and March 15, 2021. Spatz FGIA, Inc has not scientifically validated the data in Table 15 and there may be duplication of some events due to multiple sources of data collection. Some events have not been directly attributed to the Spatz3 Adjustable Balloon System.

Bond failure has been remedied with 12,614 improved devices implanted between March 2020 and March 2021.

Table 14: Spatz3 Adjustable Balloon adverse event complaints reported through OUS clinical product surveillance between August 30, 2012 and March 15, 2021

	Aug 2012 to Mar 2021		**March 2020 to March 2021**	
# of balloons	**76,000**		**12,614**	
Event	**Count**	**† Rate (%)**	**Count**	**† Rate (%)**
Serious Adverse Events				
Deflation & Migration with bowel Obstructed	23	0.030	0	0.000
Ulcer	22	0.029	0	0.000
Stomach Perforation	19	0.025	1	0.008
Death*	7	0.009	0	0.000
Esophageal Perforation	3	0.004	0	0.000

[1] See "The FDA alerts health care providers about potential risks with liquid-filled intragastric balloons" available at https://www.fda.gov/medical-devices/letters-health-care-providers/fda-alerts-health-care-providers-about-potential-risks-liquid-filled-intragastric-balloons

Dehydration	2	0.003	0	0.000
Gastric outlet obstruction	2	0.003	0	0.000
Gastritis	1	0.001	0	0.000
Allergic Reaction	1	0.001	0	0.000
Bowel Perforation	1	0.001	0	0.000
Bleeding	1	0.001	0	0.000
Pancreatitis**	0	0.000	0	0.000
Aspiration**	0	0.000	0	0.000
Device Failures leading to inability to Implant				
Inflation tube tear	181	0.238	10	0.079
Hole in the Balloon Prior/during Implantation	28	0.037	7	0.055
Procedure usability complications***	12	0.016	2	0.016
Use errors	6	0.008	1	0.008
Valve Disconnected	3	0.004	0	0.000
Inflation tube too long	1	0.001	0	0.000
Extension tube leak	1	0.001	0	0.000
Defective valve	1	0.001	0	0.000
Device Failures leading to inability to Adjust				
Procedure usability complications	9	0.012	0	0.000
Valve Disconnected	2	0.003	0	0.000
Inflation tube knotted	2	0.003	0	0.000
Broken Funnel	1	0.001	1	0.008
Cap nylon loop tear	1	0.001	0	0.000
White catheter broke	4	0.005	0	0.000
Device Failures during treatment phase				
Balloon Deflations for all reasons	1668	2.195	38	0.301
Deflation from Balloon Bond failure****	628	0.826	2	0.016
Deflation with insufficient information to determine cause	400	0.526	10	0.079
Deflation & passage in the stool	260	0.342	3	0.024
Deflation caused by fungal infection	222	0.292	8	0.063
Deflation caused by Cap Failure	44	0.058	13	0.103
Deflation caused by Balloon microholes	37	0.049	2	0.016
Spontaneous Hyperinflation	32	0.042	2	0.016
Deflation caused by Balloon Burst	31	0.041	0	0.000
Deflation & Migration with bowel Obstructed	23	0.030	0	0.000
Deflation & balloon vomited	18	0.024	0	0.000

Deflation & Migration caused by fungal infection	5	0.007	0	0.000

* 2 of the 7 deaths underwent autopsies and the deaths could not be definitively attributed to the Spatz3 Adjustable Balloon or the related procedures.

**Reported with other intragastric balloons

*** Reported usability complications during implantation procedures include improper use of the cap, insertion facilitator, valve-hold and extension tube.

**** Bond failure has been remedied with 12,614 improved devices implanted between March 2020 and March 2021 - reporting a bond failure rate of 0.016% (2/12,614).

† The event rate represents the counts of an event divided by the number of devices distributed as of the reporting cut-off on March 15, 2021. Note that the number of devices distributed may be greater than the number of devices placed

XII. 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.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The Spatz3 US Pivotal study had two co-primary effectiveness endpoints, both of which were met. These endpoints demonstrated that the Spatz3 Adjustable Balloon System was more effective than a medically supervised diet and exercise program alone for 32 weeks. At the 32-week follow-up, the %TBL was 15.0% for the Spatz3 Adjustable Balloon primary analysis group compared to 3.3% in the control group ($p<0.0001$). The difference in %TBL between Spatz3 Adjustable Balloon treatment and control groups was 11.7% (97.5% LCB 9.9%). At the 32-week follow-up, the proportion of Spatz3 Adjustable Balloon treatment group subjects who achieved ≥ 5%TBL was 91.7% (97.5% LCB 87.2%).

The proportion of Spatz3 Adjustable Balloon treatment group subjects who maintained 40% of the TBL with the Spatz3 Adjustable Balloon six months after the Spatz2 Adjustable Balloon was removed calculated from the non-imputed ITT population dataset was 74.0% excluding subjects with missing weight loss maintenance. The proportion from the multiply-imputed ITT population dataset was 73.3%.

