SetPoint System Surgeon Instructions for Use

Read all instructions, warnings and cautions carefully. Failure to follow them could lead to damage to the SetPoint System, cause it to malfunction, degrade its performance and/or result in harm.

Contact SetPoint Medical with any questions about the information contained in the **SetPoint System Surgeon Instructions for Use** (Surgeon IFU). Copies of all SetPoint System Instructions for Use (IFUs) are available on the SetPoint Medical website. Any SetPoint System-related incident or problem, which is believed to represent a safety issue, should be reported to SetPoint Medical Inc. immediately.

CONTACT INFORMATION:

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www.setpointmedical.com

Caution: Federal law restricts this device to sale by or on the order of a physician.

Surgeon Quick Reference Guide

It is important to read and understand the entire contents of this Surgeon IFU prior to use of the SetPoint System. Make sure to brief the patient on contraindications and warnings using section **Important Safety Information**.

Charger Fit Confirmation

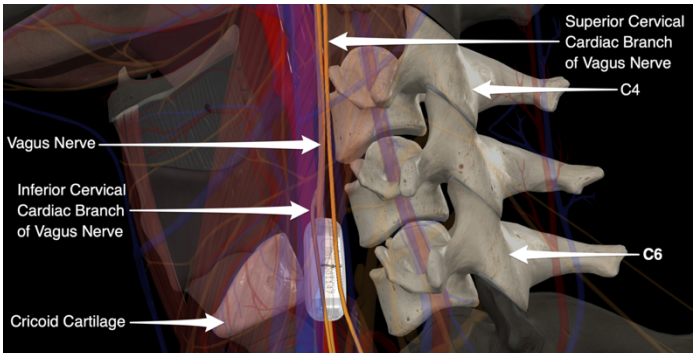
- Place the Charger around the patient's neck while they are seated upright
- Verify that the magnetic latch closes and remains latched without discomfort

See section **Charger Fit Confirmation** for more details.

Implantation Location

- On the left cervical vagus nerve
- Below both the inferior and the superior cervical cardiac branches
- Ideally between the level of the C4 and C6 cervical vertebrae, but never below the level of C7

See section **Implantation Location** for more details.



Surgical Procedure

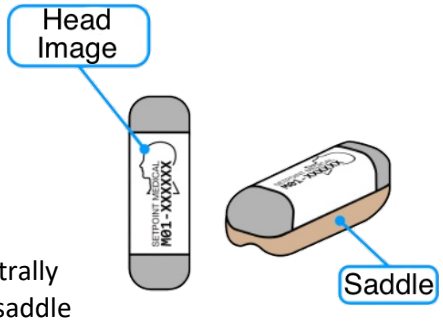
See section **Implantation** for more details.

1. Nerve Exposure

- 1.2 in (3 cm) branch-free segment of left vagus nerve

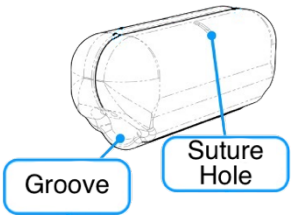
2. Implant Placement

- Place the Pod on the left vagus nerve
- Insert the Implant into the Pod, with the head-shaped marking oriented rostrally
- Visualize that nerve is seated through ends of Pod groove and is in Implant saddle
- Ensure that no extra nerve branches or other structures are entrapped in the Pod



3. Closure

- Suture Pod through suture holes with non-absorbable 5-0 Prolene on a non-cutting needle and no more than 4 throws
- Gently confirm Pod rotates and slides freely on the nerve



 1.2 in (3 cm) segment of left vagus nerve for Pod deployment	 Avoid excessive manipulation or traction on vagus nerve	 No electrocautery or RF ablation within 2 cm of Implant

The information contained herein is not a substitute for a complete and thorough understanding of all the instructions presented in the Surgeon IFU. Please refer to the relevant sections in the Surgeon IFU for all pertinent information concerning use of the SetPoint System, and safety and efficacy information.

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Introduction

This **SetPoint System Surgeon Instructions for Use** (Surgeon IFU) describes the operation and intended use of the SetPoint System and the surgical procedure for implantation. The SetPoint System is to be used only by physicians who have reviewed and understand this Surgeon IFU.

The table below shows the SetPoint System model numbers for the parts of the system that are described in this IFU.

Device Name	Model Number
Implant	M01
Charger	E04
Docking Station	C01

Table 1 - Device Names and Model Numbers

To reorder the Implant, contact SetPoint Medical and request Catalog Number 90001.

Indication for Use

The SetPoint System is indicated for the treatment of adult patients with moderately to severely active RA who have had an inadequate response, loss of response or intolerance to one (1) or more biological or targeted synthetic DMARDs.

Pediatric Use

The SetPoint System is not intended for use in the pediatric population.

SetPoint System Description

The SetPoint System includes:

- The Implant (A) which is placed within a Pod (B) and implanted on the left vagus nerve in the neck (C)
- A Charger (D) with Docking Station (F)
- A Programmer (E)

