DE NOVO CLASSIFICATION REQUEST FOR CAVACLEAR LASER SHEATH

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Laser-powered inferior vena cava filter retrieval catheter. A laser-powered inferior vena cava (IVC) filter retrieval catheter is a percutaneous catheter that uses a laser to ablate tissue and is intended to facilitate in the detachment and removal of indwelling IVC filters.

NEW REGULATION NUMBER: 21 CFR 870.5125

CLASSIFICATION: Class II

PRODUCT CODE: QRJ

BACKGROUND

DEVICE NAME: CavaClear Laser Sheath

SUBMISSION NUMBER: DEN210024

DATE DE NOVO RECEIVED: June 25, 2021

SPONSOR INFORMATION:

Spectranetics, Inc.
9965 Federal Drive
Colorado Springs, Colorado 80921

INDICATIONS FOR USE

The CavaClear Laser Sheath is indicated as follows:

The device is intended for the ablation of tissue in the removal of IVC filters that have failed a previous retrieval method.

LIMITATIONS

The sale, distribution, and use of the CavaClear Laser Sheath are restricted to prescription use in accordance with 21 CFR 801.109.

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

DEVICE DESCRIPTION

The CavaClear Laser Sheath is a 14Fr or 16 Fr laser sheath that transmits (b)(4) ultraviolet energy in (b)(4) pulse durations from Spectranetics' Excimer Laser generators to the tissue at the distal tip of the device. When the laser activates, a small amount of the tissue is ablated through photochemical, photothermal, and photomechanical interaction, vaporizing tissue overgrowth in order to allow for inferior vena cava (IVC) filter removal. The CavaClear Laser Sheath operates at repetition rates of 25-80Hz and fluence of 30-60mJ/mm^2. See **Figure 1** below.

Figure 1: CavaClear Laser Sheath

This device is identical in design, materials, and method of construction to the GlideLight Laser Sheath approved for pacemaker and defibrillator cardiac lead removal under P960042 and related supplements.

SUMMARY OF BENCH AND SHELF-LIFE STUDIES

BIOCOMPATIBILITY

The CavaClear Laser Sheath is considered an externally communicating device that is intended to come in direct contact with circulating blood for a limited duration (≤ 24 hours). In accordance with ISO 10993-1:2018 and the FDA Guidance (Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing"), (FDA, 2016), the biocompatibility of the IVC Filter Removal Laser Sheath device was evaluated with respect to cytotoxicity, sensitization, irritation/intracutaneous reactivity, acute systemic toxicity, material mediated pyrogenicity, and hemocompatibility endpoints. This testing was leveraged from P960042 and related supplements and results of testing met all testing requirements. The device has been appropriately evaluated for biocompatibility.

STERILITY

The CavaClear Laser Sheath was successfully adopted into the currently validated ethylene oxide (EO) sterilization cycle for the product family with appropriate equivalency evaluation per AAMI TIR28:2016, "Product Adoption and Process Equivalence for Ethylene Oxide Sterilization". It has been demonstrated that the validated cycle will provide a sterility assurance level (SAL) of 10^{-6}. Confirmatory bioburden testing and endotoxin testing were evaluated and found to be acceptable.

ELECTROMAGNETIC COMPATIBILITY & ELECTRICAL SAFETY

The CavaClear Laser Sheath does not contain electromagnetic or electrical components and is electrically isolated from the laser. The subject device is intended to be used with the CVX-300 Excimer Laser System and Philips Laser System, both approved under P910001 and its supplements. Electromagnetic compatibility (EMC) and Electrical safety (ES) testing were provided and leveraged from these submissions since the essential performance is equivalent and the risk profile is lower. Testing demonstrated that the system was compliant to ANSI AAMI ES60601- 1:2005/(R)2012 and A1:2012, IEC 60601-1:2005/A1:2012 / EN 60601-1:2006/A1:2013 (3.1 Edition) and IEC 60601-1-2:2014 / EN 60601- 1-2:2015 (4th Edition). Basic Safety and essential performance were evaluated under 60601-1, laser safety and performance were evaluated under IEC 60601-2-22 and 60825-1, and electromagnetic compatibility was evaluated under 60601-1-2. The device has been appropriately evaluated for electromagnetic compatibility and electrical safety with the CVX-300 Excimer Laser and Philips Laser System.