The proportion of subjects with excess weight loss (EWL) ≥ 25% was 84.0% (157/187) which was calculated from the multiply-imputed ITT population dataset.

B. Safety Conclusions

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

In the Spatz3 US Pivotal study there were no deaths and no subjects experienced any irreversible complications. There were 24 device- or procedure-related SAEs in 7 out of 187 treated subjects. Therefore, the device- or procedure-related SAE rate was 3.7%, (95% C.I.: 1.5%, 7.8%). The most frequent SAE was nausea that occurred in 6/187 treated subjects (3.2%).

A total of 2,522 device-related AEs were reported. The majority of events were mild in severity (71.1%, 1,561/2,522). There were 446 moderate severity events (20.3%) and 179 severe events (8.1%).

Almost all treatment group subjects (183/187, 98%) experienced gastrointestinal AEs, with nausea, dyspepsia and vomiting being the most frequent (90% (169/187), 74% (137/187), and 72% (134/187) of subjects, respectively). Ten (10) of the 187 treatment group subjects (5.3%) required intravenous fluid infusion or intramuscular injections of Phenergan for severe nausea and vomiting. In other system organ classes headache (44/187, 24%), hiccups (63/187, 34%), dizziness (40/187 21%), and dehydration (38/187, 20%) were the most frequent.

There were 50 treatment group subjects who had AEs and requested balloon removal (28%). Twenty-eight of them (56% (28/50)) had a downward volume adjustment. Of these 28 subjects who had downward adjustments, 21 completed the 8-month balloon implant period. Of the 31 subjects who had an early explant (16.6%, 31/187), 29 were due to AEs (15.5%, 29/187), 1 to pregnancy (0.5% 1/187), and 1 (0.5%, 1/187) to relocation.

There was report of a deflated balloon in 1 subject found during the balloon removal procedure (0.5%, 1/187). The suspected reason for the deflation was the presence of a fungus biofilm on the surface of the balloon.

The probable risks of the device are also based on OUS clinical product surveillance of the Spatz3 Adjustable Balloon System. Complaint information support that the Spatz3 Adjustable Balloon poses the general risks associated with liquid-filled intragastric balloons as a device class including, but not limited to: spontaneous hyperinflation, acute pancreatitis, esophageal perforation, gastric perforation, bowel perforation, aspiration, and death. The most frequently reported complaint is balloon deflation (2.2%). Deflation with migration (passage in stool) complaint rate is 0.34%, and bowel obstruction, which first requires migration of a deflated balloon, complaint rate is 0.03%.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The %TBL difference between treatment and control of 11.7% is comparable to or greater than other endoscopic/intragastric devices intended for weight loss. The Spatz3 Adjustable Balloon System treatment subjects (mean baseline weight of 216 lbs.) experienced an approximate weight loss over 8 months of 25 lbs. on average more than control subjects. The ITT-LOCF population experienced a mean %TBL of 10.7% more than did control subjects. The percentage of Spatz3 Adjustable Gastric Balloon System treated subjects who achieved ≥5% TBL was 91.7%; whereas, the ITT-LOCF cohort was 87.7%. Co-primary endpoints of the clinical study were met.

The probable risks of the device are based on data collected in a clinical study conducted to support PMA approval as described above and real-world complaint data. In the clinical study, the device- or procedure-related SAE rate was 7/187 subjects (3.7%, 95% C.I.: 1.5%, 7.8%). The most frequent SAE was nausea that occurred in 6/187 treated subjects (3.2%). The most serious SAE was an esophageal mucosal tear. The remaining SAEs were related to abdominal pain, vomiting, dehydration, gastroesophageal reflux disease, hypokalemia, diarrhea, and failure to thrive. The SAEs were all reversible by removing the device.

Real-world complaint data from outside US device use demonstrates that known risks associated with liquid-filled IGBs as a device class occur with the Spatz3 Adjustable Balloon System, including: gastric, bowel, and esophageal perforation; spontaneous hyperinflation; bowel obstruction; ulceration; aspiration; gastric outlet obstruction; and death. Accurate rates for these events in the US patient population can be gathered post-market.

The use of the Spatz3 Adjustable Gastric Balloon System has an acceptable safety profile in view of the patient benefits and consideration for post-market data collection.

Additional factors considered in determining probable risks and benefits for the Spatz3 Adjustable Balloon System device included:

- White females accounted for a high percentage of study subjects (87% female, 71% white). Generalizability of the results in the non-white and male populations is unknown.

- In the clinical trial, there was different oral medications provided to treatment and control subjects. This may have introduced bias in the effectiveness outcomes. For example, Aprepitant (Emend®) was given following the implantation procedure for treatment group subjects. This drug is known to affect hunger and satiety. Also, the probiotic, lactobacillus acidophilus was given to treatment group subjects throughout the course of the study. These probiotics may have provided weight loss benefits.

