DE NOVO CLASSIFICATION REQUEST FOR AMSTENT® TRACHEOBRONCHIAL COVERED STENT SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Tracheal prosthesis with cover material derived from human sources. The tracheal prosthesis with cover material derived from human sources is an expandable tubular device made of a metal material covered with a human-sourced decellularized material. It is intended to be implanted to restore the structure and/or function of the trachea or tracheobronchial tree. This device may also include a device delivery system. This device type does not include products that are intended to promote regeneration, impede inflammatory cascades, and release growth factors.

NEW REGULATION NUMBER: 21 CFR 868.3721

CLASSIFICATION: Class II

PRODUCT CODE: SDB

BACKGROUND

DEVICE NAME: AMStent® Tracheobronchial Covered Stent System

SUBMISSION NUMBER: DEN230087

DATE DE NOVO RECEIVED: December 20, 2023

SPONSOR INFORMATION:

Peytant Solutions, Inc.
3650 Annapolis Lane North, #180
Plymouth, MN 55447

INDICATIONS FOR USE

The AMStent® Tracheobronchial Covered Stent System (AMStent® System) is indicated for use in the treatment of tracheobronchial strictures produced by malignant neoplasms in adult patients.

LIMITATIONS

The AMStent® System is contraindicated for:

- Small bronchi which could impede catheter removal.

• Tracheobronchial obstruction with a lumen diameter which cannot be dilated and maintained at a minimum of 4mm.
• Patients for whom bronchoscopic procedures are not recommended.

WARNINGS

- The safety and effectiveness of the AMStent® System for use in the vascular system has not been established and can result in serious harm and/or death.
- This product has been designed for single patient use only. Do not reuse. Do not resterilize.
- Inspect the packaging and device before use. Do not use if the packaging is damaged or the device is damaged. Do not use unless the packaging sterile barrier is intact.
- Do not use if expiration date has been exceeded.
- The AMStent® delivery catheter is not intended for any use except AMStent® deployment.
- Placing an AMStent® across a major bifurcation may prevent or hinder future access for other procedures.
- Placing the AMStent® across bifurcations or side branches could impede airflow to the affected portions of the lung.
- The AMStent® cannot be repositioned in the airway after partial or full deployment.
- If the AMStent® is partially or fully deployed, the AMStent® cannot be resheathed or remounted onto the AMStent® delivery catheter.
- Do not place an AMStent® in a tumor stricture that is adjacent to a major vessel, as this may create a potential for fistula formation.
- A 0.035" guidewire is required before introduction of the AMStent® delivery catheter into the body. The guidewire must remain in place during the introduction, manipulation, and eventual removal of the AMStent® delivery catheter.
- After use, dispose of product and packaging in accordance with hospital, administrative, and/or local government policy.
- The AMStent® contains nitinol, an alloy of nickel and titanium. Persons with allergic reactions to these metals may suffer an allergic reaction to this implant. Prior to implantation, patients should be counseled on the materials contained in the device, as well as potential for allergy/hypersensitivity to these materials.