SOFTWARE

The CavaClear Laser Sheath does not contain software. The subject device is intended to be used with the CVX-300 Excimer Laser and the Philips Laser System, both of which are approved in P910001 and its supplements. Software testing was provided and leveraged from this submission. Testing was provided to demonstrate that the device, when used with the laser, meets all requirements outlined in the FDA "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" for software of major level of concern.

PERFORMANCE TESTING – BENCH AND SHELF LIFE

The following performance testing was leveraged from the identical device approved within P960042 and associated supplements:

- Laser Output Characterization
  - Pin code programming of appropriate laser operating parameters
  - Maximum and minimum fluence range and repetition rate range
  - Laser catheter system calibration test and reliability
  - Energy output verification
  - Repetition rate verification
  - System minimum energy verification

    - Lasing Lifetime
- Reliability and gas life testing
- Functional, mechanical, and durability testing
- Coupler assembly testing
- User interface functionality
- Design/human factors validation
- Catheter testing
    - Tissue ablation
    - Tip integrity
    - Energy transmission
    - Particulate testing
    - Simulated use
    - Infusion testing
    - Dimensional characteristics
    - Bond strength
    - Kink testing
    - Torque testing
    - Radiopacity

The following testing was provided in DEN210024 to support the proposed indications for use, as well as minor changes to the device packaging:

- Human factors testing

Test	Purpose	Methods	Sample Size	Acceptance Criterion	Results
Summative Human Factors Testing	(b)(4)				

- Package integrity

Pouch material and folding techniques were modified for the sterile barrier of the CavaClear Laser Sheath and thus, additional packaging validation was conducted. A visual inspection, seal strength, and bubble leak testing was performed at baseline and at the aged condition. All results met the predefined acceptance criteria and were found to be acceptable.

The device has been appropriately evaluated for performance on the bench.

PERFORMANCE TESTING - ANIMAL

Animal testing was provided in P960042 to support the safety and performance in removing chronically implanted endocardial leads. All objectives of the evaluation were accomplished, including lack of acute adverse effects on local vasculature (e.g., perforation). Given the higher risk vascular bed, this data was determined to be leverageable for the new indications for use. The device has been appropriately evaluated in pre-clinical safety studies.

SUMMARY OF CLINICAL INFORMATION

The safety and effectiveness of the CavaClear Laser Sheath for removal of IVC filters has been established through a retrospective analysis of real-world evidence, as summarized below.

Title: Multicenter, real-world study of Excimer laser sheath assisted retrieval of embedded inferior vena cava (IVC) Filters

Purpose: The study aimed to evaluate the safety and performance of utilizing an excimer laser sheath as an advanced technique during IVC filter removal procedures.

Methods: This retrospective, multicenter, real-world evidence, observational trial enrolled 265 subjects at 7 sites in the US, with 139 subjects representing data from the single-center experience and 126 subjects from 6 sites representing the multi-center experience. Sites in the multi-center dataset were selected to represent a variety of operator experience levels and overall case volumes. All cases where the laser was utilized during an IVC filter removal procedure completed between March 2012 and February 2021 were captured following abstraction of the medical records with respect to the multi-center experience or from the existing published dataset with respect to the single center experience. The study populations included all-comer patients presenting with IVC filters that were refractory to alternate removal techniques, which included 10 different filter types with an upper dwell limit of over 21 years. Data collected represents the users experience for various levels of experience, ranging from 4-5 cases (novice) up to 139 cases (expert).

Patients were predominantly female in both the single-center and multi-center experience

data with 56.1% female and 59.5% female respectively. The average patient age at the time of procedure in both the single and multi-center experience datasets was 52 ± 16 years. The primary safety endpoint of the study aimed to demonstrate a major device related complication rate, based on SIR grading, of less than 10%. The primary efficacy endpoint aimed to demonstrate that the procedural technical success rate, which was not defined and was reported based on practitioners' clinical judgement, was above 89.4%. The thresholds for success in both the safety and efficacy endpoints were based upon meta-analysis of data in existing literature. All site reported complications were independently adjudicated to assess relatedness to use of the laser and to evaluate the appropriate severity classification based on the current SIR guidelines.