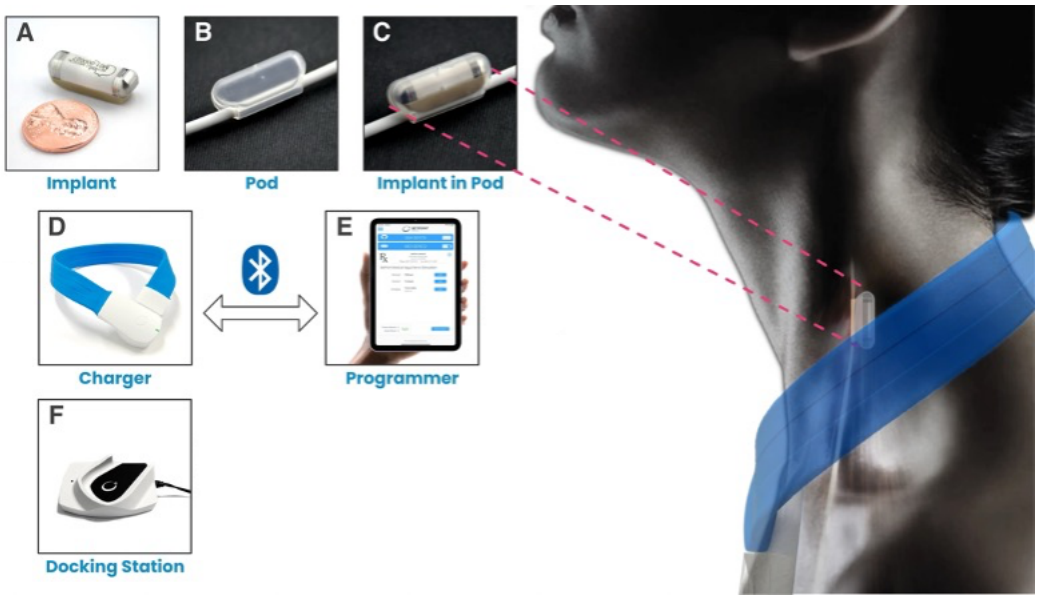

Figure 1 - SetPoint System and Components

Implant and Pod

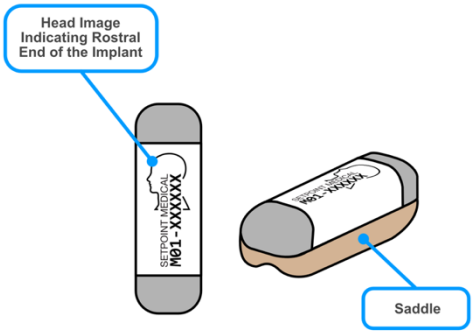

Figure 2 - Implant

The Implant is an integrated neurostimulation device. It is used to electrically stimulate the vagus nerve for 1 minute, every day. It is about 1 in (2.5 cm) long and weighs about 0.1 oz (3 g). It is surgically implanted next to the vagus nerve on the left side of the neck. The Implant is placed inside a Pod, which is a flexible cover made of silicone. The Pod helps hold the Implant in place.

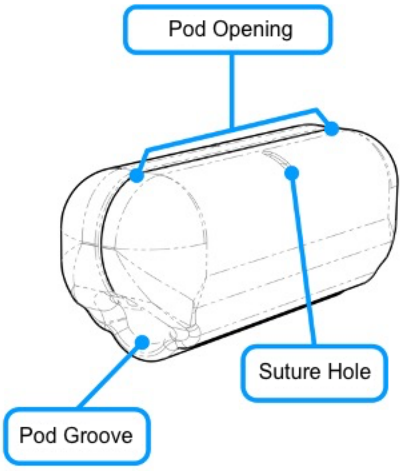

Figure 3 - Pod

The SetPoint System implantable components are supplied sterile, using an ethylene oxide (EO) process, and are only intended for single use. The Implant and two Pods (provided on plastic holders) are packaged in a sealed inner tray covered with an inner lid that prevents them from moving during transit (see Figure 4). The second Pod is provided for use only as a backup if the first Pod is damaged during deployment or while being sutured closed and is identical to the first Pod. The plastic holder is only intended for use during storage and must be discarded before the Pod is implanted. It is not meant for introduction into the surgical field.

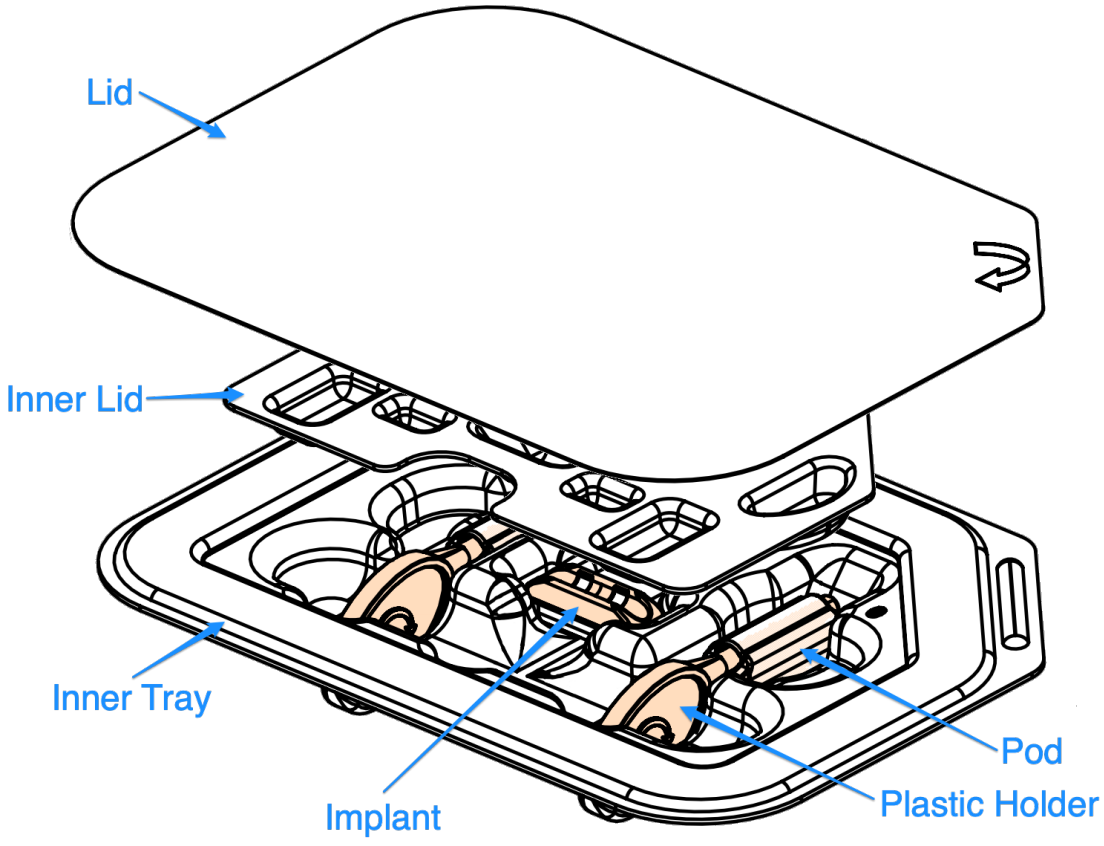

Figure 4 - Inner Tray Contents

The inner tray is packaged in a sealed outer tray, which displays the product labeling. The outer tray rests in a paperboard tray support and is packaged with a Patient ID Card inside a paperboard product box, which also displays the product labeling. This product box is sealed with tamper evident labels. The product box must be stored within the following environmental conditions.

Temperature	Humidity	Altitude
50 to 104 °F (10 to 40 °C)	15 to 93 %RH	Up to 9,843 ft (3,000 m)

Table 2 – Storage Conditions

Charger and Docking Station

The Charger is a device worn around the patient's neck. It is used for charging the Implant at home and for programming the Implant at the clinic. The Docking Station is provided to charge and hold the Charger between uses.

For more information regarding the use of the Charger or Docking Station, please refer to the **SetPoint System Prescriber Instructions for Use** or **SetPoint System Patient Instructions for Use** which are available on the SetPoint Medical website.

Programmer

The Programmer is an app installed on an Apple iPad® that is only used by a trained healthcare professional. It is used with the Charger to program the Implant or to turn off or resume stimulation, if necessary. Additionally, it gives the healthcare professional information about the use of the Implant and Charger, such as how many doses have been delivered or missed, and Implant battery charge levels.