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

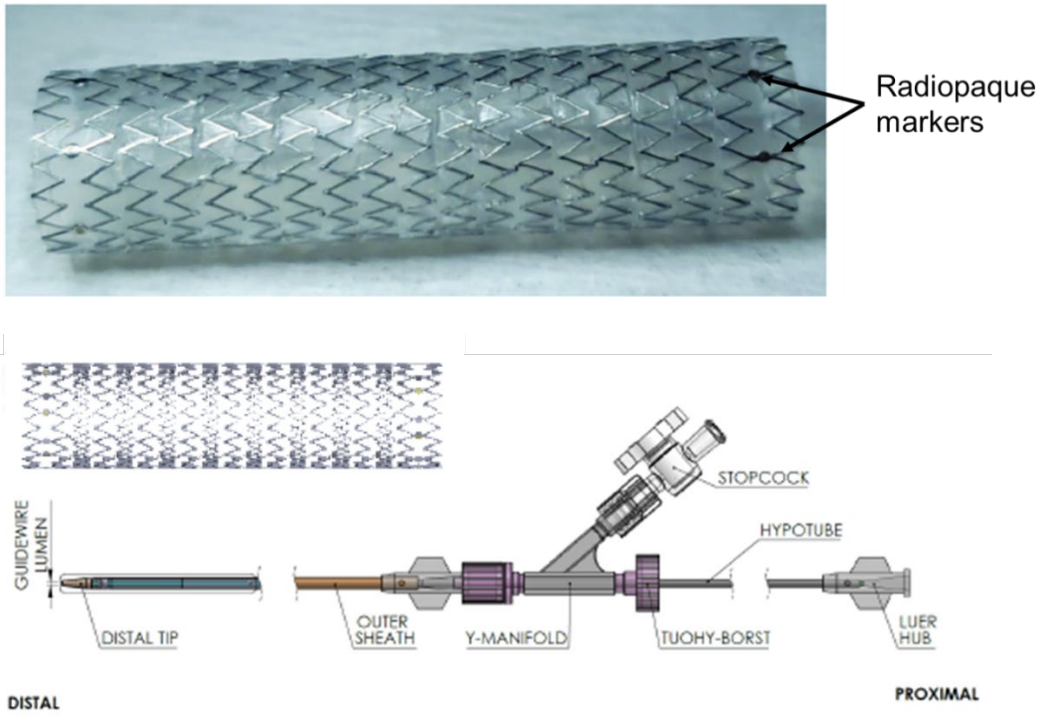
DEVICE DESCRIPTION

Peytant Solutions, Inc. developed the AMStent® Tracheobronchial Covered Stent System (AMStent System) to provide patency of the tracheobronchial tree in patients suffering from tracheobronchial strictures produced by malignant neoplasms. Like other nitinol devices that are also used for treating tracheobronchial strictures produced by malignant neoplasms, the AMStent System consists of a self-expanding metallic stent

(SEMS) that has a covering material over the interstices of the stent, and the stent is provided preloaded on a delivery catheter (Figure 1). The difference is that the AMStent covering is made from human-sourced decellularized amniotic membrane (DCAM), while the existing stents utilize synthetic cover materials (e.g., polyurethane, ePTFE, or silicone).

The AMStent is an open-cell, self-expanding, nitinol stent (10mm diameter x 40mm length) with a DCAM cover that is attached to the stent with polyethylene terephthalate (PET) sutures. The AMStent is preloaded on a flexible, "pull-back," AMStent delivery catheter. The AMStent delivery catheter is positioned in the tracheobronchial stricture with the assistance of a standard 0.035" guidewire, that is not provided with the AMStent System, under bronchoscopic and / or fluoroscopic visualization. Radiopaque markers are located on each end of the AMStent and on the distal end of the AMStent delivery catheter to facilitate placement.

Figure 1: *The AMStent system stent (above) and delivery catheter (below)*



Third-party Components and Accessories: The device is delivered with a 0.035" guidewire under bronchoscopy and includes radiopaque markers for detection via fluoroscope. The guidewire and fluoroscope are not included in the device. The device also requires saline and a 10cc syringe.

SUMMARY OF NONCLINICAL/BENCH STUDIES

The non-clinical/bench studies conducted on the Peytant Solutions AMStent System are summarized in the sections below. Note that certain tests were conducted in DEN200047, including some of the engineering/bench testing and shelf-life testing.

BIOCOMPATIBILITY

AMStent System materials with direct or indirect patient contact, representative of the final finished product, were tested based on ISO 10993-1: 2018 and FDA guidance "*Use of International Standard ISO 10993-1, "Biological evaluation of medical devices – Part 1:Evaluation and testing within a risk management process*" issued September 8, 2023. The stent related materials were tested for long-term (>30 day) duration and the delivery catheter materials were tested for a limited (≤24 hours) duration. Cytotoxicity testing of the AMStent primary package (tray with Tyvek lid) was conducted to provide additional assurance of biological safety. The results of all biological tests demonstrated that the patient contacting materials of the AMStent System device are biocompatible.

SHELF-LIFE

All testing of the complete AMStent System including packaging, delivery catheter, and AMStent, to include independent characterization of the DCAM cover, has demonstrated continued intended function over a minimum of 90 days. As a result, the current shelf life is established at 90 days from the date of sterilization.

