DE NOVO CLASSIFICATION REQUEST FOR
XLUMENA AXIOS STENT AND DELIVERY SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Pancreatic drainage stent and delivery system.** A pancreatic drainage stent is a prescription device that consists of a self-expanding, covered, metallic stent, intended for placement to facilitate transmural endoscopic drainage of pancreatic pseudocysts. This stent is intended to be removed upon confirmation of pseudocyst resolution. This device may also include a delivery system.

NEW REGULATION NUMBER: 21 CFR 876.5015

CLASSIFICATION: II

PRODUCT CODE: PCU

BACKGROUND

DEVICE NAME: AXIOS STENT AND DELIVERY SYSTEM

SUBMISSION NUMBER: K123250

DATE OF DE NOVO: FEBRUARY 19, 2013

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REQUESTER'S RECOMMENDED CLASSIFICATION: II

INDICATIONS FOR USE

The AXIOS Stent and Delivery System is indicated for use to facilitate transgastric or transduodenal endoscopic drainage of symptomatic pancreatic pseudocysts ≥ 6 cm in size, with ≥ 70% fluid content that are adherent to the bowel wall. Once placed, the AXIOS Stent functions as a port allowing passage of standard and therapeutic endoscopes to facilitate debridement, irrigation and cystoscopy. The stent is intended for implantation up to 60 days and should be removed upon confirmation of pseudocyst resolution.

LIMITATIONS

The sale, distribution, and use of the AXIOS Stent and Delivery System is limited to prescription use only.

The AXIOS Stent has been shown to be MR Conditional and can be scanned safely under the following conditions:

- Static magnetic field of 3-Tesla or less
- Maximum spatial gradient magnetic field of 720 Gauss/cm or less
- Maximum whole body averaged specific absorption rate (SAR) or 2-W/kg for 15 minutes of scanning.

The safety of the delivery system has not been evaluated in the MR environment, and, therefore, the delivery system should not be used within the MR environment.

Limitations on device use are also achieved through the following statements included in the Instructions for Use:

> *Placement of the AXIOS™ Stent should be performed by physicians familiar with endoscopic ultrasonography and endoscopic stent placement techniques.*
>
> *The AXIOS Stent implantation should not exceed 60 days.*

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

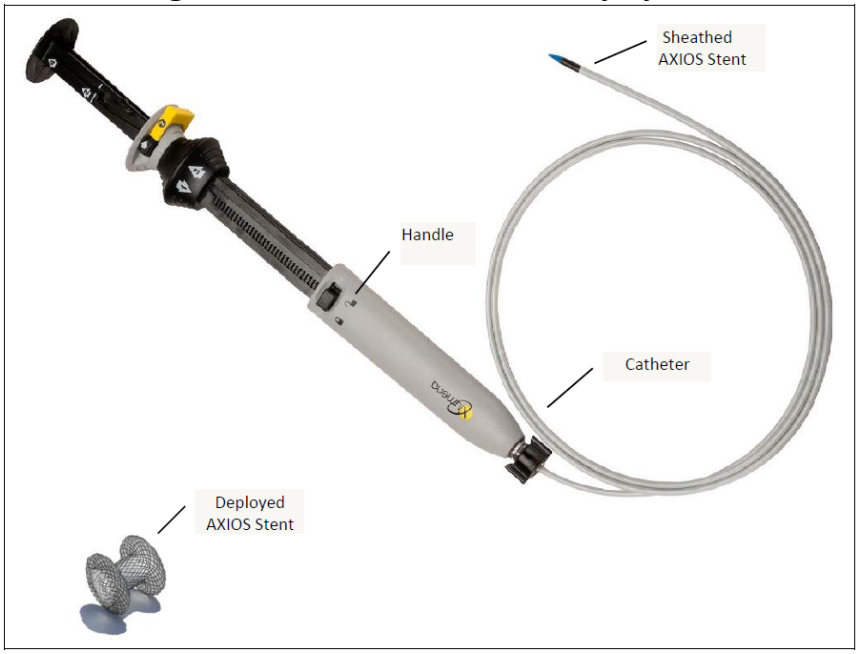
DEVICE DESCRIPTION

The AXIOS Stent and Delivery System consists of two major components, the catheter-based delivery system and the implantable stent, as shown in Figure 1 below. The stent is a flexible, fully-covered, self-expanding Nitinol stent, which is preloaded within the catheter-based delivery system.

The system is intended to cannulate the transgastric or transduodenal wall into a pancreatic pseudocyst for endoscopic drainage. The stent serves as a conduit for passive drainage of pseudocyst contents directly into the GI tract. The large lumen diameter provides a short path and may allow secure access to the pseudocyst interior for additional diagnostic or therapeutic procedures.