For more information regarding the use of the Programmer, please refer to the **SetPoint System Prescriber Instructions for Use** which is available on the SetPoint Medical website.

Patient Identification (ID) Card

The Patient ID Card is included in the Implant packaging. The Patient ID Card should be filled out per instructions that accompany the card (see Figure 5) and provided to the patient after the surgery, and before they leave the hospital. Device information, such as model number, serial number and device identifier, can be completed using one of four device stickers provided on the outer tray label in the Implant packaging (see Figure 6). Patients should be instructed to always have their Patient ID Card on hand and present it during security screenings, such as at airports. Additionally, the QR code on the card provides access to critical information regarding the implant, which is necessary to ensure that any treatments are compatible with it. Instruct the patient to always present the Patient ID card to healthcare professionals, dentists, or estheticians before pursuing any additional medical, medical imaging or beauty treatments. Neglecting to inform these professionals about the Implant may cause harm to the SetPoint System and/or may lead to complications with the treatment. If the patient changes doctors, or loses their card, they should contact SetPoint Medical for a replacement card.

Figure 5 - Sample Patient ID Card (Front and Back)

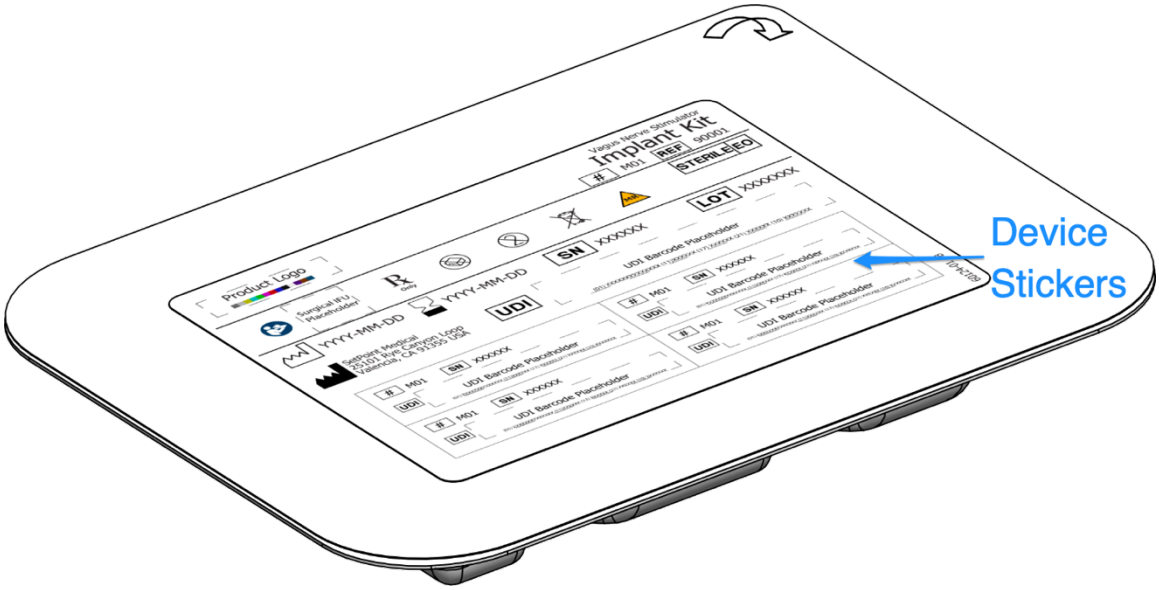

Figure 6 - Device Stickers on Outer Tray Label

Important Safety Information

Read all instructions, warnings and cautions carefully. If you have any questions, contact SetPoint Medical. If you do not follow these guidelines, the SetPoint System could get damaged, not work correctly, and/or result in harm.

Contraindications

There are certain situations in which the SetPoint System should not be used because the risk(s) are greater than the potential benefit(s).

The SetPoint System should not be used:

- If the patient has had certain health procedures that would interfere with how the device works, for example,
  - If they have had surgery to remove the vagus nerve (vagotomy).
  - If they have had their spleen removed (splenectomy).
- If you determine that it might not be safe for them to have the surgery, for example,
  - If they have spine disease in their neck that makes it risky to place a breathing tube (intubate).
  - If they cannot be safely given anesthesia for surgery.
- If they cannot safely use SetPoint Charger, for example,
  - If their neck is too large to wear SetPoint Charger.
  - If they have a pacemaker or a defibrillator implanted.

Warnings & Precautions

It is important that both you and the patient use the SetPoint System safely to avoid injury or damage to the SetPoint System or other devices. Here are some key safety tips:

- Instruct the patient to always present the Patient ID card to healthcare professionals, dentists, or estheticians before pursuing any additional medical, medical imaging or beauty treatments. If they do not, the treatment may cause harm to the SetPoint System and/or may lead to complications with the procedure.
- Instruct the patient not to scuba dive or enter a hyperbaric chamber after receiving the Implant. The safety of high pressure has not been established and these conditions could damage the device.
- Do not use the Implant or Pod if either device shows damage, the packaging shows signs of significant damage, the sterile packaging is breached, the tamper evident label indicates that the package has been opened, or if the product is beyond its expiration date. If you do, you might implant a non-functional device or one with compromised sterility.
- Do not over-manipulate the vagus nerve throughout the surgical procedure. If you do, it may result in adverse effects such as hoarseness or vocal cord paresis.
- Do verify adequate vagus nerve exposure of at least 1.2 in (3 cm) prior to Pod placement. If you do not, it may result in adverse effects such as hoarseness or vocal cord paresis.
- Do verify that the Implant and Pod are placed freely on the vagus nerve with no entrapped branches. If you do not, it may result in adverse effects such as hoarseness or vocal cord paresis.
- Do not re-use the Implant or Pod with another patient. If you do, it will not be sterile.
- Do adhere to local e-waste regulations when disposing of any part of the SetPoint System. If you do not, it can result in environmental contamination with hazardous substances.

Medical Imaging Warnings

There are various types of medical imaging technologies in common use. Although X-rays, computed tomography (CT), ultrasound imaging (sonography), positron emission tomography (PET) are all safe to perform after the patient receives their Implant, it is vital that they always show their Patient ID card to any healthcare professional performing these procedures. Specifically for magnetic resonance imaging (MRI), although they can have scans 2 weeks after implantation, they can only be performed under certain conditions as outlined in **SetPoint System Magnetic Resonance Imaging (MRI) Safety Information Manual**. This is referred to as MR Conditional and must be discussed with your MRI technician.

