



Memorandum

SUMMARY of P960042/S031 GlideLight 80Hz Laser Sheath (12, 14, or 16Fr) Spectranetics

EXECUTIVE SUMMARY

This PMA/S was submitted to gain approval for an additional product line within the Spectranetics Laser Sheath family with a higher maximum repetition rate that will allow the physician to use less force and take less time during a lead extraction procedure. The new device (originally referred to as the “(b) (4)”, but finally termed the “GlideLight Laser Sheath” in A001) will operate at a maximum of 80 Hz, while the predecessor device (the market approved SLSII Laser Sheath) operates at a maximum of 40 Hz.

To support their request, the firm provided the following:

- Extensive bench testing
- A risk assessment taking into account post market performance of the predecessor SLS II 40 Hz device
- OUS performance data of the subject device
- Simulated use testing by nine physicians regarding ease of use and scenarios in which the device might not be suitable for use
- Process validation activities to evaluate the manufacturing changes necessary to implement the requested change.

Regulatory Background

The predecessor SLS II device was approved in January 1998 for the same indications requested for the subject GlideLight Laser Sheath device- transvenous removal of chronically implanted pacing or defibrillation leads. The firm plans to continue to market the predecessor device after approval of the new device.

Pre-IDE Conversations

The firm submitted two pre-IDEs to discuss their proposed test plan for the 80Hz Laser Sheath: (b) (4). The same review team that participated on the discussions regarding these pre-IDEs participated on the review of the subject submission. During these pre-IDE conversations, FDA communicated concerns with the adequacy of the proposed bench testing, (b) (4).

(b) (4) Detailed email comments were sent to the sponsor in December 2010.

Indications and Contraindications for Use

The firm lists their indications and contraindications for use on page 13 of the submission; no changes have been made relative to the predecessor SLS II 40 Hz device.

Indications for Use

The laser sheath is intended for use as an adjunct to conventional lead extraction tools in patients suitable for transvenous removal of chronically implanted pacing or defibrillator leads constructed with silicone or polyurethane outer insulation.

Contraindications

Use of the Laser Sheath is contraindicated:

- When emergency thoracotomy with cardiopulmonary bypass cannot be performed immediately in the event of a life threatening complication;
- When fluoroscopy is not available;
- In patients in whom superior venous approach cannot be used;
- When the proximal end of the pacing lead is not accessible to the operator;
- When the lead will not fit into the inner lumen of the laser sheath.

LEAD REVIEWER COMMENTS: I do not believe the change from 40Hz to 80Hz should impact the appropriateness of the Instructions for Use. The firm does, however

(b) (4)

. In addition, the clinical reviewer agreed with the firm's provided indications and contraindications for use statement.

Device Description

A detailed description of the device is provided on page 9 of the submission is paraphrased and quoted below:

Design: The GlideLight laser Sheath 80 Hz Laser Sheath consists of optical fibers arranged in a circle between inner and outer polymer tubing. The fibers terminate at the distal end within a polished tip and at the proximal end within the coupler that connects to the Excimer Laser System. At the distal tip, the fibers are protected by inner and outer stainless steel bands, which form a radiopaque marker. The inner lumen of the device is designed to allow a pacing lead to pass through, as the device slides over the lead towards the tip of the lead implanted in the heart.

Function: The laser sheath transmits ultraviolet energy from the Spectranetics CVX-300 Excimer Laser System to the tissue at the distal tip of the device with the intention of ablating a small amount of the tissue, thereby freeing the lead from overgrowth in a controllable fashion.

Detailed Description of Changes

The repetition rate for the SLS devices is controlled by a pin code on the proximal coupler assembly at the proximal end of the device. The coupler connects the sheath with the Spectranetics CVX Excimer Laser System (P910001), and the pin code identifies the device to the laser system (including the applicable maximum frequency). The only changes required for the requested increase in frequency from 40 Hz to 80Hz, therefore, is to the pin code and labeling of the proximal coupler assembly.

Separately, the CVX Excimer laser system itself underwent software upgrades to support its use with the GlideLight 80Hz Laser Sheath. These changes were submitted under P910001/S049 and reviewed. The submission included testing to demonstrate that when the GlideLight Laser Sheath is connected to the laser coupler, the system generates the appropriate signal for the sheath, the software recognizes this signal, the software correctly identifies/sets the laser operating parameters, and the sheath can be calibrated. The proposed software changes were approved on 25 Oct 2011.

Risk Assessment

The firm assessed the risks of the proposed increased frequency of the GlideLight Laser Sheath by conducting a Preliminary Hazard Assessment (PHA), Design Failure Modes and Effects Analysis (DFMEA), and a Process Failure Modes and Effects Analysis (PFMEA). The firm points to the low number of post market issues with the 40 Hz SLSII device as evidence of the general safety of the device. The largest concern that remains of all design and manufacturing mitigation is the potential for misuse of the device, which is mitigated by the Instructions for Use.

In the original submission, the firm did not clearly indicate if the subject device had been used or approved outside the US (OUS).

