SUMMARY OF SAFETY AND PROBABLE BENEFIT (SSPB)

I. GENERAL INFORMATION

Device Generic Name: Pediatric Esophageal Atresia Anastomosis Device

Device Trade Name: Flourish™ Pediatric Esophageal Atresia Device

Device Procode: PTK

Applicant's Name and Address: Wilson-Cook Medical Inc.
4900 Bethania Station Road
Winston-Salem, NC 27105

Date(s) of Panel Recommendation: None

Humanitarian Device Exemption (HDE) Number: H150003

Humanitarian Use Device (HUD) Designation Number: HUD # 10-0239

Date of HUD Designation: October 28, 2010

Date of Notice of Approval to Applicant: May 12, 2017

II. INDICATIONS FOR USE

The Flourish Pediatric Esophageal Atresia Device is indicated for use in lengthening atretic esophageal ends and creating an anastomosis with a non-surgical procedure in pediatric patients, up to one year of age with esophageal atresia without a tracheoesophageal fistula (TEF) or in pediatric patients up to one year of age for whom a concurrent TEF has been closed as a result of a prior procedure. This device is indicated for atretic segments < 4cm apart.

The indication for use statement has been modified from that granted for the HUD designation. The HUD designation was "for lengthening atretic esophageal ends and creating an anastomosis with a non-surgical procedure in pediatric patients, up to one year of age with esophageal atresia without a currently existing tracheoesophageal fistula (TEF), or for whom a concurrent TEF has been closed as a result of a prior procedure." It was modified for the HDE approval to include the device trade name and specify that atretic segments must be < 4cm apart.

III. CONTRAINDICATIONS

The Flourish Pediatric Esophageal Atresia Device is contraindicated for the following:

- Patients older than one year of age or with teeth as it may damage the oral catheter.
- Patients who have an existing TEF.
- For creation of an anastomosis other than in the esophagus.

- For atretic segments > 4cm apart.
- Patients without an established and appropriately sized gastrostomy tract.
- Patients having gastrostomy site signs of significant infection.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Flourish Pediatric Esophageal Atresia Device labeling.

V. DEVICE DESCRIPTION

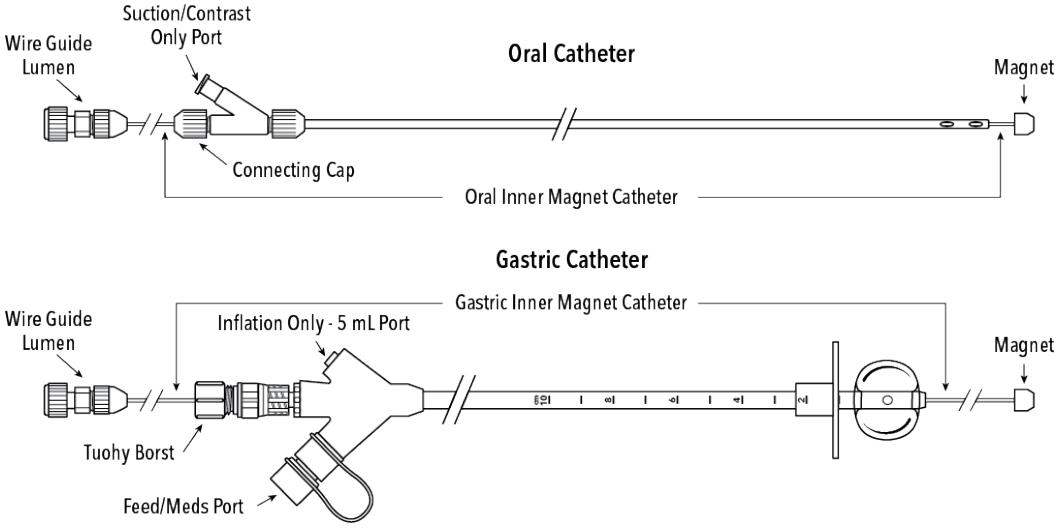
The Flourish Pediatric Esophageal Atresia Device consists of an oral/esophageal catheter and a gastric catheter. The oral/esophageal catheter is a 10 Fr two-lumen catheter. One lumen is for injection of contrast to confirm anastomosis; the other is for suction of saliva.