Figure 7 - MR Conditional

Medical Procedure Warnings

Instruct the patient to use caution with any medical procedure that introduces electrical current, electromagnetic radiation, or thermal energy into tissues in the neck area. The Implant may absorb, intensify, or reflect these energy sources, resulting in localized heating that could damage the device or nearby nerves and vascular structures. This damage may result in pain or discomfort, loss of vocal cord function, or even possibly life-threatening injury if there is damage to blood vessels. Note that these risks are present whether the Implant is active or suspended. It is vital that they always show their Patient ID card to any healthcare professional performing these procedures so that they can carefully evaluate potential interactions and risks. Before proceeding with any procedure that delivers energy to the tissues surrounding the Implant, the healthcare professional should consider alternatives that avoid energy transfer. Specific examples of higher risk procedures around the implantation site that need to be avoided because they could damage the Implant, cause it to malfunction, and/or result in harm including severe injury:

- Shortwave diathermy, microwave diathermy, ultrasound diathermy or other procedures that induce heat in internal tissues. This does not include diagnostic ultrasound which is permitted.
- Electrosurgery/electrocautery, and ablation techniques that utilize any form of electromagnetic radiation or electrical current to cut, coagulate, or thermally destroy tissues. For electrocautery, do not use within 2 cm of the Implant. If using monopolar electrocautery, place the return pad such that the current path is not across the Implant.
- Transcutaneous electrical nerve stimulation (TENS), electroconvulsive therapy or other procedures that apply electrical current through skin surface electrodes.
- Extracorporeal shock wave lithotripsy or other procedures that use pressure waves or induce mechanical forces to break up internal structures.
- Radiation therapy, including forms of photon beam radiation therapy such as x-rays, gamma rays, proton beam therapy, brachytherapy, stereotactic radiosurgery, cobalt machines, and linear accelerators.

Radio Frequency (RF) Warnings

After receiving the implant, the patient should not enter any environment with a posted FCC Notice, Caution or Warning sign indicating the presence of high-intensity radio frequency (RF) fields that surpass normal public exposure limits without seeking medical guidance first. These areas are typically indicated by restricted environment signs like those in Figure 8. Exposure to high levels of RF could cause the Implant to malfunction or lead to tissue damage in the vicinity of the device.

Figure 8 - Restricted Environment Signage

Education, Training, and Services

In addition to the information provided in this Surgeon IFU, supplementary training materials including, but not limited to, a training presentation, surgical videos, and a training model are available and can be provided upon request. Additional training, if requested, can be arranged with your local SetPoint Medical representative.

Surgical Procedures

Surgical procedures for the SetPoint System should be performed by a surgeon with expertise in the surgical anatomy of the carotid sheath, its contents, and its surrounding structures, and with experience in safe dissection and manipulation of these structures and of cranial nerves such as the vagus nerve.

Implantation Location

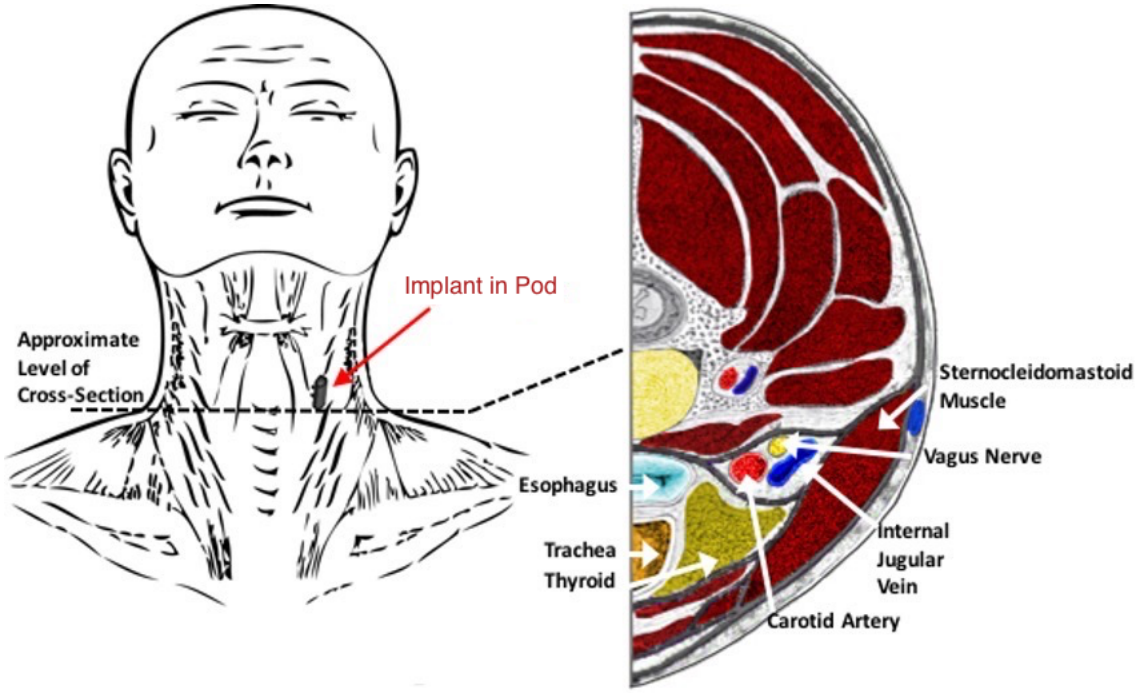

Figure 9 - Implant Location

The Implant must be placed on a segment of the left cervical vagus nerve that is at least 1.2 in (3 cm) long and free from any branches. A suitable segment is typically half-way up between the clavicle and the mastoid process and below both the inferior and superior cervical cardiac branches.

Ideal placement for the Implant to optimize communication with the Charger is between the level of the C4 and C6 cervical vertebrae. The Implant should never be placed below the level of the C7 cervical vertebra. An example placement is illustrated in Figure 10.