Results: The primary safety endpoint for the study was met with device related major complication rates of 2.9% (95% CL=0.8%, 7.2%), and 4.0% (95% CL=1.3%, 9.0%) demonstrated by the single and multi-center experience datasets, respectively. The upper confidence limits (UCLs) for both the single and multi-center experience datasets were below the Primary Safety Performance Goal (PG) of 10%.

Of 42 complications from the single-center experience dataset, 2 events were evaluated to be probably related to laser use (SIR Grade B complication, IVC injury with extravasation), 24 complications were evaluated to be possibly related to laser use, and 16 complications were evaluated to be not related to laser use. There were no major or minor complications that were evaluated to be definitely related to the use of laser. Of 24 complications from the multi-center experience dataset, 1 was evaluated to be definitely related to laser use (Minor: IVC injury with extravasation), 7 were evaluated to be probably related to laser use, 11 were evaluated to be possibly related to laser use, and 5 were evaluated to be not related to laser use. Please see Table 1 below for more detailed information on complications.

The primary efficacy endpoint for the study was met with procedural technical success rates of 95.7% (95% CL=90.8%, 98.4%), and 95.2% (95% CL=89.9%, 98.2%) for the single and multi-center clinical experience datasets, respectively. The lower confidence limits (LCLs) for both the single and multi-center experience datasets were above the Primary Efficacy Performance Goal (PGs) of 89.4%. Procedure failure was reported for 6 patients in each dataset for reasons including failure to capture the filter apex, failure to ablate tissue, or other reasons, including filter fracture.

Subgroup analyses were conducted for the single-center data and the multiple-center data separately. Regarding the primary safety endpoint for the multi-center data, the reported p-values for a subgroup analysis for whether a prior retrieval attempt was made (and failed) compared to when an attempt was not made was determined to be 0.0706, with rates of 0.0% (0/53) when a prior attempt was made and 7.0% (5/71) with no prior attempt. For the single-center experience, all procedures had a prior retrieval attempt before using the subject device. Please note that the device is only indicated for patients who have previously had a failed retrieval attempt.

Regarding the primary effectiveness endpoint for the single-center data, a potential effect was seen for gender, with a p-value=0.0853, with rates of 91.7% (55/60) for the male

subgroup and 98.7% (77/78) for the female subgroups. FDA believes that these differences may be due to low sample sizes in each group and does not have a reason to believe the subject device is less effective in the male population. No significant difference was noted for the multi-center data in this subgroup.

Conclusion: The results of this study demonstrate a high procedural technical success rate and a low major device related complication rate across both the single and multi-center experience datasets suggesting that a laser sheath can be used as an addition to the IVC filter retrieval armamentarium after failure of other methods for complex embedded filters without significantly increased risk of IVC filter related complications.

Table 1: Patient Demographics and Study Results

	Single-Center Experience	**Multi-Center Experience**
Patient Demographics		
Number of Subjects	139	126
Age (years)	52±16 (138)	52±16 (126)
Gender	Female: 56.1% (78/139) Male: 43.2% (60/139)	Female: 59.5% (75/126) Male: 40.5% (51/126)
Filter Dwell Time (months)	57.1±51.8 (136)	69.7±62.0 (110)
Prior failed retrieval attempts	100.0% (139/139)	42.1% (53/126)
Study Primary Endpoints		
Procedural Technical Success Rate	95.7% (133/139) [90.8%, 98.4%]	95.2% (120/126) [89.9%, 98.2%]
Device Related Major Complication Rate	2.9% (4/139) [0.8%, 7.2%]	4.0% (5/126) [1.3%, 9.0%]
Complications*		
Overall Site Reported Complication Rate	30.2% (42/139)	18.3% (23/126) [24][2]
Complication relatedness to use of laser[1]	Definitely Related: 0/42 Probably Related: 2/42 Possibly Related: 24/42 Not Related: 16/42	Definitely Related: 1/24[3] Probably Related: 7/24 Possibly Related: 11/24 Not Related: 5/24
Device Related Major Complication Rate	**2.9% (4/139) [0.8%, 7.2%]**	**4.0% (5/126) [1.3%, 9.0%]**
IVC perforation	1	0
Filter fracture with embolization	2	0
Filter penetration	1	0
IVC injury with extravasation	0	2
Hematoma, major	0	2
Hemorrhage	0	1
Procedure Related Major Complication Rate	**3.6% (5/139) [1.2%, 8.2%]**	**4.0% (5/126) [1.3%, 9.0%]**
IVC perforation	1	0