The gastric catheter is a modified two-lumen 18 Fr/ 5 cc balloon retention catheter. One lumen is for balloon inflation/deflation. The second lumen is modified by the addition of the gastric magnet catheter, essentially creating a lumen within a lumen. This modified arrangement allows for initial placement of a wire to guide introduction of the gastric magnet catheter assembly. Once the wire guide is removed from the gastric magnet catheter, flushing can occur through this created lumen or through an added accessory lumen.

Feed is delivered through the original accessory feed port adjacent to the adapted central port. The inflated balloon holds 5 mL liquid.

The distal end of each of the internal catheters is fitted with a bullet-shaped neodymium iron boron (NdFeB) magnet, which features a central hole for insertion of up to a 0.038-inch guide wire. When the two (2) catheters are aligned tip to tip the magnets have opposite polarities; thus attracting each other. They are cylindrically shaped and have a diameter of 6.35 mm. Each magnet catheter is 56.5" in length. Figure 1 illustrates the complete device.

Figure 1- Flourish Pediatric Esophageal Atresia Device:



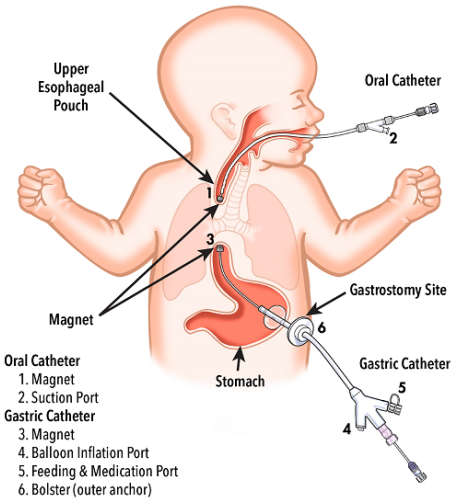
Principles of Operation

In a candidate infant, the distance between the atretic segments is assessed under fluoroscopy using metal probes. After identification of the pouches, the oral/esophageal catheter is inserted orally and advanced until the magnet is located at the distal end of the upper pouch. The gastric catheter is inserted over a wire guide, under fluoroscopy through a mature stoma and advanced until the magnet is located at the distal end of the lower pouch. The gastric catheter is secured to the stomach wall internally with a balloon and externally with a bolster. See Figure 2 - Flourish Pediatric Esophageal Atresia Device Placement, below.

Within three (3) to thirteen (13) days, the traction caused by the magnets allows the esophageal sacs to approximate. Biplane chest radiographs are taken to assess the distance between magnets. Once approximated, the surrounding tissues grow together while the tissue between the magnets necroses causing development of an anastomosis, thereby creating a connected passage from mouth to stomach.

Once an anastomosis has been confirmed through fluoroscopy, the magnets are removed. The oral/esophageal inner magnet catheter at proximal end of the oral/esophageal catheter is cut. A new wire is introduced through the oral/esophageal inner magnet catheter through the newly formed anastomosis and exits through the gastrostomy port. The oral/esophageal catheter is pushed distally toward the stomach until magnets are in the stomach, below the anastomosis. Then, the oral/esophageal inner magnet catheter is gently pushed and the gastric catheter is pulled until the system exits from gastrostomy site, thus removing the gastrostomy tube, oral/esophageal and gastric inner magnet catheters, and the magnet pair as a unit. A new orogastric tube or nasogastric tube is placed for one (1) to three (3) days.