An endosonographic exam is performed to locate the pancreatic pseudocyst, measure the size, assess the fluid content, and evaluate wall adherence of the pseudocyst. Once the endosonographic exam is complete, an access tract is created using conventional access tools. The stent and delivery system is then inserted into the endoscope and the stent is delivered.

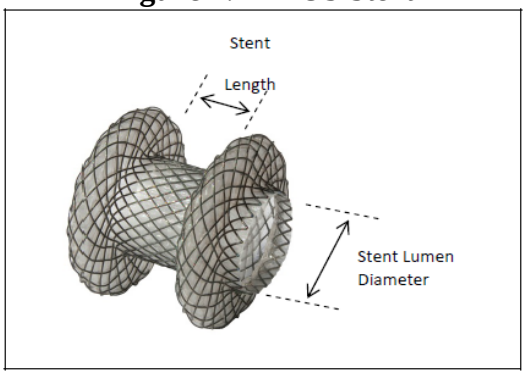
Figure 1: AXIOS Stent and Delivery System



Stent

As shown in Figure 2 below, the AXIOS Stent is designed with a duplicate "anchor" or "flange" on each end to achieve tissue apposition and prevent migration. The stent is radiopaque and is fully covered with silicone to prevent leakage, minimize tissue in-growth, and facilitate removal. The large diameter is intended to facilitate efficient drainage.

Figure 2: AXIOS Stent



The AXIOS Stent will be provided in two lumen diameters and one length, for a total of two different stent models, to accommodate the various anatomy and cyst content. The stent sizes are provided in Table 1 below.

Table 1: AXIOS Stent Sizes

Catalog Number	AXS-10-10	AXS-15-10
Stent Lumen Diameter (mm)	10	15
Stent Length (mm)	10	10

Delivery System

The AXIOS Delivery System consists of a catheter and an integrated handle with manual controls for positioning and deploying the AXIOS stent. The AXIOS Delivery System is sized to fit within commercially available echoendoscopes with a working channel of 3.7 mm diameter or larger. The Delivery System catheter is 138 cm in working length and attached directly to the endoscope handle. The AXIOS Delivery System requires an access site of at least 10 Fr.

The AXIOS Stent and Delivery System is provided sterile, disposable and intended for use during a single patient procedure.

Refer to the instructions for use for complete information for stent deployment and removal, including a list of warnings, precautions and contraindications.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The materials for the stent and delivery device are listed in Tables 2 and 3 below:

Table 2: Stent Materials

Component Name	Material	Patient Contact
Stent	Nitinol (Nickel-Titanium)	Direct
Covering (b)(4) Trade Secret	Silicone (b)(4) Trade Secret	Direct
Stent Covering	Silicone (b)(4) Trade Secret/CCI	Direct
Stent Lubricant	Silicone Lubricant (b)(4) Trade Secret/CCI (b)(4) Trade Sec	Direct

Table 3: Delivery System Materials

Component Name	Material	Patient Contact
Catheter	(b)(4) Trade Secret/CCI	
RO Marker (b)(4) Trade Secret/C Catheter (b)(4) Trade Secret/CCI		Direct
Outer Sheath (b)(4) Trade Secret/CCI		
Outer Sheath Coating (b)(4) Trade Secret/CCI		
Nose Cone (b)(4) Trade Secret/CCI		
Handle		
(b)(4) Trade Secret/CCI		None

Winged Luer, (b)(4) Trade Secret/CCI		

The stent is classified as an implanted device with tissue contact for an extended duration (>30 days). In accordance with ISO10993-1, Biological evaluation of medical devices, the following tests were performed on the stent:

- Cytotoxicity
- Sensitization
- Implantation
- Sub-chronic toxicity
- Genotoxicity
- Acute systemic toxicity
- Irritation

The (b)(4) Trade Secret/CCI lubricant was not a part of the biocompatibility studies, since this lubricant was added subsequent to the biocompatibility testing and after the completion of the clinical study. In order to assess the biocompatibility of the final, finished, sterilized device, with the (b)(4) Trade Secret/CCI lubricant, the following additional testing and information was provided:

- Device master file (b)(4) Trade Secret/CCI
- 6-month animal study of two different stent lubricants to evaluate local tissue response
- Toxicological risk assessment of ethyltriacetoxysilane, a component o (b)(4) Trade Secret/C
- Cytotoxicity testing of the AXIOS stent (b)(4) Trade Secret/CCI coating
- Biocompatibility testing reports of the (b)(4) Trade Secret/CCI
- (b)(4) Trade Secret/CCI 0 product profile for comparison
- Summary of OUS adverse events of the AXIOS stent with the (b)(4) Trade Secret/CCI
- Toxicological risk assessment of the AXIOS stent with the (b)(4) Trade Secret/CCI coating