MR COMPATIBILITY

The AMStent was tested for safety in the Magnetic Resonance Imaging (MRI) environment on fully finished and sterilized AMStents that had been deployed from the AMStent delivery catheter. Testing was conducted in accordance with ASTM F2052-15, ASTM 2213-06, ASTM 2119-07. Testing was conducted at 3-Tesla (magnetic field interactions, and artifacts). MRI-related heating was conducted at 1.5 Tesla/64 MHz, and 3 Tesla/128 MHz.

Testing resulted in a recommendation for the following MRI Compatibility labeling:

MR Conditional

Magnetic Field Interactions: translational attraction was 2 degrees.

MRI-Related Heating: expected maximum temperature rise of 3.1°C after 15 minutes of continuous scanning.

Artifacts: image artifact extends approximately 5 mm from the implant using69 gradient echo pulse sequence and a 3 Tesla System

PACKAGING

Engineering bench testing of the AMStent System packaging was conducted in as follows:

- Distribution testing in accordance with ASTM D4169: 2016;
- Bubble Leak testing in accordance with ASTM F2096-11;
- Seal Strength testing in accordance with ASTM F88-15;
- Visual inspection in accordance with ASTM F1886/F1886M-16.

In addition, due to its direct contact with the AMStent delivery catheter, cytotoxicity testing of the PETG tray in accordance with ISO 10993-5: 2009 was conducted, as noted above. Results of this testing indicated the tray to be non-cytotoxic.

PERFORMANCE/BENCH TESTING

Performance testing of the AMStent System on the catheter, stent, and stent cover. This included stent deployment, compression and recoil, expansion force, dimensional, fatigue, and corrosion tests, as well as puncture testing of the DCAM cover. Specific testing related to stent corrosion and Ni ion release was performed as recommended in the FDA guidance *Technical Considerations for Non-Clinical Assessment of Medical Devices Containing Nitinol*. The products used for testing had undergone all processing, including sterilization, and underwent simulated distribution prior to conducting the tests. These engineering bench tests were conducted on product that had not been intentionally aged, although many had been real-time aged as discussed in the individual test reports. Testing was also conducted on product and packaging that had been intentionally aged for a minimum of 90 days to ensure continued performance as intended over the labeled shelf life. The testing was satisfactory to show the device performs as intended and is safe for use.

HUMAN TISSUE CONTROLS

The AMStent System process for obtaining and preparing human tissue for use as a stent cover is sufficient and meets regulatory requirements for the use of human cells, tissues, and cellular and tissue-based products (HCT/P's). The AMStent System includes a human-sourced decellularized amniotic membrane cover. The process of obtaining DCAM material for use in manufacture of the AMStent System includes the key steps as shown in Table 1. Each step is to be conducted in accordance with 21 CFR 1271 requirements and Current Good Tissue Practice (CGTP) requirements. To ensure adherence to 21 CFR 1271 and reduce the risk of transmitting communicable diseases, facilities involved in the processing of DCAM coupons to be used on the AMStent are required to be an FDA registered facility and approved in writing by Peytant Solutions, Inc.

Risk control measures implemented include:

- Source material selection;
- Processing;
- Terminal sterilization;
- Compliance with 21 CFR 1271;
- Annual scientific review of literature and AATB bulletins to identify new and emerging diseases; and
- Labeling discloses the use of human-sourced material and residual risk of communicable disease.

Table 1: *DCAM Material Recovery, Processing, Manufacturing and Release Overview*

DCAM Step	Description
Donor eligibility assessment	Evaluation of whether potential donor meets criteria including maternal risk and health history, donor screening, testing, and consent
Placenta Recovery (Birth Tissue Procurement)	(b) (4)
(b) (4)	
Manufacturing	(b) (4)
Final Review for Product Release	Review of documentation by trained Clinical and Quality function personnel or designee to ensure all requirements have been met from donor eligibility assessment through final manufacturing prior to approving product for release to distribution

Prior to releasing AMStent Systems for distribution, extensive product release activities are completed. These are completed to ensure that the donated birth tissue was appropriately processed as intended. This is required to result in the intended human-sourced decellularized amniotic membrane material and ensure that:

- Donor eligibility and material processing and handling were conducted in accordance with 21 CFR 1271 requirements; and
- The final product meets all specifications.