In A001, they clarified that at the time of the original submission, no post market data was available for the 80 Hz device (only the 40 Hz model). However, the GlideLight Laser Sheath received a CE mark in December 2011, and as of February 2012 information was available on the limited release of the product. The report provided indicated 81 leads were extracted in 49 completed cases at 6 sites. Four complaints and three adverse events were reported.

There were no concerns with the firm's conclusions that (when used as intended) the GlideLight Laser Sheath provides a favorable risk/benefit ratio.

The firm's response to A001 providing information on OUS experience of the subject device was reviewed. It was concluded that the risks of the new laser were acceptable given the post market performance since no events were directly attributed to the new, higher repetition rate. It was noted that all three adverse events, when reviewed in detail, resulted in perforations. This is not concerning, though, because perforations are a known occurrence with the device and the risk is not expected to be different with the subject device compared to its predecessor. In addition, a limited roll out will be conducted by the firm to provide more detailed information on the procedural success and adverse event rates.

Preclinical Testing- Design Verification Bench Testing

The firm conducted the following general design verification activities:

- The laser lifetime (ensuring that the GlideLight Laser Sheath can properly transmit twice the number of laser energy pulses as the predecessor 40 Hz device).

- The force to ablate tissue (providing supporting evidence for the firm's claim that there is a significant statistical difference between the force needed to ablate tissue using the 80Hz device vs the predecessor 40 Hz device).

The firm also conducted four additional tests recommended by FDA during pre-IDE discussions in order to demonstrate safety of the new device and support the proposed marketing claims:

- Competitive Device Comparative Testing: thermal and mechanical histological effects were compared for the predecessor SLS II device, the proposed GlideLight Laser Sheath, and two laser sheaths from Cook; both soft (porcine myocardium) and hard (bovine Achilles tendon) tissues were used.
- 80 Hz vs 40Hz Histopathology Analysis Testing: Ablation and coagulation thicknesses were compared between 40Hz and 80Hz data sets and acceptability was determined based on pre-set criterion.
- Worst Case Scenario Testing: laser sheaths were tested for ablation and coagulation thickness at varying repetition rates (60, 80, 100, and 115Hz) using a worst case advancement rate and tissue penetration depth.
- Temperature Profile Testing: temperature probes were used to measure tissue heating; data was compared to an acceptance criterion from literature.

Software. As discussed above under the Detailed Description of Changes section, all software testing was found acceptable and approved under a different submission-P910001/S049.

The firm's original testing was largely acceptable and supportive of the marketing claims requested. These concerns were resolved as indicated below:

- While the firm evaluated thermal ablation and coagulation, it was initially unclear if an assessment of mechanical disruption caused by laser induced bubble formation and stress wave generation was conducted. In A001, the firm indicated that such an assessment was conducted (and no evidence of disruption was seen). The additional analysis and discussion was reviewed and found acceptable. There are no further concerns regarding potential mechanical disruption effects of the increased repetition rate.
- The worst case scenario testing included no justification for the selected tissue depth (the firm selected 6.5 mm instead of 9mm, which the review team believed would present the worst case impact on the tissue). The firm provided a rationale for this selection in A001: varying the laser pulse frequency while holding the advancement rate constant can provide worst case scenario testing as long as sufficient depth is reached to obtain representative tissue samples. This additional justification was found to be acceptable. There are no further concerns with the worst case testing.

Preclinical Testing- Simulated Use

The firm's design validation activities included a Physician Simulated Use and Label review as well as a review of the Instructions for Use. Nine physicians familiar with the predecessor SLS II device participated in the simulated use testing; this testing involved simulated lead extractions and a questionnaire asking for comparison between the 40 Hz and 80Hz device with respect to force used and the time required to complete the operation.

The size of the simulated use testing study was quite small (only nine physicians), but since each was an expert with extraction, there was not a concern with the number. While the study seemed acceptable, the labeling should be updated to include the results from the simulated use testing to better educate the user. The firm's response in A001 provided edits to the indications for use and training materials (discussed further below). Further edits were discussed interactively with the firm (06 and 10 April 2012) to reach arrive at a document that was acceptable. No concerns remain at this time.

Clinical Evidence

No clinical evidence was provided in support of the premarket approval of this submission. However, the sponsor indicated during interactive communication that a limited roll out and launch will be conducted in order to gain detailed information on procedural success and adverse event rates.

The need for premarket clinical data for the subject device change was discussed and it was determined that clinical data was not necessary for the premarket approval of this device for a number of reasons including the following:

- The device itself is identical in design and use to the 40 Hz approved predecessor, therefore, the risks associated with usage are expected to be similar in nature, allowing the data provided for the predecessor device to be representative of the proposed device.
- The OUS data provided for the newer 80Hz device confirms the basic assessment that device performance would be similar. The limited roll out and launch proposed by the firm should also provide confirmatory data of the review team's assessment of the extent of the changes and the expected impact on performance.
- Bench testing provided an effective method of assessing tissue damage concerns of the higher frequency device.
- The instructions for use and training materials were carefully reviewed together with the physician handling and simulated use study to ensure they inform users of the risks with the change in frequency.
- The physicians who are most likely to use the subject device are experienced clinicians familiar with the device and laser operation.