The delivery system is classified as an externally communicating device, with tissue contact for limited duration (<24 hours). In accordance with ISO 10993-1, the following tests were performed on the delivery device:

- Cytotoxicity
- Sensitization
- Irritation or intracutaneous reactivity
- Acute systemic toxicity

SHELF LIFE/STERILITY

The stent and delivery system are sterilized by ethylene oxide (EO) to ensure a sterility assurance level of 10^{-6}, and are not intended for re-sterilization or reuse. The sterilization process validation and routine monitoring comply with ISO 11135-1:2007 Sterilization of Health Care Products -- Ethylene Oxide -- Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices. EO and ethylene chlorohydrins (ECH) residuals were measured to ensure that they were within the specified limits of ISO 10993-7:2008 Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization residuals. The device was found to be non-pyrogenic after Limulus Amebocye Lysate (LAL) testing.

The device is packaged in a (b)(4) Trade Secret/CCI with a (b)(4) Trade Secret/CCI lid. Packaging validation testing was performed to demonstrate the ability of the packaging to protect the stent and delivery system from hazards. The sterilized product was subjected to package performance testing after conditioning, and the trays were visually inspected and subjected to gross leak detection (bubble) and seal strength (peel) testing as stated in ISO 11607. The evaluation of the packaging system demonstrated that the product was protected, sterility was retained, and pouch seals would allow aseptic opening.

The stent and delivery system are labeled with a shelf life of 12 months. The shelf life testing included package integrity testing and functional testing of devices aged using accelerated aging to simulate 13 months. The accelerated aging calculation was based on the Von't Hoff's Q10 theory. The functional testing was performed using the same protocols as the functional testing discussed in the bench testing section below, with the same acceptance criteria. This testing included tensile testing of the delivery device, deployment force testing, removal testing, dimensional testing of the stent, expansion and compression force testing, and fatigue testing of the stent. The functional testing demonstrated that the aged stent performed equivalently to the non-aged stent. The packaging testing demonstrated package integrity and maintenance of the sterile barrier in the aged devices.

MAGNETIC RESONANCE (MR) COMPATIBILITY

Testing was conducted by an independent laboratory to evaluate the magnetic resonance (MR) safety and compatibility of the AXIOS Stent. Testing was conducted with a single 15x10mm stent and a (b)(4) Trade Secret/CCI System; testing evaluated implant displacement force, implant torque, radiofrequency-induced heating, and image artifacts. The testing showed a deflection angle of (b)(4) Trade Secret/ no torque was observed.

Radiofrequency-induced heating measured a maximum temperature rise (b)(4) Trade Secret C. The implant displayed an artifact that appeared moderate for the shape and size of the device and is addressed in the labeling.

Based on the test results, the stent was labeled as MR Conditional. The safety of the delivery system has not been evaluated in the MR environment, and therefore the delivery system should not be used within the MR environment.

PERFORMANCE TESTING – BENCH

The following design verification testing was performed to evaluate the AXIOS Stent System:

- Deployment testing
- Expansion force testing
- Compression force testing
- Dimensional testing
- Corrosion
- Tensile strength testing
- Fatigue/durability

Sterilized and packaged devices were exposed to environmental conditions and simulated transit testing prior to undergoing testing. Both 15 mm x 10 mm and 10 mm x 10 mm stent models were tested.

Deployment Testing

(b)(4) Trade Secret/CCI

g.

- (b)(4) Trade Secret/CCI

Expansion and Compression force testing

(b)(4) Trade Secret/CCI

Dimensional Testing

(b)(4) Trade Secret/CCI

Tensile Strength Testing

(b)(4) Trade Secret/CCI

(b)(4) Trade Secret/CCI

- (b)(4) Trade Secret/CCI

(b)(4) Trade Secret/CCI

- (b)(4) Trade Secret/CCI

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All samples met the acceptance criteria.

Fatigue/Durability Testing

(b)(4) Trade Secret/CCI

Corrosion

(b)(4) Trade Secret/CCI

PERFORMANCE TESTING – ANIMAL

An animal study was designed and performed to evaluate the safety and performance of the AXIOS stent when performing endoscopic drainage in a chronic animal model. The stent characteristics were evaluated, including chronic performance (long-term patency, removability and migration), occurrence of adverse events, and histopathology. A total of four 10 x 10 mm stents were used in a porcine model. The animals underwent a surgical procedure to appose the stomach to a 3-4 inch section of the small intestine using

non-absorbable suture material, 5 weeks prior to the AXIOS procedure. In each animal, the stent was deployed between the wall of the animal's stomach and the small intestine. Each implant was left in place for approximately 5 weeks, at which time the stents were removed using an endoscopic snare. The animals were survived for 4 additional weeks after the stent was removed to determine if there were any adverse reactions post-removal. The animals were euthanized at 8 weeks post implant, and histopathological evaluation was performed.