Figure 2- Flourish Pediatric Esophageal Atresia Device Placement:



VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conventional procedures used in the treatment of lengthening atretic esophageal ends that are < 4cm apart and creating an anastomosis (in pediatric patients up to one year of age

with esophageal atresia without a tracheoesophageal fistula (TEF) or in pediatric patients up to one year of age for whom a concurrent TEF has been closed as a result of a prior procedure) include surgical repair via thoracotomy or thoracoscopy. There are currently no commercially available devices in the U.S. indicated to treat esophageal atresia.

VII. MARKETING HISTORY

The Flourish Pediatric Esophageal Atresia Device has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (i.e., complications) associated with the use of the device.

Potential complications during the procedure include inability to approximate the atretic gap with the magnets or rupture of the balloon in the gastrostomy device.

Potential complications during the device indwelling period include ulceration or tissue irritation around the stoma, and trauma to the patient's gum due to constant catheter pressure.

Potential complications also include recurrent tracheoesophageal-fistula and inflammation.

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

The integrity and performance testing of the Flourish Pediatric Esophageal Atresia Device was evaluated through testing summarized in Table 1.

Table 1. Non-Clinical Performance Testing

Test	Acceptance Criteria	Result(s)
Oral inner magnet catheter magnet joint (in compression)	Compressive force ≥ 1.5 lbf.	Pass
Gastric inner magnet catheter magnet joint (in compression)	Compressive force ≥ 1.5 lbf.	Pass
Oral inner magnet catheter magnet joint (in tension)	Tensile force ≥ 4.5 lbf.	Pass
Gastric inner magnet catheter magnet joint (in tension)	Tensile force ≥ 4.5 lbf.	Pass
Flow rate through feeding lumen (gastrostomy tube) with magnet catheter in place	Flow rates must meet or exceed 9 cm^3/min.	Pass
Balloon burst volume (determination of balloon	Minimum burst volume for a 5 cm^3 rated balloon must meet or exceed 10 cm^3.	Pass

Test	Acceptance Criteria	Result(s)
integrity of enteral feeding devices with retention balloon)		
Balloon volume maintenance (test integrity of the inflation system to maintain balloon volume)	Failure to inflate is failure of the liquid from the filling device (syringe) to enter the retention balloon. Failure of retention is discoloration of or leakage on the clean surface beneath the enteral feeding device.	Pass
Balloon concentricity (test the concentricity of the balloon)	Balloon concentricity ratio for a 5 cm^3 rated balloon must not exceed 2:1.	Pass
Balloon size and shaft size (evaluate the retention balloon shaft size)	The balloon section may wrinkle but shall not tear or distort, and the enteral feeding device shaft or tip may offer resistance but if distortion or stretching occurs it is considered a failure.	Pass
Balloon integrity in simulated gastric fluid (assess the ability of the retention balloon to withstand gastric acidity levels without rupture, therefore, maintaining its functional purpose of retention)	Units must remain inflated.	Pass
Balloon integrity (evaluate the integrity of the retention balloon of the enteral feeding device)	Any balloon burst during any period of the time of the test shall have failed the test. Any balloon that does not burst but which does deflate during any period of the time of the test shall have failed the test. Any balloon that does not burst but which does deflate during any period of the test because of some form of leakage shall be an invalid test sample.	Pass
Compressive force of magnets	Shall not exceed 60 N/cm^2 (at 2 mm inter-magnet space).	Pass
Glued joint disconnection by unscrewing	Must not unscrew when subjected to a minimum of 0.35 Nm of torque for 10-15 seconds.	Pass
ENFit fluid leakage test (per AAMI/ANSI/ISO 80369-3)	Leakage by pressure decay test method shall not leak by more than 0.005 $Pa \cdot m^3/s$ while being subjected to an applied pressure of between 300 kPa and 330 kPa over a hold period between 15s and 20s using air as the medium or;	Pass