Filter fracture with embolization	2	0
Filter penetration	1	0
IVC injury with extravasation	0	2
Hematoma, major	0	2
Hemorrhage	0	1
Access site hematoma	1	0
Device Related Minor Complication Rate	**15.8% (22/139) [10.2%,23%]**	**11.1% (14/126) [6.2%, 17.9%]**
IVC injury with extravasation	9	4
IVC perforation	1	0
Filter fracture	1	0
Filter fracture with embolization	1	0
Pseudoaneurysm	1	0
Access site hematoma	3	0
Caval thrombus	0	1
Filter fracture with embedded fragments	0	3
Retrieval tool fracture	0	5
Other	6	1
Procedure Related Minor Complication Rate	**26.6% (37/139) [19.5%, 34.8%]**	**15.1% (19/126) [9.3%, 22.5%]**
IVC injury with extravasation	9	4
IVC perforation	1	0
Filter fracture	1	0
Filter fracture with embolization	1	3
Pseudoaneurysm	1	0
Access site hematoma	3	0
Caval thrombus	0	2
Filter fracture with embedded fragments	2	3
Retrieval tool fracture	0	5
IVC stenosis	2	0
Small extravasation	1	0
Additional procedures required for filter retrieval due to filter tilt	2	0
Back pain	1	0
Caval narrowing	1	0
Deep vein thrombosis	0	1
Other	12	1
[1]All complications were independently adjudicated for SIR grade and assessed for relatedness to use of laser		

[2]One subject reported multiple complications/SIR grades – Multi-Center
[3]One complication evaluated to be definitely related to use of the laser was a minor complication in the multi-center experience dataset
*Device related: Device related complications are also procedure related complications; Procedure related: Procedure related complications also includes complications that are not device related; Major Complication definition (per SIR grading): C. Require therapy, minor hospitalization (<48 hours); D. Require major therapy, unplanned increase in level of care, prolonged hospitalization (>48 hours); E. Permanent adverse sequelae; F. Death; Minor Complication definition (per SIR grading): A. No therapy, no consequence; B. Nominal therapy, no consequence; includes overnight admission for observation only.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

TRAINING

Training is required for use of the CavaClear Laser Sheath for IVC filter removal. Training includes the following topics:

- Device design and key features
- Review of indications and contraindications
- Review of potential complications
- Laser sheath preparations
- The use of the laser sheath to remove IVC filters
- Post-removal of laser sheath

LABELING

The labeling consists of Instructions for Use and packaging labels. The Instructions for use include the indications for use; a description of the device, contraindications, warnings, precautions; a detailed summary of the clinical data collected in support of the device; a shelf life; and instructions for the safe use of the device. The labeling satisfies the requirements of 21 CFR 801.109.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of Laser-powered inferior vena cava filter retrieval catheters:

Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
Infection	Sterilization validation Shelf life testing Pyrogenicity testing Labeling

Identified Risks to Health	Mitigation Measures
Adverse tissue reaction	Biocompatibility evaluation
Device damage during use resulting in clinical sequelae such as embolic concern or prolonged procedure	Non-clinical performance testing Clinical performance testing
Soft tissue damage from laser, such as IVC injury, extravasation, and perforation	Laser generator compatibility testing *In-vivo* safety testing, Clinical performance testing Labeling Training
IVF filter damage, including fracture and embolization, due to laser interaction	Non-clinical performance testing Clinical testing Labeling Training