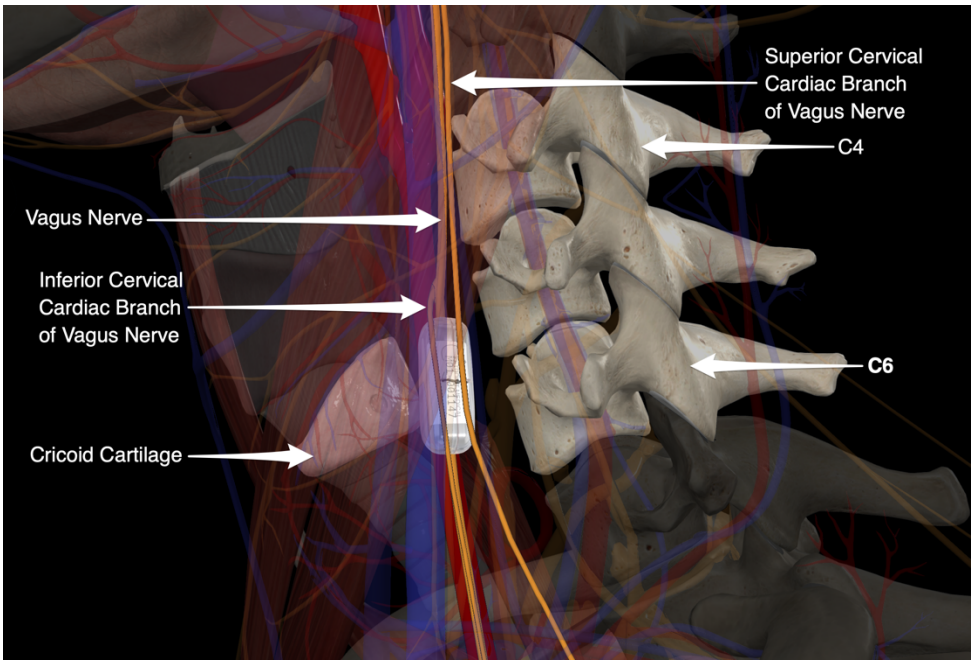

Figure 10 - Relationship Between Implant Implantation Location and Vagus Nerve Branches

Charger Fit Confirmation

To confirm fit of the Charger prior to the implantation procedure, it is recommended that the following steps be performed:

1. Prior to the implant procedure, either place the Charger, or instruct the patient to place the Charger around their neck while they are seated upright.
2. Verify that the magnetic latch closes and remains latched without discomfort.
3. Remove the Charger or instruct the patient to remove the Charger.

Implant Preparation

⚠ **Warning:** Do not use the Implant or Pod if either device shows damage, the packaging shows signs of significant damage, the sterile packaging is breached, the tamper evident label indicates that the package has been opened, or if the product is beyond its expiration date. If you do, you might implant a non-functional device or one with compromised sterility.

1. Carefully open the product box and remove the outer tray. Set aside the Patient ID Card to fill out after the surgery is complete.
2. The outer tray should be opened by pulling the tab on the lid as shown in Figure 11. Set aside the outer tray lid and label with the device stickers on it (see Figure 6 on page 9), to adhere to the Patient ID Card.

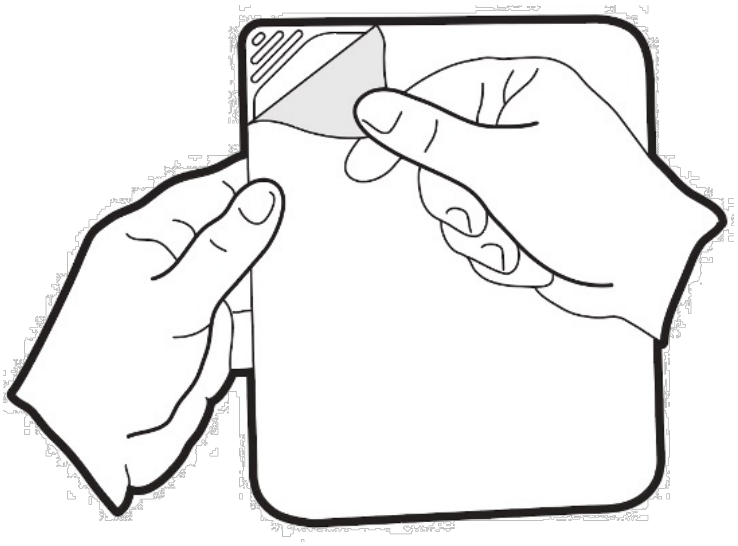

Figure 11 - Opening Tray by Pulling Tab

3. Present the outer tray so that the inner tray can be removed in the sterile field.
4. The inner tray should be opened by pulling the tab on the lid as shown in Figure 11.
5. Remove the inner lid and discard (see Figure 4 on page 7).
6. Place the inner tray on the surgical tray or other sterile surface in the sterile field.
7. If at any point during the surgical procedure the Implant is dropped from a height of over 6 in (15 cm), discard the Implant and utilize the backup.

Implantation

⚠ **Warning:** Do not over-manipulate the vagus nerve throughout the surgical procedure. If you do, it may result in adverse effects such as hoarseness or vocal cord paresis.

Using standard surgical techniques, make a single transverse incision on the left ventral surface of the neck, dissect the fascia and musculature to expose the carotid sheath, and identify the vagus nerve. Then:

1. Locate and expose a segment of the left vagus nerve that is free of branches by circumferentially dissecting the surrounding tissue.

⚠ **Warning:** Do verify adequate vagus nerve exposure of at least 1.2 in (3 cm) prior to Pod placement. If you do not, it may result in adverse effects such as hoarseness or vocal cord paresis.

2. Confirm with a surgical ruler that at least 1.2 in (3 cm) of nerve segment has been exposed to allow for manipulation and insertion of the Pod.
3. If using vessel loops, place under the nerve utilizing standard surgical techniques.
4. Remove a Pod from its plastic holder and discard the plastic holder (see Figure 4 on page 7).
5. The following are recommended techniques for Pod deployment to accommodate anatomical variations.
    a. Flat Method:
        i. Hold the Pod open facing upwards (see Figure 12a) and use forceps to clamp it in the open position along its midline (see Figure 12b).
        ii. Insert the Pod under the nerve (see Figure 12c) and align it such that the nerve is positioned at the Pod groove (see Figure 3 on page 7 and Figure 12d).

iii. Slowly release the forceps, allowing the Pod to return to its original shape (see Figure 12e), closing around the nerve (see Figure 12f). If needed, use forceps to gently maneuver the Pod so that nerve is resting in the Pod groove and the Pod opening is facing upwards.