Test	Acceptance Criteria	Result(s)
	Positive pressure liquid leakage test method shall show no signs of leakage, sufficient to form a falling drop of water, over a hold period of 30 to 35 seconds while being subjected to an applied pressure of between 300 kPa and 330 kPa.	
ENFit stress cracking (per AAMI/ANSI/ISO 80369-3)	Evaluated for leakage (by pressure decay or positive pressure, see above) post stress cracking (27,5 N applied for a minimum of 5 seconds).	Pass
ENFit resistance to separation from axial load (per AAMI/ANSI/ISO 80369-3)	Shall not separate from the reference connector over a hold period between 10 and 15 seconds while being subjected to a disconnection applied axial force between 32 N and 35 N.	Pass
ENFit resistance to separation from unscrewing (per AAMI/ANSI/ISO 80369-3)	Shall not separate from the reference connector for a hold period between 10 and 15 seconds while being subjected to an unscrewing torque of between 0.0198 N·m to 0.02 N·m.	Pass
ENFit resistance to overriding (per AAMI/ANSI/ISO 80369-3)	Shall not override the threads or lugs of the reference connector while being subjected to an applied torque of between 0.15 N·m to 0.17 N·m over a hold period between 5 and 10 seconds.	Pass
ENFit disconnection by unscrewing (per AAMI/ANSI/ISO 80369-3)	Shall separate from the reference connector with an applied unscrewing torque up to 0.26 N·m.	Pass

B. Additional Studies

Biocompatibility

The Flourish Pediatric Esophageal Atresia Device has prolonged contact with the mucosal membrane during clinical use (<30 days). Biocompatibility of the device was evaluated through testing summarized in Table 2.

Table 2. Biocompatibility Testing

Component	Evaluation	Comments
Esophageal & Gastric Inner Catheter	Previously cleared in K101095	The component is identical to the catheter in a previously cleared device with the same nature of mucosal membrane contact and duration of exposure (<30 days).
Gastric Outer Catheter	Previously cleared in K130674	
Esophageal Outer Catheter	Previously cleared under K043203	

Component	Evaluation	Comments
Magnets	MEM elution cytotoxicity test	The test article showed no evidence of causing cell lysis or toxicity.
	Intracutaneous reactivity study in rabbits	There is no difference between the test article overall mean irritation score and control extraction, no irritation was observed.
	Guinea Pig Maximization Sensitization test	The test article showed no signs of causing delayed dermal contact sensitization in the guinea pig and is not considered a sensitizer.
	Systemic toxicity study in rats following a 13-week subcutaneous implantation study	The test article showed no evidence of systemic toxicity following subcutaneous implantation in rats, and not irritant to local tissues compared to the negative control materials.
	Toxicological risk assessment based on ICP-MS analysis	The amounts of each leachable compounds identified from the analysis were below the toxicological threshold and not expected to pose an unacceptable systemic toxicity risks to the patients.

Sterilization

The Flourish Pediatric Esophageal Atresia Device is sterilized using ethylene oxide (EO), and the sterilization process is validated to provide a sterility assurance level (SAL) of 10^{-6} in accordance with international standards for sterilization processes for medical devices, ANSI/AAMI/ISO 11135-1:2014. A validated post-sterilization aeration process assures that residual levels of EO and ECH (ethylene chlorohydrin) are within acceptable limits specified by ISO 10993-7:2008(R) 2012.

Shelf Life and Package Integrity

Shelf-life testing was conducted under accelerated aging and real time conditions to support device functionality for a 1 year shelf-life. The devices were also evaluated to determine whether the device functionality was maintained. Samples passed the testing; thereby demonstrating that device functionality was maintained. Package integrity was evaluated using finished, packaged, and sterilized devices that underwent simulated distribution, environmental conditioning, and aging, and were subjected to dye penetration and seal strength testing. Samples passed the testing, thereby demonstrating

ability of the packaging to maintain a sterile barrier for the claimed 1-year product shelf life.

X. SUMMARY OF CLINICAL INFORMATION

The supportive clinical information was obtained from literature as well as compassionate/emergency use cases submitted to the FDA.