- Overall, 31/187 Spatz3 Adjustable Balloon System subjects had the device removed early (16.6%). This high removal rate may impact patient's ability to fully benefit from use of the device. This also creates moderate uncertainty in the benefit and risk associated with device use. However, the adjustable volume design of the Spatz3 Adjustable Balloon should help mitigate early termination of therapy for some patients.

- The real-world evidence on device safety from Spatz3 Adjustable Balloon System global product experience includes surveillance data that has not been scientifically validated and there may be duplication of some events due to multiple sources of data collection. Additionally, some events have not been directly attributed to the Spatz3 Adjustable Balloon System.

- The current non-surgical options available for weight loss in patients with obesity vary in effectiveness and mechanisms of action. This device provides an additional therapeutic option.

1. Patient Perspective
   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for weight loss in adult patients with obesity with a BMI of 35.0 - 40.0 kg/m^2 or a BMI of 30.0 - 34.9 kg/m^2 with one or more obesity-related comorbid conditions in conjunction with a supervised weight control program, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the Spatz3 Adjustable Balloon System when used in accordance with the indications for use. Subjects treated with the Spatz3 Adjustable Balloon System lost on average 15.0% of their baseline weight compared to 3.3% weight loss in control subjects. About 92% of subjects treated with the Spatz3 Adjustable Balloon System lost at least 5% of their baseline weight. The safety profile for the Spatz3 Adjustable Balloon System is reasonable, with seven subjects experiencing twenty-four device- or procedure-related SAEs among 187 subjects in whom received the Spatz3 Adjustable Balloon placed in the US pivotal study. Most AEs were mild or moderate and were reversible with device removal. In conclusion, the Spatz3 Adjustable Balloon system is safe and effective for weight loss in patients with BMI between 35.0 and 40.0 kg/m^2 or a BMI of 30.0-34.9 kg/m^2 with one or more obesity-related comorbid conditions when used in conjunction with a supervised weight control program.

XIV. CDRH DECISION

CDRH issued an approval order on [date of approval order]. The final clinical conditions of approval cited in the approval order are described below.

In addition to the Annual Report requirements, continued approval of the PMA is based, in part, on your completion of a post-approval study (PAS) described below. The Spatz3 PAS will be conducted per the PAS protocol v1.3c, dated October 13, 2021.

PMA Post-Approval Study - The Spatz3 Post Approval Study is a multicenter, open-label study for the continuing evaluation and periodic reporting of the safety and effectiveness of the Spatz3 Adjustable Balloon System for weight loss in adults with obesity 22 years and older with a BMI of 35.0 - 40.0 kg/m^2 or a BMI of 30.0 to 34.9 kg/m^2 with one or more major obesity-related comorbid conditions who have failed to achieve and maintain weight-loss with a supervised weight control program. Subjects will be treated with the Spatz3 Adjustable Balloon System in conjunction with a diet and exercise plan. Subjects will be treated with the Spatz3 Adjustable Balloon for 8 months and subjects who lose at least 5% of their initial body weight will be followed for an additional 6 months to assess for weight-loss maintenance.

The study will be conducted at up to 30 US centers. The enrollment at each site will range from 20 to a maximum of 60 subjects. The study is an all-comers study that will enroll the first patients to receive the Spatz3 Adjustable Balloon System at each center in the US following FDA approval of the PMA. Once the study has implanted 50% of the projected sample size of 537 subjects, and there are enough participating centers that are actively implanting devices to ensure treatment of 537 subjects, any center that has reached its designated study enrollment maximum may implant the device in patients outside of the study. A PAS interim report will be submitted to FDA when a center is ready to begin treating subjects outside of the study informing FDA that the above conditions are met.

The primary study endpoint is to demonstrate that the rate of device or procedure-related serious adverse events (SAEs) is less than 8% at 8 months. The secondary study endpoint is to demonstrate that the mean percent total body weight loss (%TBL) is not less than 11% TBL at 8 months. Other 8-month study endpoints include: weight loss measured by percent excess weight loss (%EWL) and device- and/or procedure-related adverse events. The study will also provide rates with confidence intervals of balloon deflation with migration and other important device risks. Mean %TBL and %EWL will be measured at 6-months post-balloon removal in subjects who lost at least 5% TBL during the 8-month balloon therapy.

You must meet the following timelines for:

- complete initiation of all study sites within 7 months of the PMA approval date;
- first study subject enrolled within 4 months of the PMA approval date;
- 50% of subjects enrolled within 7 months of the PMA approval date;
- 100% of subjects enrolled within 16 months of the PMA approval date;
- follow-up the last patient at the last study site within 30 months of the PMA approval date; and

- submit a final report to the Agency within 33 months of the PMA approval date.

You must submit separate periodic PAS reports on the progress and data of the Spatz3 Post Approval Study as follows:

- PAS Progress Reports every six months until subject enrollment has been completed, and annually thereafter.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports (i.e., every 3 months), in addition to your periodic (6-months) PAS Progress Reports, until FDA notifies you otherwise.
- An interim PAS Progress Report will be provided once all subjects have been explanted.

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

XV. 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.