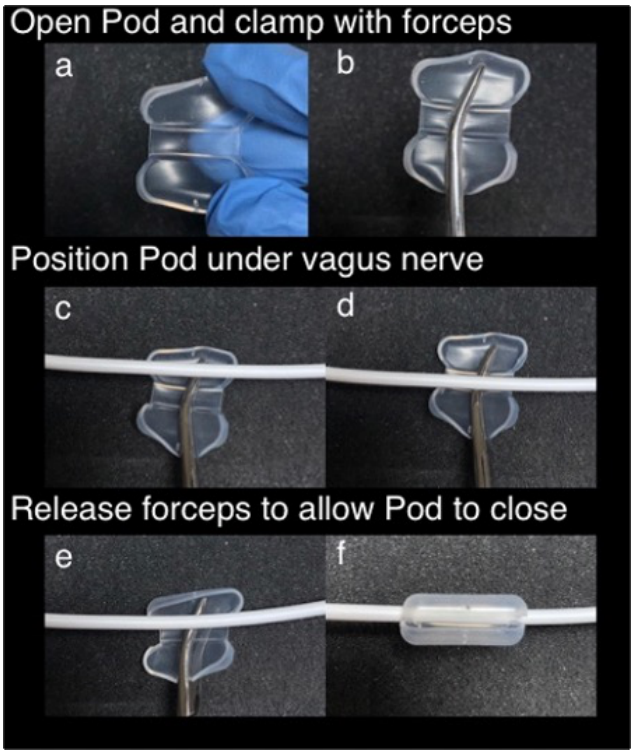

Figure 12 - Pod Implantation: Flat Method

b. Fold Method:
   i. Hold the Pod open facing downwards by pressing on both sides (see Figure 13a).
   ii. Fold the Pod off axis (see Figure 13b) and use curved forceps to clamp the Pod perpendicular to the Pod groove (see Figure 3 on page 7 and Figure 13c). Turn the forceps so that the Pod opening is facing upwards (see Figure 13d).
   iii. Introduce the Pod under the vagus nerve, gently rotating the forceps by approximately 90 degrees to minimize touching the nerve.
   iv. Once the mid-line is positioned under the nerve, rotate the Pod so that the opening is facing upwards (see Figure 13e).
   v. Slowly release the forceps, allowing the Pod to return to its original shape (see Figure 13f and Figure 13g), closing around the nerve (see Figure 13h). If needed, use forceps to gently maneuver the Pod so that nerve is resting in the Pod groove and the Pod opening is facing upwards.

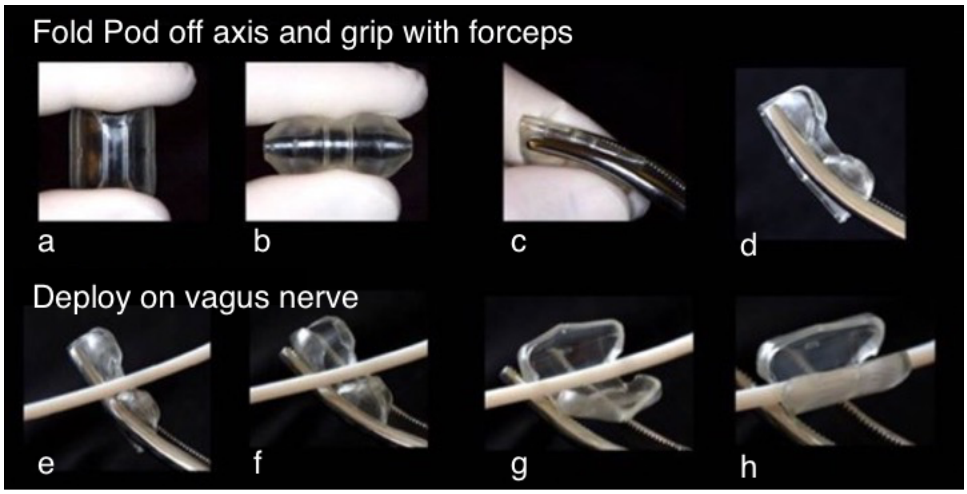

Figure 13 - Pod implantation: Fold Method

6. Insert the Implant into the Pod, (see Figure 15a-d) with the head-shaped marking on the Implant oriented rostrally (see Figure 14).

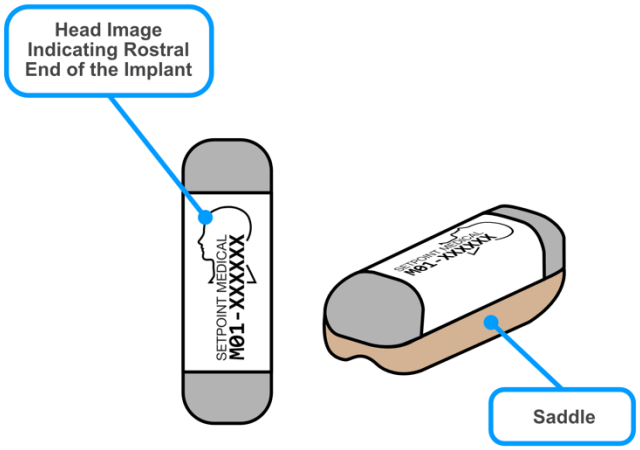

Figure 14 - Head-shaped Marking Indicating Rostral End of the Implant

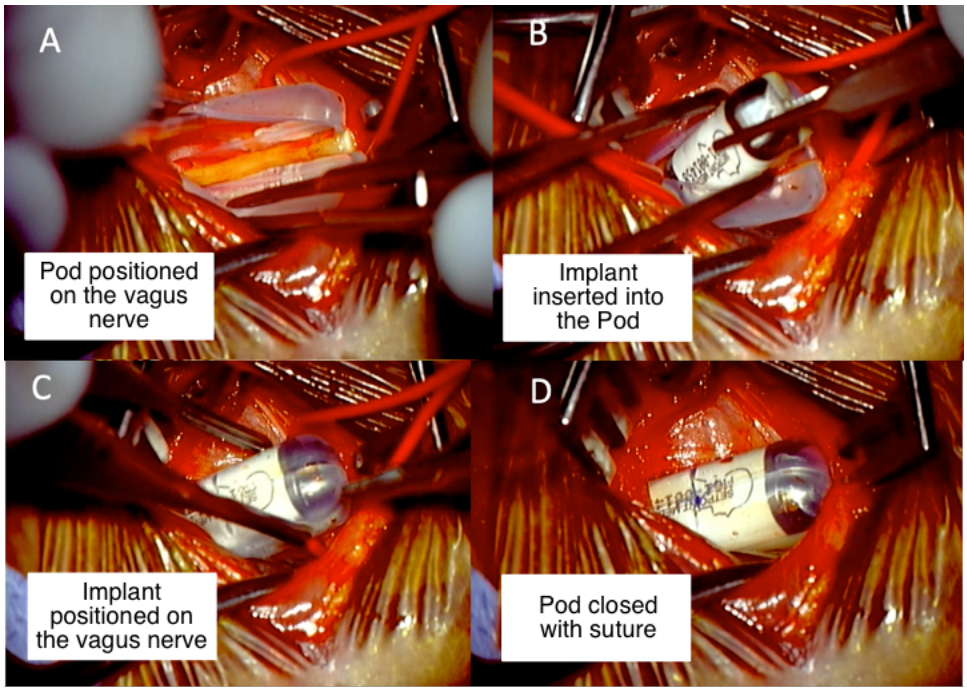

Figure 15 - Pod and Implant Implantation Method

7. Close the Pod around the Implant.
8. While minimizing Pod movement, suture the Pod closed through the suture hole in the Pod (see Figure 16) with a non-absorbable 5-0 Prolene suture on a non-cutting needle. Limit the number of throws in the knot to a maximum of four to avoid excessively pulling on the device or nerve.