Clinical results supporting product approval were derived from a case series in Argentina[1] (n=9) and cases performed as emergency use in the U.S. (n=7) for a total of 16 cases (three (3) of these cases were reported in references 2 and 3). Principal short-term clinical results are summarized in Table 3 and demonstrate a high rate (100%) of success in creating anastomoses. Patients frequently required dilatation of the anastomotic site (13/16 or 81.3%).

Clinical Result	**Outcomes with Flourish**	**N**
Successful creation of an anastomosis	100%	16/16
Death	0%	0/16
Anastomotic leak	0%	0/16
Stricture at anastomosis site requiring endoscopic dilation	81.3.%	13/16
Stricture at anastomosis site requiring surgical intervention	6.3%	1/16
Long Term Clinical Outcomes with Flourish™		
Gastroesophageal reflux disease	33%	2/6*
Tracheomalacia	33%	2/6*
Esophageal dysmotility requiring treatment	50%	3/6*
Asthma	50%	3/6*
Recurrent pulmonary infections	50%	3/6*

*Patients from the Argentinian series having longer term follow up.

There were nine (9) patients with previously untreated esophageal atresia who were treated by magnetic compression anastomosis at a single center in Argentina as described in the article "Magnetic gastrointestinal anastomosis in pediatric patients," by Zaritzky et al[1]. The average age of the patient was 3 months (range 23 days to 5 months). Of the nine (9) patients, six (6) had Type A esophageal atresia (an esophageal pouch and a gastric pouch with no tracheoesophageal fistula, or TEF) and three (3) had Type C esophageal atresia (an esophageal pouch and a gastric pouch with a TEF) and underwent surgical repair of the TEF prior to magnetic compression anastomosis treatment. The gap between the upper and lower pouches was evaluated by placement of metal probes viewed on anterioposterior (AP) and lateral chest x-rays. Only children with a gap of 4 cm or less between the esophageal and gastric pouches were treated with the catheter-based device.

Additionally, all nine (9) patients previously underwent surgical gastrostomy and had a mature gastrostomy tract at the time of catheter-based treatment. Primary esophageal

anastomosis was achieved in an average of 4.2 days (range 3 to 6 days) in the nine (9) patients with previously unrepaired esophageal atresia.

No patient experienced an anastomotic leak. One patient developed sepsis 48 hours after magnet placement. In this case, the catheter-based magnets were removed, the patient was treated with antibiotics, and the catheter-based magnets were replaced to complete the magnetic treatment. Eight (8) patients developed anastomotic strictures that required dilatation and two (2) of these patients with intractable esophageal stenosis also underwent placement of 10 mm diameter fully covered stents after dilatation. One patient (who underwent several dilatations and stent placement) ultimately required surgical re-anastomosis.

Three (3) of the 9 esophageal atresia patients were lost to long-term follow up. Regarding oral capabilities, the six (6) patients with long-term follow-up data were reported to be ingesting normal residue diets for their age.

Regarding other conditions, of the 6 subjects with longer term follow-up, two (2) patients were diagnosed with gastroesophageal reflux disease (GERD) and tracheomalacia. Three (3) patients were diagnosed as having esophageal dysmotility requiring treatment and three (3) patients developed asthma or recurrent pulmonary infections. None of the patients have scoliosis or rib deformities. Of note, one patient (17 months old at the time of publication) carried concurrent diagnoses of GERD, tracheomalacia, esophageal dysmotility, and asthma/recurrent pulmonary infection. This patient was at the 15th growth percentile for age at the time of publication.

In addition to the nine (9) infants described above, there were two (2) cases described in the article, "Staged repair of esophageal atresia: Pouch approximation and catheter-based magnetic anastomosis," by Lovvorn et al[3]. In the first patient with long-gap esophageal atresia, the esophageal pouches were approximated with three (3) sutures to promote continued esophageal lengthening and reduction in tension over time. To facilitate central canalization and to spare the patient repeat thoracotomy, magnetic compression anastomosis was performed. Anastomosis was achieved and the patient experienced resolution of hypersalivation and swallowed all oral secretions without difficulty. Repeat esophagogram, obtained six (6) weeks after magnetic catheter removal, demonstrated an anticipated tight, but patent, narrowing at the anastomosis which was dilated with a balloon to full luminal caliber. As a routine means to ensure luminal integrity, esophageal dilators were passed weekly for three (3) consecutive weeks. At the time of publication (nearly eight (8) months after magnet removal), the patient was swallowing salivary secretions well and progressing with oral feedings.