MATERIAL CHARACTERIZATION AND LOT RELEASE

The AMStent is covered in a human-sourced decellularized amniotic membrane material. To characterize the composition of this material, the following tests were performed

(Table 2). Results of the material characterization activities demonstrate that the processing of the DCAM material both within and across lots is appropriately controlled to result in DCAM material that is consistently able to meet final product specifications based on user requirements. Qualitative and quantitative criteria have been identified and implemented for an acceptance and lot release evaluation to ensure the safety and effectiveness of the AMStent System is maintained across product lots.

Table 2: *DCAM Material Characterization Attributes Overview*

Characterization Attribute	Characterization Tests
Mechanical Strength	(b) (4)
Nucleic Acids and Cell Debris	
Collagen Quality	
Collagen Type and Content	
Visual Quality	
Presence of Manufacturing Residuals	

ANIMAL STUDIES

Two large animal studies were conducted that provide information to support the safety and effectiveness of the AMStent System. Both studies were conducted in compliance with Good Laboratory Practices (GLP) in accordance with 21 CFR 58. The first was a chronic (average 92 day) study to evaluate the in-vivo safety, implantability, migration, systemic effects, and usability of the AMStent compared to a control device. The second was an acute study to evaluate the in-vivo safety, implantability, removability, and usability of the AMStent following deployment. Both studies met their success criteria and study objectives, and the results support the safety and performance claims for the AMStent System.

SUMMARY OF CLINICAL INFORMATION

Not applicable. Validation of the AMStent System did not require clinical evaluation in human subjects.

LABELING

The labeling for the device is sufficient and consists of a package label, patient tracking card, and

the Instructions for Use. The package labeling satisfies the requirements of 21 CFR 801.109 to include a prescription use symbol, the patient tracking card satisfies the tracking requirements of 21 CFR 1271.290, and the Instructions for Use satisfies the medical device labeling requirements of 21 CFR 801 and specific human tissue labeling requirements for 21 CFR 1271.55.

Please see the Limitations section above for important contraindications, warnings, and precautions presented in the device labeling.

RISKS TO HEALTH

The table below (Table 3) identifies the risks to health that may be associated with the tracheal prosthesis with cover material derived from human sources.

Table 3: *Risk/Mitigation table*

Risks to Health	**Mitigation Measures**
Device mispositioning, migration, erosion, and fracture	Animal performance testing Non-clinical performance testing Labeling
Adverse tissue reaction	Biocompatibility evaluation
Device repositioning or removal during implantation	Animal performance testing Non-clinical performance testing Labeling
Infection	Material characterization and infection control measures Sterility testing Shelf-life testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the tracheal prosthesis with cover material derived from human sourcesis subject to the following special controls:

(1) Human tissue characterization and infection control measures must be provided for all human cells, tissues, and cellular and tissue-based products (HCT/P's), including documentation demonstrating:
   (i) Determination of donor eligibility, based on donor screening and testing for relevant communicable disease agents and diseases;
   (ii) Testing of all donor tissue for evidence of infection by relevant communicable disease agents, including (but not limited to): Human immunodeficiency virus type 1 and type 2, Hepatitis B and C viruses, and *Treponema pallidum*;
   (iii) Material sourcing from facilities that are registered for handling and processing of HCT/P materials and that incorporate the following procedures:
      (A) The facility must monitor environmental conditions for contamination or cross-contamination of HCT/Ps or equipment, or accidental exposure of HCT/Ps to

communicable disease agents;

(B) Processing must ensure materials have undergone defined decellularization processing and demonstrate sufficient viral inactivation potency across RNA, DNA, enveloped, non-enveloped virus types, and viruses native to the tissue, and removal of residual human nucleic acids via lot-based testing;

(C) A distinct identification code must be affixed to the HCT/P container that relates the HCT/P to the donor and to all accompanying records pertaining to the HCT/P, except for Personally Identifiable Information, and must enable tracking from the donor to the consignee or final disposition; and

(D) All HCT/P material must be kept in quarantine until completion of the donor-eligibility determination;

(iv) Material characterization activities demonstrating that the processing of the human-derived material both within and across lots is appropriately controlled to result in material that is consistently able to meet final product specifications.