In addition, the firm's proposed limited roll out of the subject device was discussed, which appears to be an acceptable method of confirming that the provided (and reviewed) training

materials and instructions for use adequately inform the user of the risks and mitigation of the new higher frequency. There are no outstanding questions that require post market evaluation via a formal Post Approval Study and no further concerns with this section of review.

Instructions for Use and Physician Training

The firm has added a general statement to the Instructions for Use that describes the new 80Hz device. Other editorial changes were necessary to account for the increased repetition rate as well.

The physician training is based on the training used with the market approved predecessor 40 Hz device and includes the following:

- Classroom training in laser safety and physics;
- A didactic presentation of laser operation followed by a demonstration of the CVX-300 Excimer Laser System;
- Hands-on training in the use of the CVX-300 Excimer Laser System in lead removal;
- Observation of the removal of at least two leads with the Laser Sheath performed by an experienced Laser Sheath user;
- Removal of at least two leads in the presence of a second physician experienced in lead removal techniques and a fully trained Spectranetics representative.

The Instructions for Use as well as the physician training were reviewed and found largely acceptable. It was noted that the results and feedback from the simulated use study needed to be incorporated into labeling. For example, no mention is made of situations and circumstances where the 80Hz device would not be appropriate. In A001, the firm provided some revisions to the instructions for use and training materials, such as the note that several parameters are controllable by the physician (calibration, fluence, and repetition rate). The changes were not sufficient, however, to convey (1) that data has not been provided for the 80 Hz device and (2) that caution should be used since less force is required for advancement. Interactive communications via email with the firm (06 and 10 April 2012) resolved the remaining concerns.

There was also an initial concern with the box labeling- as noted by the simulated use physician participants, the name of the device was confusing [REDACTED] (b) (4). In A001, the firm revised the name of their 80 Hz device to GlideLight, therefore, addressing this concern.

Labeling Claims

Four specific labeling claims regarding the new 80Hz device are requested in the submission:

- [REDACTED] (b) (4)
- Advancement force with 80Hz is up to 55.88% less than the advancement force with 40Hz ablation.

- Ablation rate of 80Hz is up to 141.72% faster than 40Hz at similar advancement forces.
- Reduced advancement force of 80Hz lowers the forces applied to leads during extraction, when compared to 40Hz.

The firm points to the results of their bench testing and provides a Marketing Claims Summary Report as well to support their request.

The proposed claims were reviewed. Clarification of the language of the first claim was needed. The firm accepted FDA's wording change proposal to clearly indicate that the tissue effects in question are those of coagulation and ablation. No concerns remain with the language of the claims proposed.

Note that an additional marketing claim was originally proposed by the sponsor, but removed after interactive discussions regarding concerns that the claim was promotional in nature. (b) (4)

Packaging, Shelf Life and Sterilization

The firm indicates that there have been no changes to the sterilization process relative to the predecessor device. In response to FDA concerns in the Major Deficiency letter, the sponsor confirmed that the packaging materials and configuration as well as shelf life requested for the GlideLight Laser Sheath are identical to that of the predecessor SLS II device.

There are no concerns with the absence of packaging, sterilization, or shelf life testing given that no changes have been made to the device itself that would impact the adequacy of the packaging or the testing already provided and reviewed to demonstrate a 2 year shelf life. There are no concerns with this section of review.

Biocompatibility

No biocompatibility testing was conducted on the proposed GlideLight Laser Sheath device.

The absence of biocompatibility testing is not concerning since there have been no changes to the materials or manufacturing processes used.

Manufacturing

The change from 40 Hz to 80 Hz required manufacturing process changes to the laser test station and proximal couple assembly station. Process validation (using a sample size of 24 devices- 8 from each of 3 size options) was conducted to ensure that the changes to the manufacturing processes are not problematic from a quality control perspective. Firmware validation was also conducted.

The manufacturing process changes and their validation in the original submission were reviewed. The changes and validation activities described in the original submission were largely appropriate, but that some clarification was necessary to confirm. The responses to these concerns were provided in A001 and reviewed. No concerns remain as clarified

further below:

- The original submission indicated that the Laser Test Procedure had been updated for the new device, but that updated version was not provided. In A001, the firm included the Laser Test document applicable to the entire family of SLS devices and clarified that the reference to the 80Hz repetition rate was based on modifications to the laser unit and not the laser test procedure. The provided document and additional information are acceptable and no concerns remain.
- No rationale for the sample size used in the process validation activities was provided in the original submission. In A001, the firm clarified that the protocol called for a minimum of 24 units tested with an acceptance criterion of 100% verification at final inspection. In fact, 41 devices were built as part of a site change process qualification activity and used for the current validation. This sample size is acceptable.
- No details were provided in the original submission regarding the one unit that failed process validation testing. In A001, the firm clarified that a final inspection of the failed specimen showed missing or dead fibers. The firm's current procedure calls for a rework in such cases and, after the rework, the device was reprocessed and successfully retested. No concerns remain with the test results.