The devices were successfully deployed in all four cases. No stents migrated, and all 4 remained patent during the implant period. Slight tissue ingrowth into the stent was noted in three of the animals, which did not interfere with stent removability or patency. All four stents were easily removed.

SUMMARY OF CLINICAL INFORMATION

Feasibility

A non-randomized feasibility clinical study was conducted by a single site, Tokyo Medical University, to evaluate the clinical feasibility of transenteric pancreatic pseudocyst drainage using endoscopic ultrasonography (EUS) guidance. The results were published in April 2012 in the journal, "Gastrointestinal Endoscopy."

The study included a retrospective case series of the use of the AXIOS stent system to treat pancreatic pseudocysts. A total of 15 subjects were treated with the AXIOS stent for drainage of pancreatic pseudocysts. Technical success was evaluated as the ability to deploy, implant, and remove the AXIOS stent. Clinical success was assessed as pseudocyst resolution through the period of implantation and through follow-up visits at 1, 3, and 6 months. All stents were deployed and removed without difficulty. The stents were implanted for 8-82 days, and were patent at removal. The pseudocyst was resolved in all subjects.

Pivotal

A prospective, multi-center, single-arm study was conducted under an IDE, (b)(4) Trade Secret/CCI, to assess the safety and effectiveness of the AXIOS device for transmural drainage of symptomatic pancreatic pseudocysts. The study enrolled 33 subjects at seven sites.

Eligibility criteria stipulated that the pancreatic pseudocyst is greater than or equal to 6 cm in size, with 70% or more fluid content and adherent to the bowel wall, and the subjects had to be between 18 and 75 years old.

Following successful stent placement, subjects underwent an abdominal CT or abdominal ultrasound and an endoscopy with endoscopic ultrasonography at the 30 day post-stent placement visit. If the pseudocyst had resolved (decreased in size to $\leq$ 3 cm), the stent was removed. If the pseudocyst had not resolved at the 30 day visit, the stent would remain in place and the pseudocyst would be re-evaluated at the 60 day visit. All remaining stents were removed at the 60 day visit. If the pseudocyst had not resolved at the 60 day visit, a pigtail stent would be placed through the remaining fistula tract after AXIOS stent removal.

Safety was evaluated with regard to stent placement, stent migration, and tissue response for the period up to 7 days after stent removal. Effectiveness was measured by pseudocyst resolution (of at least 50% reduction in size) and device performance. Telephone follow-up at 3 and 6 months post removal was also performed.

Intent-to-Treat (ITT): The ITT population (n=33) included all subjects who met eligibility criteria, provided written consent and underwent the index procedure for AXIOS stent placement.

Modified Intent-to-Treat (mITT): The mITT (n=30) is a subset of the ITT subjects who received an AXIOS stent during the index procedure (i.e., underwent successful AXIOS stent placement).

- Three (3) of the 33 subjects enrolled did not receive the AXIOS Stent. In these subjects, stent placement was attempted but was not successful. These subjects received standard care (i.e., pigtail stents) for their condition. These subjects were excluded from the mITT and per-protocol analyses, and were followed for safety endpoints only.

Per-Protocol (PP): The per protocol population (n=29) is a subset of the ITT subjects that received an AXIOS stent during the index procedure (i.e., underwent successful AXIOS stent placement) and had an evaluable clinical outcome.

- As noted in the mITT population above, three subjects did not receive the AXIOS Stent and are excluded from the PP analysis.
- Another subject underwent successful placement of the AXIOS stent, but was excluded as this subject had pigtail stents and a nasocystic tube placed through a separate (second) puncture site alongside (not through) the AXIOS stent and clinical outcome was not evaluable.

All subjects continued to be assessed and observed throughout the study based on their willingness to attend the planned follow-up visits and/or post discharge evaluations.

Effectiveness Endpoints

The effectiveness endpoints were defined as follows:

- Stent lumen patency at 30 days and/or 60 days
- Stent removability at 30 days and/or 60 days
- Technical success, defined as: placement of the AXIOS Stent using the AXIOS Delivery System and removal of the AXIOS Stent using a standard endoscopic snare.
- Clinical success, defined as: at least a 50% decrease in pseudocyst size, based on radiographic analysis, at 30 days and/or 60 days.