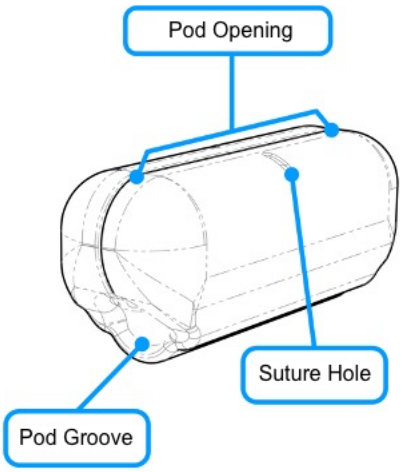

Figure 16 - Pod Suture Hole

⚠ **Warning:** Do verify that the Implant and Pod are placed freely on the vagus nerve with no entrapped branches. If you do not, it may result in adverse effects such as hoarseness or vocal cord paresis.

9. Visualize that the nerve is seated through the ends of the groove of the closed Pod and is in the Implant saddle. Ensure that there are no extra nerve branches or other structures entrapped in the Pod.

10. Verify the closed Pod does not constrict the nerve or vascular tissue by using either a gentle sliding movement of the Pod on the nerve or a slight rotation of the Pod.

Using standard surgical techniques, close the musculature, fascia and skin. Frequent irrigation of the implantation site with generous amounts of bacitracin or equivalent solution can be performed prior to closure for infection control. To minimize scarring, the incision should be closed with cosmetic closure techniques.

Fill out the Patient ID Card and adhere one of the device stickers (see Figure 17) onto the correct location on the card (see Figure 18). The filled-out card should be provided to the patient after surgery.

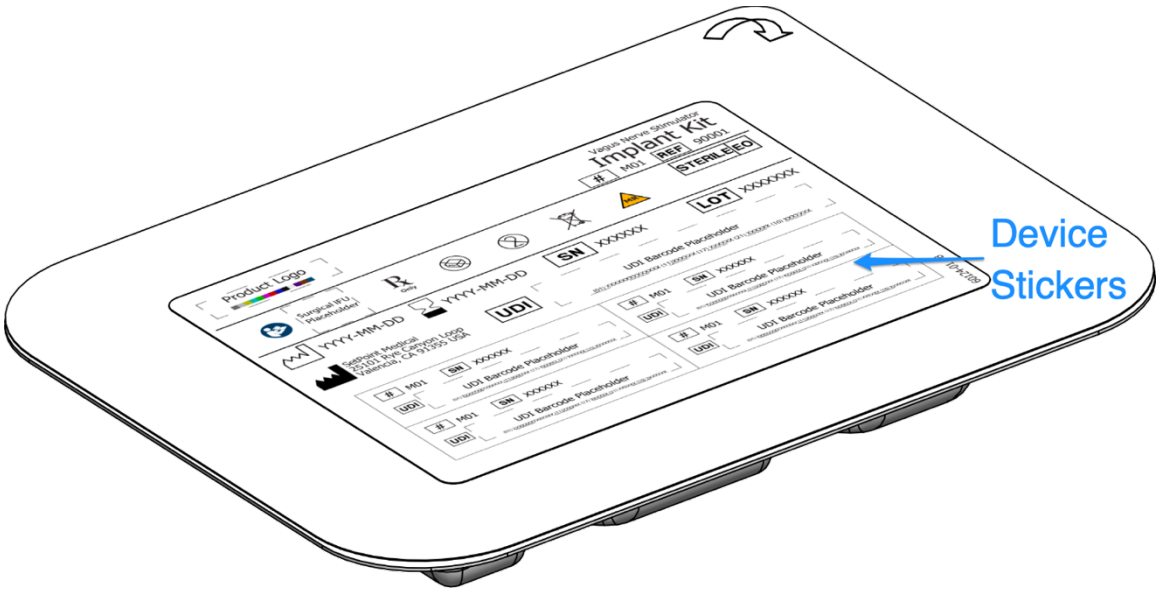

Figure 17 - Device Stickers on Outer Tray Label

Figure 18 - Sample Patient ID Card (Front and Back)

Explantation and Reimplantation

The adverse events associated with explantation or reimplantation are similar to those associated with implantation, but the risk of occurrence of such events is likely to be greater because the presence of scarring around the chronically implanted device makes removal more difficult. If Implant removal is contemplated, SetPoint Medical should be notified prior to explantation or reimplantation surgery.

Therapy programming on the Implant should be suspended, if possible, prior to surgery.

⚠ **Warning:** Do not over-manipulate the vagus nerve throughout the surgical procedure. If you do, it may result in adverse effects such as hoarseness or vocal cord paresis.

If performing a reimplantation, prepare the new Implant as per instructions in section **Implant Preparation**. Using standard surgical techniques, make a single transverse incision on the left ventral surface of the neck, dissect the fascia and musculature to expose the carotid sheath. Then:

1. Expose the Implant in the Pod by incising any tissue capsule surrounding it along the Pod opening (see Figure 16 on page 18) with the suture visible.
2. Cut the suture and open the Pod.
3. Remove the Implant from the Pod.
4. If performing an explantation, cut the Pod in halves by cutting parallel to the groove in the Pod (see Figure 16 on page 18) and then remove the halves.
5. If performing a reimplantation, inspect the Pod for damage, specifically the integrity of the suture holes.
    - If the Pod is undamaged, leave it in place, place the new Implant by following steps 6-10 in the **Implantation** section (page 15)
    - If the Pod is damaged, cut the Pod in halves by cutting parallel to the groove in the Pod (see Figure 16 on page 18) and then remove the halves. Place the new Pod and Implant by following steps 3-10 in the **Implantation** section (page 15).

Using standard surgical techniques, close the musculature, fascia and skin. Frequent irrigation of the incision site with generous amounts of bacitracin or equivalent solution can be performed prior to closure for infection control. To minimize scarring, the incision should be closed with cosmetic closure techniques.

The old Patient ID Card should be retrieved and discarded. If performing a reimplantation, fill out the new Patient ID Card and adhere one of the device stickers (see Figure 17) from the new Implant onto the correct location on the card (see Figure 18). The new, filled-out card should be provided to the patient after surgery.

⚠ **Warning:** Do not re-use the Implant or Pod with another patient. If you do, it will not be sterile.

⚠ **Warning:** Do adhere to local e-waste regulations when disposing of any part of the SetPoint System. If you do not, it can result in environmental contamination with hazardous substances.

Contact SetPoint Medical to request a return merchandise authorization (RMA) for the explanted Implant and Pod, if removed.