Similar to the first patient, the second patient underwent stretching of the two (2) pouches, with a gap distance that gradually decreased over a two (2) month span. This patient had subsequent placement of the magnetic catheters with resulting anastomosis. This patient also underwent balloon dilation starting at 12 days post-procedure for anastomotic stenosis and had placement of an 8 Fr orogastric tube to facilitate a routine dilating regimen over four (4) consecutive weeks (to achieve proper luminal diameter). At the time of publication (four (4) months after magnet removal), the patient was swallowing oral secretions well, but according to the authors, had persistent stenosis likely related to the fibrotic healing response of the salivary leak that complicated the original suture-approximation procedure.

For the other five (5) emergency use cases in infants ages 2 to 8 months, anastomosis was achieved in 4 to 10 days. Three (3) of these five (5) infants required dilations for stenosis, starting from 6 weeks to 2 months. One had to undergo serial dilations and, at a year and a few months, had a recalcitrant stricture, one required multiple dilations and three (3) months post anastomosis was receiving training in swallowing and speech, one had no further treatment due to need for ventilator support for a pre-existing congenital anomaly, one had serial dilations and a subsequent esophageal stent, and one required surgery to correct an undiagnosed TEF.

The above results provide data from 16 total patients, 13 of which developed anastomotic strictures that required balloon dilation and/or esophageal stenting. This rate is higher than what is reported for standard of care surgical repair (typically 30-40%)[4]; however, anastomotic repair can avoid several surgical complications and several patients have been reported to be able to swallow secretions and ingest oral diets normally in the months post procedure. Therefore, it is concluded that probable benefits outweigh the risks of device use.

XI. 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. 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.

XII. RISK - PROBABLE BENEFIT ANALYSIS

Patients with esophageal atresia cannot eat, as the upper portion of the esophagus ends in a blind pouch and is non-continuous with the lower portion of the esophagus, which is also a pouch. A child with esophageal atresia typically presents with excessive oral secretions, feeding intolerance, and/or respiratory difficulties at birth[5] and are fed through a gastrostomy tube. Associated anomalies are frequently seen in children with EA, occurring in more than 50% of patients, described as VACTERL (vertebral, anorectal, cardiac, trachea-esophageal, renal, and limb) defects.[4] Morbidity/mortality depends on associated conditions.

Current standard of care therapy is surgical repair of thoracotomy, although thorascopic repair has also been used.Both types of treatments (thoracotomy and thorascopic repair) have been shown to be effective in creating an anastomosis.

Risks of surgical repair include those of general anesthesia as well as postoperative pain. Complications related to surgical procedures include anastomotic leak, stricture, gastroesophageal (GE) reflux, fistula recurrence, and motility abnormalities. Of these, leaks present in the immediate/ short-term postoperative period while the others including stricture, tracheoesophageal fistula recurrence, GE reflux, and feeding/respiratory difficulties are medium- to long-term complications. Anastomotic leaks occur in up to

15–20% of patients. Anastomotic strictures develop in 30–40% of cases most of which respond to fluoroscopic dilatations. GE reflux is common in postoperative patients with significant reflux occurring in up to 40% of cases. Recurrent trachea-esophageal fistula is seen in five (5) (14%) of patients.[4]

Pediatric thoracotomy incisions, even when muscle-sparing approaches are used, have been associated with several long-term complications, including shoulder weakness, winged scapula, and thoracic scoliosis. Because of these morbidities as well as cosmesis after thoracotomy, interest in neonatal thoracoscopic repair for short-gap EA has been increasing among pediatric surgeons.[4]

Regarding magnetic anastomosis, probable benefit has been demonstrated, with anastomosis being achieved in all 16 described cases. Additional probable benefits also include ability to swallow secretions and ingest oral diets normally as well as fewer short-term (e.g., anesthesia) and long-term complications (e.g., scoliosis and thoracic wall deformities).