The evaluation of effectiveness was based on the ITT population with regard to Technical Success (AXIOS stent placement and removal) and the Per Protocol population to characterize the AXIOS stent lumen patency, overall clinical success, and the overall effectiveness of the AXIOS Stent and Delivery System.

Effectiveness Results

The effectiveness results are summarized below:

- 90.9% of subjects had successful stent placement (30 stents of 33 procedures)
- 93.1% of subjects (27 of 29) had stent lumens that were patent at stent removal,
- 96.6% of stents (28 of 29) were successfully removed using standard endoscopic tools; one was inadvertently dislodged during recanalization of the AXIOS stent with the gastroscope for debridement,
- Clinical success, defined as at least 50% decrease in pseudocyst size at time of stent removal, was observed for 86.2% (25 of 29 pseudocysts).

Table 4: AXIOS Overall Effectiveness

Effectiveness Measure	Study Subset	Overall Effectiveness by Endpoint
Technical success, defined as		
- Placement of the AXIOS stent, and	ITT	90.9% (30/33)
- Removal of the AXIOS stent using standard endoscopic tools	mITT	96.7% (29/30)
Stent Lumen Patency	Per-Protocol	**93.1% (27/29)**
- Debridements		31.0% (9/29)
- Supplemental stenting (stent-in-stent)		10.3% (3/29)
Clinical Success, defined as at least a 50% decrease in pseudocyst size, based on radiographic analysis	Per-Protocol	**86.2% (25/29)**
Overall Effectiveness	**Per-Protocol**	**86.2% (25/29)**

Patency

Stent patency was evaluated throughout the study and met the efficacy endpoint if the stent was patent at removal (at 30 or 60 days). The protocol defined drainage at the pseudocyst, including partial drainage, as a patent stent. As shown in Table 4 above, overall stent patency in the per-protocol group was measured at 93.1% (27/29). Nine of the 29 subjects required at least one debridement procedure to maintain stent patency, and 3 of the 29 subjects received supplemental stenting (placement of a pigtail stent through the AXIOS stent). Of these three subjects to receive supplemental stenting, two required the supplemental stents to maintain stent patency, and were found to have non-patent stents at the time of stent removal. The third subject to receive supplemental stenting had a partially draining AXIOS, and the supplemental stent was placed at the physician's discretion to improve drainage. The subject had partial drainage at the time of stent removal and is considered a stent patency success.

Removal

Stent removal was indicated at the time of pseudocyst resolution (≤ 3 cm in diameter) or at the 60 day post procedure visit. The sponsor states that a total of 30 stents were examined at the 30 day visit. Nineteen of these were successfully removed prior to or at the 30 day visit.

Additionally, one stent was inadvertently dislodged during a debridement procedure prior to the 30 day visit. The remaining 10 stents were successfully removed at the 60 day visit.

Removal was performed using standard endoscopic tools (snares, forceps, etc.). All stents were removed with no injury to the tissue, including the non-evaluable subject. Additionally, the stent which was inadvertently dislodged was removed without clinical sequelae, but it is not counted as a successful stent removal due to the accidental nature of the stent dislodgement. Therefore, the overall removal rates were 96.6% (28/29) in the PP group, and 96.7% (29/30) in the ITT group.

Technical Success

A total of 30 stents were placed during 33 procedures. These included 10x10 stents (n=18) and 15x10 stents (n=12). Successful placement was demonstrated in 90.9% of subjects. All stents were removed with no injury to the tissue.

Clinical Success

Post-procedure, pseudocyst resolution was evaluated by various imaging modalities including abdominal CT, transabdominal ultrasound, MRI and/or endoscopic ultrasonography, at 30, and in some cases, 60 days. Clinical success was defined as at least 50% decrease in pseudocyst size at stent removal. An overview of pseudocyst size reduction over time in the PP subset is shown in Figure 3.

Figure 3: Pseudocyst Size Reduction (Per-Protocol, N=29)

Twenty stents were removed at or before the 30 day visit. The remaining nine subjects were re-evaluated at the 60-day visit. Summary data for the clinical success endpoint is presented in Table 5 below.