(2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:

(i) Deployment testing to evaluate the accuracy and repeatability of any delivery system;
(ii) Compression and expansion forces;
(iii) Dimensional testing;
(iv) Fatigue and corrosion testing; and
(v) Compatibility of the device in a magnetic resonance (MR) environment.

(3) Animal performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including an animal study with chronic time points to evaluate device migration, occlusion, and granuloma formation.

(4) The device must be demonstrated to be biocompatible.

(5) Labeling must include:

(i) Magnetic resonance compatibility information;
(ii) Labeling must include a detailed summary of the device-related and procedure-related complications pertinent to the use of human-derived material and appropriate warnings;
(iii) A summary of bench and in vivo testing that describes the duration of testing;
(iv) Descriptions of claims and functionality must be limited to device functionality information demonstrated from performance testing; and
(v) A shelf life.

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

(7) Performance data must support the shelf-life of the device by demonstrating continued sterility, package integrity, tissue integrity, and device functionality over the identified

shelf life.

BENEFIT-RISK DETERMINATION

The AMStent System is intended for use in the treatment of tracheobronchial strictures produced by malignant neoplasms (cancerous tumors). Tracheobronchial strictures may also be referred to as tracheobronchial stenosis and define a condition where the airways narrow making it harder to breathe. When the tumor is wholly within the central airway, it is often treated by mechanical removal, to the extent possible, and thermal techniques (e.g., LASER, electrocoagulation, photodynamic therapy, argon plasma and cryoextraction).[1] Fully or partially covered self-expanding metallic stents may then be used to maintain the opening of the airway. Pre-stenting treatments are less likely when the tumor is outside of the central airway. By the time patients need this type of intervention, they are typically at the end of their life. In most studies, the median life expectancy is usually less than 3 months after stent placement.[2]

Nitinol/metal stents have a history of palliative use providing relief to labored breathing and end of life comfort. With it, however, they also have a history of mispositioning, migration, erosion, infection, and fracture. These probable risks are greatly outweighed by the probable benefit that comes with improved breathing experienced by patients who have these implants placed. To address these risks, the performance analysis for this device included an animal study which showed less stent migration, less mucus accumulation and occlusion, and fewer obstructive granulomas relative to a marketed stent, although this was for a small sample size and not repeated in other studies. Additionally, there remains uncertainty as to the device's performance in patients living 90-days post implant as that is the extent of the tested use life assessed in the in vivo animal study.

While The AMStent® System maintains the general benefits of a tracheal stent in the palliative care setting (i.e, providing relief to labored breathing and end of life comfort), it does include a new risk of disease communication due to the use of human derived amnion tissue. This is mitigated, however, by the adherence to human tissue characterization and infection control measures. The calculated risk of disease transmission is <1:1million instances of the use of the DCAM covers. This risk is greatly outweighed by the benefit of this device for palliative care.

Patient Perspectives

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

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

> The AMStent® Tracheobronchial Covered Stent System (AMStent® System) is indicated for use in the treatment of tracheobronchial strictures produced by malignant neoplasms in adult patients.

The probable benefits outweigh the probable risks for the AMStent® Tracheobronchial Covered Stent System. The device provides benefits, and the risks can be mitigated using general controls and the identified special controls.

References

1. Guibert N, et al. Airway stenting: Technological advancements and its role in interventional pulmonology. *Respirology*. 2020 Sep; 25(9): 953-962. doi: 10.1111/resp.13801. Epub 2020 Mar 11.
2. Holden VK, et al. Safety and Efficacy of the Tracheobronchial Bonastent: A Single-Center Case Series. *Respiration*. 2020;99(4):353-359. doi: 10.1159/000506815.

CONCLUSION

The De Novo request for the AMStent® Tracheobronchial Covered Stent System is granted, and the device is classified as follows:

Product Code: SDB
Device Type: Tracheal prosthesis with cover material derived from human sources
Regulation Number: 21 CFR 878.3721
Class: II