The rate of anastomotic stricture appears to be higher than that of surgical repair with current data suggesting occurrence in 80% or more of patients. These patients required serial balloon dilatations, esophageal stenting, and/or surgery for stricture resolution. Other described complications in some of the patients that have had the device have included gastroesophageal reflux disease, tracheomalacia, esophageal dysmotility, recurrent asthma, and recurrent pulmonary infections. In small case series, these occurred in up to 50% of subjects treated with the device.

A. Probable Benefit Conclusions

Demonstration of probable benefit included results from 16 infants. These 16 infants included nine (9) with previously untreated esophageal atresia and seven (7) emergency use cases. Some of these 7 cases had previously undergone either thoracotomy or thorascopy for approximation of pouches; however, anastomosis was not achieved. Magnetic anastomosis was achieved in all patients, ranging from 3 to 13 days.

B. Safety Conclusions

The risks of the device are based on data collected in nine (9) infants with previously untreated esophageal atresia and seven (7) emergency use cases to support HDE approval as described above. Some of these seven (7) cases had previously undergone either thoracotomy or thorascopy for approximation of pouches; however, anastomosis was not achieved.

In total, 13 of the 16 patients (81.3%) developed a narrowing in their esophagus (anastomotic stricture) that required a balloon dilation procedure and/or stent to repair. In one patient, surgery was required 10 days post procedure to correct an undiagnosed TEF and surgically create primary anastomosis. Other reported complications included gastroesophageal reflux disease, tracheomalacia, esophageal dysmotility, recurrent asthma, and recurrent pulmonary infections.

C. Probable Benefit-Risk Conclusions

The probable benefits of achieving anastomosis, ability to swallow secretions and ingest oral diets normally, and fewer short- and long-term surgical complications outweigh the risks of a higher rate of anastomotic strictures requiring further treatment.

Additional factors to be considered in determining probable risks and benefits for the Flourish device include that in children who have undergone previous operative techniques; this magnetic device may spare them the morbidity of a repeat thoracotomy and its associated risks.

In addition, FDA solicited feedback from three (3) external members of the CDRH "Network of Experts" to supplement the understanding of the limited clinical information available. The majority of experts favored using the device as an alternative tool to surgery. The following excerpts were provided as feedback to the FDA.

"The additional benefits to magnetic anastomosis (not mentioned above) include avoidance of wound infection and potential for rib and spine issues. In addition, the technique allows for a less invasive, and likely more tolerated therapy for esophageal atresia, which can be important for children with comorbidities, such as the associated VACTERL syndrome and congenital cardiac anomalies, who may not tolerate thoracotomy as well."

"In addition, children who undergo the typical stretching of the pouches and delayed repair of esophageal atresia are commonly 6-9 months of age at the time of primary repair attempt. During this time, many of these children develop oral aversion. This is also a long time to undergo intermittent stretching procedures, intermittent fluoroscopy (radiation risks), no feeding by mouth, and the concerning and potential risk of aspiration of saliva which pools in the proximal esophageal pouch, and could lead to subsequent pneumonia."

"In comparison to surgical repair, the vast majority of surgeons who have performed or attempted to perform a thoracoscopic repair have low number of cases, high complications (which are not necessarily reported and published), and these operations can take an exceedingly long time to perform (>6-8 hours compared to 1-2 hours in an open procedure) due to a lack of expertise, familiarity, and volume."

"Additional advantages of magnetic technique over the surgical repair include the following: the learning curve of performing the magnetic technique appears to be short, the procedure may be easier to perform (surgeons are usually adept at using fluoroscopy and passing catheters), the magnetic technique takes less amount of time, and has a very low anastomotic leak rate."