Table 5: AXIOS Clinical Success

Effectiveness Measure	Subset	30-day Visit	60-day Visit
Clinical Success			
At least a 50% decrease in pseudocyst size	Per-Protocol	75.9% (22/29)	77.8% (7/9)
Percent Decrease In Size			
≥40% decrease in size	Per-Protocol	79.3% (23/29)	77.8% (7/9)
≥30% decrease in size		86.2% (25/29)	77.8% (7/9)
Pseudocyst Diameter			
Pseudocyst diameter ≤3cm	Per-Protocol	62.1% (18/29)	77.8% (7/9)

Seven subjects did not achieve pseudocyst resolution at the 30-day visit as defined by at least a 50% decrease in pseudocyst size, including two subjects with supplemental stenting (pigtail stent through the AXIOS stent), two subjects whose AXIOS stents were removed prior to the 30-day visit without pseudocyst resolution (clinical success failures), and three remaining subjects with patent AXIOS stents. Four additional subjects had patent stents remain in place because they had not met the 30-day definition of stent resolution, defined as a pseudocyst diameter of ≤3cm, although they met the clinical success definition. Of the nine subjects with AXIOS stents in place at the 60-day visit, all achieved pseudocyst resolution (at least a 50% decrease in pseudocyst size), including the two subjects with supplemental stenting. However, since pseudocyst resolution required the use of supplemental stenting, these two subjects are treated as clinical success failures.

The results showed an overall clinical success effectiveness rate of 86.2% (25/29) in the PP population. As stated above, the overall clinical success effectiveness rate includes the following four failures: two subjects who achieved less than a 50% decrease in pseudocyst size, and two subjects with supplemental stenting (a pigtail stent through the AXIOS stent).

Safety Endpoints

The safety endpoint was defined as the freedom from major complications through the post-stent removal study period. A subject was considered to have a successful safety outcome by the time of the one week post-stent removal visit if the following applied:

- Absence of access site-related bleeding requiring transfusion
- Absence of access site-related infection requiring intravenous or intramuscular antibiotics and/or extended hospitalization
- Absence of tissue injury, defined as ulceration to the submucosa at the site of stent implant
- No surgery for access-site related perforation required

- No stent migration/dislodgement into the pseudocyst or enteral lumen
- No serious adverse event classified as implant-associated or implant/surgical procedure associated

The safety outcome measure will be met if 85% of subjects are free of major complications through the 1 week post-removal visit.

Safety Results

The safety results for the above mentioned safety endpoints are summarized in Table 6 below.

Table 6: Freedom from Major Complications

Safety Endpoint	ITT N=33	Per Protocol N=29
Subjects are free of access site-related bleeding requiring transfusion	100% (33/33)	100% (29/29)
Subjects are free of access site-related infection requiring intravenous or intramuscular antibiotics and/or extended hospitalization	97% (32/33)	96.6% (28/29)
Subjects are free of surgery for access-site related perforation	100% (33/33)	100% (29/29)
Treated subjects are free of stent migration/dislodgement into the pseudocyst or enteral lumen	97% (32/33)	96.6% (28/29)
Subjects are free of tissue injury (ulceration to the submucosa) at stent site persisting through 1-week post-stent removal	100% (33/33)	100% (29/29)
Treated subjects are free of serious adverse event classified as implant associated or implant/endoscopic procedure-associated	84.8% (28/33)	86.2% (25/29)
Overall Safety	84.8% (28/33)	86.2% (25/29)

There were a total of 45 adverse events (AEs) reported among 33 subjects. There were 29 AEs post-index procedure and 16 AEs post-removal. Four events were considered to be related to both the index procedure and device. One event that was considered related to the device and/or index procedure was abdominal pain with chills 3 days post-index procedure. This subject underwent early removal of the stent.

There were 5 subjects with major complications, including 2 probably device-related and 3 probable procedure-related events. One subject developed back and left shoulder pain, 1 subject developed an acute GI bleed related to a pseudoaneurysm requiring embolization and transfusions and 1 subject developed an infected pseudocyst that was associated with stent migration and required hospitalization for intravenous antibiotics. These complications were also recorded as SAEs. The overall safety was 84.8% (28 of 33) for the ITT subjects, and 86.2% (25 of 29) for the PP subjects.

There were 25 serious adverse events (SAEs) that occurred among 16 of the 33 ITT subjects (48.5%). The most common post-procedure SAEs were abdominal pain (n=4), nausea and vomiting (n=2) and infection (n=2). None of the 10 post-removal SAEs occurred more than once.

There were 7 SAEs (21.2%) that were related to the procedure or device among the ITT subjects. The 4 SAEs (3 subjects) that were related to the procedure included abdominal pain, abdominal pain with syncope and GI bleeding, fever and left shoulder/back pain (1 each), while the 3 SAEs (3 subjects) that were related to the device included abdominal pain, infection and mucus overgrowth (1 each).

Nineteen subjects were reviewed to determine if there was a relationship of the dimensions of the stent and AEs. Among 7 subjects with AEs that were related to either the stent or index procedure, 4 subjects received the 10 x 10 mm stent and 3 received the 15 x 10 mm stent. Among the 10 subjects undergoing debridement procedures, there was an equal distribution of 10 x10 mm and 15 x10 mm stents.