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the laser-powered inferior vena cava (IVC) filter retrieval catheter is subject to the following special controls:

1) Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. Testing must include:
   i. Evaluation of major and minor complications associated with IVC filter removal; and
   ii. Evaluation of success rates of IVC filter removal.
2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be evaluated:
   i. Dimensional testing must demonstrate that the device is compatible with the intended anatomy and compatible with all labeled accessories.
   ii. Mechanical testing on all joints must demonstrate that the device can withstand tensile and torsional forces encountered under challenging clinical use conditions.
   iii. Simulated use testing must demonstrate that the device can be inserted, tracked, activated, and removed without device damage and that the device is able to function as intended (e.g., remove IVC filter without damage) under challenging clinical use conditions.
   iv. Performance testing must demonstrate that the product is visible under fluoroscopic techniques.
   v. Performance testing must demonstrate that the device does not kink when subjected to clinically relevant tortuosity.
3) Compatibility testing with laser generators must include:
   i. Electrical safety, electromagnetic compatibility (EMC) testing, and electromagnetic interference (EMI) testing must be conducted for all devices that contain electrical components.

ii. Software verification, validation, and hazard analysis must be conducted for all devices that contain software.
iii. Laser output characterization and performance testing, including verification of calibration reliability, energy output, and repetition rate, and laser lifetime testing, must be conducted.

4) All patient-contacting components must be demonstrated to be biocompatible.
5) Performance data must demonstrate the sterility and non-pyrogenicity of patient contacting components of the device that are provided sterile.
6) Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and system functionality over the established shelf life.
7) *In vivo* safety testing must demonstrate that the device does not cause soft tissue damage or device damage under worst case clinical use conditions.
8) Labeling must include the following:
   i. A detailed summary of the device technical parameters and materials of the device;
   ii. A summary of the clinical performance testing conducted with the device; and
   iii. A shelf life.
9) A training program must be provided to ensure that users can safely and reliably use the device per its instructions for use.

BENEFIT-RISK DETERMINATION

The risks of the device are based on data collected in a clinical study described above.

Risks for use of the CavaClear Laser sheath are low, as demonstrated by the supporting clinical data. The device related major complication rate was observed to be approximately 3-4%, which is similar to the expected rate for other advanced filter extraction techniques. Complications experienced in this study include IVC injury causing extravasation, IVC injury causing hematoma, IVC injury causing perforation, filter fracture, and filter embolization. These complications occurred at expected rates. Device related minor complications, determined to be minor based on SIR grading, were experienced at rates of approximately 10-15% in the clinical study, and were similar in nature to the ones described above. Risks are further mitigated through labeling and a comprehensive training program.

The probable benefits of the device are also based on data collected in a clinical study as described above.

The probable benefits of the CavaClear Laser Sheath are demonstrated by the supporting clinical data, which indicated a technical success rate of approximately 95%. Reasons for failed technical success include inability to grasp filter, failure to ablate tissue, and filter fracture. For chronically embedded IVC filters, the observed technical success rate was high, indicating that the CavaClear Laser Sheath provides clinical benefits to patients with firmly adherent and otherwise difficult to extract devices.

Additional factors to be considered in determining probable risks and benefits for the CavaClear Laser Sheath include:

This device is intended for patients who have failed previous retrieval attempt(s) and the clinical data shows a high technical success rate in these patients who otherwise may have limited options for IVC filter removal.

The sponsor has made efforts to mitigate risks through labeling and development of a comprehensive training program for new physician users, incorporating best practices for managing potential complications.

For the intended patient population with firmly adherent IVC filters that have failed a previous retrieval method, the benefit risk profile derived from the provided real world evidence has been demonstrated to be acceptable.

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 device is intended for the ablation tissue in the removal of IVC filters that have failed a previous retrieval method.

The probable benefits outweigh the probable risks for the CavaClear Laser Sheath. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the CavaClear Laser Sheath is granted and the device is classified as follows:

> Product Code: QRJ
> Device Type: Laser-powered inferior vena cava filter retrieval catheter
> Regulation Number: 21 CFR 870.5125
> Class: II