"The magnetic device would be ideal for children in whom re-operative thoracotomy may be high-risk. This would include patients with serious comorbidities and those who have undergone previous thoracotomy. However, there is also the potential opportunity to use this as a first line therapy for all children with esophageal atresia, as this therapy can be instituted much earlier in life than the current standard of care"

”While the use of magnetic catheters in the case of patients with isolated esophageal atresia seems to be the most logical scenario, the high rate of stenosis requiring subsequent intervention(s) in combination with the lack of sufficient comparative data make it difficult to define whether or magnetic catheters should be considered in subjects that with a history of related procedures.”

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

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and probable benefit of this device when used in accordance with the indications for use. Esophageal anastomosis was achieved in the majority of described cases, both as first line, as well as second line therapy. The probable benefits of earlier anastomotic repair and fewer surgical complications outweigh the risks of a higher rate of anastomotic strictures requiring balloon dilation and/or esophageal stenting. This is coupled with thorough labeling, obtained opinions from experts in the field with the majority favoring device use, and an acceptable training program and post-approval study in place.

Therefore, it is reasonable to conclude that the probable benefit to health from using the device for the target population outweighs the risk of illness or injury, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment when used as indicated in accordance with the directions for use.

XIII. PANEL RECOMMENDATION

This HDE was not taken to a meeting of the Gastroenterology-Urology Devices Panel because the preclinical and clinical issues raised by the HDE did not require panel review for the proposed indication.

XIV. CDRH DECISION

CDRH has determined that, based on the data submitted in the HDE, the Flourish Pediatric Esophageal Atresia Device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from using the device outweighs the risks of illness or injury. CDRH issued an approval order on May 12, 2017. The final conditions of approval cited in the approval order are described below.

Conditions of Approval include providing data from a post-approval study (PAS). The study objective is for continued evaluation of device safety and probable benefit after device approval. This is a prospective, single-arm, new enrollment observational study conducted in a minimum of 15 sites, including 1 site in the United States. A minimum of 20 subjects will be followed for 2 years after treatment with the Flourish Pediatric Esophageal Atresia Magnetic Device. The frequency of follow-up assessments will be consistent with the standard of care. The primary safety endpoint is the rate of the following: stricture at the anastomotic site leading to the need for intervention; peri-anastomotic leaks; and other

adverse events and/or complications potentially related to the device or procedure (including, but not limited to: GERD, tracheomalacia, esophageal dysmotility, and/or recurrent asthma or pulmonary infections). The secondary endpoint (for evaluation of probable benefit) is successful anastomosis formation, defined as creation of a lumen connecting the upper esophageal pouch to the lower esophageal pouch as demonstrated by union of the device magnets and an esophagram showing connected flow of contrast agent. Descriptive analyses will be presented for all study endpoints.

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 the device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

1. Zaritsky M. Ben R. Johnston K. Magnetic gastrointestinal anastomosis in pediatric patients. J Ped Surg. 2014. 49:1131-1137.

2. Dorman RM, Vali K, Harmon CM, Zaritzky M, Bass KD. Repair of esophageal atresia with proximal fistula using endoscopic magnetic compression anastomosis (magnamosis) after staged lengthening. Pediatr Surg Int. 2016 May;32(5):525-528.

3. Lovvorn H, Baron M, Danko M, et al. Staged repair of esophageal atresia: Pouch approximation and catheter-based magnetic anastomosis. J Ped Surg Case Reports. 2014; (2): 170-175.

4. Sodhi KS., et al. Postoperative appearances of esophageal atresia repair: retrospective study of 210 patients with review of literature - what the radiologist should know. Acta Radiol. 2013 Mar 1;54(2):221-5.

5. Kunisaki, S.M., et al. Surgical Advances in the Fetus and Neonate: Esophageal Atresia. Clin Perinatol 2012 (39) 349–361.