Clinical results summary

Overall, 86.2% (25 of 29) of the PP subjects achieved the primary clinical effectiveness endpoint. The mean pseudocyst diameter decreased from a baseline of 9.0 cm to 3.1 cm at 30 days (29 subjects), and 1.6 cm at 60 days (10 subjects). Successful removal of the stents occurred in 29 of 30 subjects (97%) with one subject having an accidental dislodgement of the stent on post-stent placement day 18.

The study results showed that the stent facilitates successful pseudocyst drainage, either as a function of the stent alone, the stent and debridement procedures, or the stent with the placement of a pigtail stent through the AXIOS lumen. All scenarios would be considered a clinical success in clinical practice. Despite the occurrence of two SAEs requiring hospitalization, there were no life-threatening events which were determined to be related to the procedure or the device.

LABELING

Labeling has been provided which includes the instructions for use and an appropriate prescription statement as required by 21 CFR 801.109. The labeling includes:

- directions for selection of stent size, creation of the access tract, stent deployment and stent removal;
- summary effectiveness data from the 33 subject multi-site clinical study;
- adverse event data from the clinical study;
- potential complications from the use of the device; and
- warning statements to mitigate potential risks in the clinical setting, such as:
    - Placement of the AXIOS™ Stent should be performed by physicians familiar with endoscopic ultrasonography and endoscopic stent placement techniques;
    - The AXIOS Stent implantation should not exceed 60 days;
    - Long-term patency of this stent has not been established. Periodic evaluation of the stent is advised; and
    - Care is required during dilation, debridement, irrigation, and cystoscopy procedures through the stent, to prevent air/fluid leak and/or stent dislodgement.

RISKS TO HEALTH

Table 7 identifies the risks to health that may be associated with use of pancreatic drainage stents and delivery system and the measures necessary to mitigate these risks.

Table 7: Risk/Mitigation Table

Identified Risk	**Mitigation Method**
Adverse Tissue Reaction or Infection	Biocompatibility testing Sterility testing Labeling
Partial expansion of stent	Clinical experience In-vitro (bench) testing Labeling
Failure to deliver stent	Clinical experience In-vitro (bench) testing Labeling
Stent occlusion	Clinical experience Labeling
Stent ingrowth/failure to remove stent	Clinical experience Labeling
Stent migration (passive dislocation)	Clinical experience In-vitro (bench) testing Labeling
Stent dislodgement (active dislocation)	Clinical experience In-vitro (bench) testing Labeling
Tissue ulceration	Clinical experience In-vitro (bench) testing Labeling
Procedural complications	Clinical experience Labeling

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the AXIOS Stent and Delivery System is subject to the following special controls:

Performance Testing

The device and elements of the delivery device that may contact the patient must be demonstrated to be biocompatible.

Performance data must demonstrate the sterility of patient-contacting components of the device.

Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the requested shelf life.

Non-clinical testing data must demonstrate that the stent and delivery system perform as intended under anticipated conditions of use. The following performance characteristics must be tested:

(A) Deployment testing of the stent and delivery system must be conducted under simulated use conditions.
(B) Removal force testing must be conducted. The removal force testing must demonstrate that the stent can be safely removed, and that the stent will remain in place when subjected to forces encountered during use.
(C) Expansion force testing must be conducted. The expansion force must demonstrate that the forces exerted by the stent will not damage the tissue surrounding the stent.
(D) Compression force testing must be conducted. The compression force must demonstrate that the stent will withstand the forces encountered during use.
(E) Dimensional verification testing must be conducted.
(F) Tensile testing of joints and materials must be conducted. The minimum acceptance criteria must be adequate for its intended use.
(G) Fatigue testing must be conducted. Material strength must demonstrate that the stent will withstand forces encountered during use.
(H) Corrosion testing must be conducted. Corrosion resistance must demonstrate that the stent will withstand conditions encountered during use.

Non-clinical testing must evaluate the compatibility of the stent in a magnetic resonance (MR) environment.

Well-documented clinical experience must demonstrate safe and effective use, and capture any adverse events observed during clinical use.

Labeling

Labeling must include the following:

(A) Appropriate instructions, warnings, cautions, limitations, and information related to the safe use of the device, including deployment of the device, maintenance of the drainage lumen, and removal of the device.

(B) A warning that the safety and patency of the stent has not been established beyond the duration of the documented clinical experience.

(C) Specific instructions and the qualifications and clinical training needed for the safe use of the device, including deployment of the device, maintenance of the drainage lumen, and removal of the device.