Appendix A – Explanation of Symbols Used on Packaging and Devices

Symbol	Title	Reference	Description
21 CFR 801.109: Prescription Devices			
	Prescription Only	(b) (1)	Caution: Federal law restricts this device to sale by or on the order of a physician
ASTM F2503			
	Magnetic Resonance (MR) Conditional	Fig. 5	An item with demonstrated safety in the MR environment within defined conditions including conditions for the static magnetic field, the time-varying gradient magnetic fields and the radiofrequency fields
	Magnetic Resonance (MR) Unsafe	Fig. 9	An item which poses unacceptable risks to the patient, medical staff or other persons within the MR environment
WEEE Directive 2012/19/EU			
	Symbol for the marking of EEE	Annex IX	Separate collection for electrical and electronic equipment
IEC 60417			
	Non-ionizing Electromagnetic Radiation	5140	To indicate elevated, potentially dangerous, levels of non-ionizing radiation
	For Indoor Use Only	5957	To identify electrical equipment designed primarily for indoor use
IEC 60529			
IP22	Degree of Protection	N/A	Protected against solid foreign objects of 0.5 in (12.5 mm) Ø and greater; Protection against vertically falling water drops when enclosure is tilted up to 15°.
ISO 15223-1: 5.1. Manufacture			
	Manufacturer	5.1.1	Indicates the medical device manufacturer
	Date of Manufacture	5.1.3	Indicates the date when the medical device was manufactured
	Use-By Date	5.1.4	Indicates the date after which the medical device is not to be used
	Batch Code	5.1.5	Indicates the manufacturer's batch code so that the batch or lot can be identified
	Catalog Number	5.1.6	Indicates the manufacturer's catalog number so that the medical device can be identified
	Serial Number	5.1.7	Indicates the manufacturer's serial number so that a specific medical device can be identified

	Model Number	5.1.10	Indicates the model number or type number of a product
ISO 15223-1: 5.2. Sterility			
	Sterilized Using Ethylene Oxide	5.2.3	Indicates a medical device that has been sterilized using ethylene oxide
	Do Not Use If Package Is Damaged and Consult Instructions for Use	5.2.8	Indicates that a medical device that should not be used if the package has been damaged or opened and that the user should consult the instructions for use for additional information
ISO 15223-1: 5.3. Storage			
	Temperature Limit	5.3.7	Indicates the temperature limits to which the medical device can be safely exposed
	Humidity Limitation	5.3.8	Indicates the range of humidity to which the medical device can be safely exposed
	Atmospheric Pressure Limitation	5.3.9	Indicates the range of atmospheric pressure to which the medical device can be safely exposed
ISO 15223-1: 5.4. Safe Use			
	Do Not Re-Use	5.4.2	Indicates a medical device that is intended for one single use only
ISO 15223-1: 5.7. Others			
	Unique Device Identifier	5.7.10	Indicates a carrier that contains unique device identifier information
ISO 7010			
	Refer to Instruction manual/booklet	M002	To signify that the instruction manual/booklet must be read
	General Warning Sign	W001	To signify a general warning

Applicable Standards and Regulations

21 CFR 801 Medical Devices – Labeling

ASTM F2503 – 23 Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment

Directive 2012/19/EU of the European Parliament and of the Council of 4 July 2012 on waste electrical and electronic equipment (WEEE)

IEC 60417:2024 Graphical Symbols for use on Equipment

IEC 60529:1989/AMS2:2013/COR1:2019 Degrees of protection provided by enclosures (IP Code)

ISO 15223-1:2021 Medical devices – Symbols to be used with information to be supplied by the manufacturer – Part 1: General requirements

ISO 7010:2019 Graphical symbols – Safety colors and safety signs – Registered safety signs

Appendix B – Clinical Studies Safety

Adverse Events

Adverse events are side effects, complications, or discomforts related to a procedure or treatment. This Appendix describes adverse events associated with the SetPoint system that may occur during the surgery to insert or remove the Implant or associated with stimulating the vagus nerve (referred to as vagus nerve stimulation or VNS)

Clinical Studies

The SetPoint System has been evaluated in two U.S. clinical studies enrolling 257 patients (the pilot study enrolled 15 patients and RESET-RA enrolled 242 patients). Adverse events reported by the study doctor as related to either the surgery or stimulation associated with the SetPoint System are summarized below.

At the time of FDA review for the SetPoint System, patients on average had been living with the Implant and receiving stimulation for longer than 1 year, with some patients, those enrolled in the pilot study, receiving treatment for over 5 years.

Nearly all adverse events reported during the clinical studies were mild to moderate in severity, and nearly all adverse events were considered non-serious by the study doctor (98% non-serious). No patients during the study experienced a life-threatening complication related to the SetPoint System, and no deaths were reported for any cause. During the clinical studies, no new safety issues were identified.

Surgery (Insertion of the Implant)

- Symptoms at incision site (such as pain, redness, swelling, numbness, rash, and tingling) occurred in about 6 out of 100 patients (about 6%).
- Vocal cord paresis (impaired motion of the vocal cord) occurred in about 5 out of 100 patients (about 5%). It was typically experienced as mild to moderate hoarseness, but it also included difficulty breathing or difficulty swallowing in two cases. Some patients elected to have additional treatment with speech therapy or injections of bulk fillers to the vocal cords.
- Hoarseness occurred in about 3 out of 100 patients (about 3%).
- Eye symptoms (eyelid swelling or drooping of upper eyelid) occurred in about 1 out of 100 patients (about 1%).
- Difficulty swallowing occurred in about 1 out of 100 patients (about 1%).

The following occurred in less than 1 out of 100 patients (less than 1%), all were non-serious:

- Headache or migraine
- Wound infection
- Complication with suture
- Cough
- Sore throat
- Difficulty breathing
- Diarrhea
- Rash
- Scar pain
- Inflammation and blood clot at intravenous (IV) site

Stimulation Therapy

Stimulation therapy was well-tolerated by patients. When patients reported symptoms considered related to stimulation, the symptoms either self-resolved over time or resolved with an adjustment to the strength of stimulation. The most common complaint was mild to moderate pain or discomfort related to stimulation, occurring in about 3 out of 100 patients (about 3%). Other symptoms, occurring in less than 1 out of 100 patients (less than 1%), are listed below.

- Toothache
- Retching
- Nausea
- Metallic taste
- Choking sensation
- Cough
- Sore throat
- Near fainting
- Poor quality sleep
- Spasm near device
- Jaw pain (TMJ)

Charger

One patient reported a rash after wearing the Charger.

Surgery (Removal of the Implant)

In one patient, the larynx (voice box) was accidentally injured. It was successfully repaired during the surgery and did not require hospitalization. Antibiotics and a drainage tube in the neck were required until the injury healed.