(D) Information on the patient population for which the device has been demonstrated to be effective.

(E) A detailed summary of the clinical experience pertinent to use of the device.

(F) A detailed summary of the device technical parameters.

(G) A detailed summary of the device- and procedure-related complications pertinent to use of the device.

(H) An expiration date/shelf life.

BENEFIT/RISK DETERMINATION

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in a clinical study described above. There were 3 severe adverse events (SAEs) that were related to the device: abdominal pain with hyperplastic tissue reaction, infection of pseudocyst and stent migration, and embedded hyperplastic tissue at stent site. Additionally, there were 3 subjects with procedure-related SAEs. These SAEs included 1) back and shoulder pain after stent placement; 2) abdominal pain, GI bleeding, and syncope; and 3) fever. There were a total of 45 adverse events (AEs) reported among 33 subjects. There were 29 AEs post-procedure and 16 AEs post-removal. One event (bleeding) was found to be related to the device and four events (abdominal pain, two occurrences of nausea after eating, and chills) were considered to be related to both the procedure and device. The most common non-serious adverse events included abdominal pain (27%), nausea (15%) and fever (12%). No other event occurred in more than 10% of the subjects or accounted for more than 3 events.

It is difficult to determine the impact of the device in terms of the development of a harmful event versus what would occur as a result of the natural course in a patient with severe pancreatitis and a large symptomatic pseudocyst. This device is limited to implantation duration for a maximum of 60 days. Harmful events are more likely to be related to the underlying disease (severe pancreatitis and pseudocyst) than the stent placement procedure or the stent. In addition, the stent is easily removed if necessary.

The probable benefits of the device are also based on nonclinical laboratory and animal studies as well as data collected in a clinical study as described above. Clinical success was defined as the reduction of $\geq$ 50% in the diameter of the pseudocyst within 60 days of stent placement. Overall, 86.2% (25 of 29) of the per-protocol subjects achieved the primary clinical effectiveness endpoint. The mean pseudocyst diameter decreased from a baseline of 9.0 cm to 3.1 cm at 30 days, and 1.6 cm at 60 days. In addition, the use of this device provides an access port allowing

passage of standard and therapeutic endoscopes to facilitate debridement, irrigation and cystoscopy.

It seems very likely that a patient with the given indication for use would achieve a substantial clinical benefit. This patient population represents the most severe outcomes of both acute and chronic pancreatitis. The other options for this patient group include the placement of trans-enteric or trans-cutaneous plastic stents which are both ineffective, or surgery which carries at least 5% mortality. The effectiveness endpoints were evaluated at both a 30 and 60 day visit; however, the determination of clinical success in the resolution of the pancreatic pseudocyst was based on the cumulative results at 60 days. The protocol called for all stents to be removed at 60 days regardless of pseudocyst resolution. This study did not evaluate the recurrence of pancreatic pseudocysts after stent removal; however, pseudocyst recurrence is not uncommon in patients with severe pancreatitis, and this would not be a reflection on the overall effectiveness of the stent device.

Additional factors to be considered in determining probable risks and benefits for the AXIOS Stent and Delivery System include: the limitations of the study design, technical expertise required to use the stent system, and lack of alternative treatments. This was a non-blinded, non-randomized study which enrolled 33 subjects. However, because of the magnitude of the illness associated with infected pancreatic pseudocysts, and the limited results with other non-surgical interventions (such as the placement of plastic stents), it was reasonable to proceed without a blinded and randomized clinical trial.

Additionally, the use of this stent system is very dependent on the operation of a skilled endoscopist or surgeon familiar with endoscopic ultrasonography and endoscopic stent placement.

The placement of non-metallic endoscopic stents has been the standard of care for this population, although there are significant limitations of these stents in terms of the drainage of pseudocyst necrotic debris because of the narrow lumens. Surgical intervention is generally avoided because of the substantial post-operative morbidity and up to 5 % mortality.

There are no currently available devices that serve the purpose outlined in the indications for use for the AXIOS Stent and Delivery System. This treatment will be desirable for patients in that it will enhance the potential for resolution of their pancreatic injury during the treatment phase of the disease.

In conclusion, given the available information above, the data support that for transgastric or transduodenal endoscopic drainage of symptomatic pancreatic pseudocysts $\geq$ 6 cm in size, with $\geq$ 70% fluid content that are adherent to the bowel wall, the probable benefits outweigh the probable risks for the AXIOS Stent and Delivery System. The device provides substantial benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The *de novo* for the AXIOS Stent and Delivery System is granted and the device is classified under the following:

Product Code: PCU
Device Type: Pancreatic drainage stent and delivery system
Class: II
Regulation: 21 CFR 876.5015