VNS Therapy® System Depression Physician's Manual

Pulse™ Generator—Model 102
Pulse Duo™ Generator—Model 102R
Demipulse® Generator—Model 103
Demipulse Duo® Generator—Model 104
AspireHC® Generator—Model 105
AspireSR® Generator—Model 106
SenTiva® Generator—Model 1000
SenTiva DUO™ Generator—Model 1000-D
Symmetry™ Generator—Model 8103

Lead—Model 302
PerenniaFLEX® Lead—Model 304
PerenniaDURA® Lead—Model 303

For Healthcare Professionals

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- 304 - 2009

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For a list of symbols and glossary terms used with the VNS Therapy System, go to www.livanova.com.

1.1 Brief Device Description

1.1.1 The VNS Therapy System

The LivaNova® VNS Therapy® System, used for vagus nerve stimulation (VNS), consists of the implantable VNS Therapy generator, lead, and external programming system used to change stimulation settings. The generator is an implantable, multiprogrammable pulse generator that delivers electrical signals to the vagus nerve. The generator is housed in a hermetically sealed titanium case and is powered by a single battery. Electrical signals are transmitted from the generator to the vagus nerve by the lead. The lead and the generator make up the implantable portion of the VNS Therapy System.

The VNS Therapy Programming System includes a computer pre-installed with VNS Therapy programming software and a programming wand. The physician uses the programming system to read and change generator settings.

1.2 Intended Use / Indications

The VNS Therapy System is indicated for the treatment of chronic or recurrent depression in patients that are in a treatment-resistant or treatment-intolerant major depressive episode.

1.3 Contraindications

- **Vagotomy —** The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy.
- **Diathermy —** Do not use shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (hereafter referred to as diathermy) on patients implanted with a VNS Therapy System. Diagnostic ultrasound is not included in this contraindication. Energy delivered by diathermy may be concentrated into or reflected by implanted products such as the VNS Therapy System. This concentration or reflection of energy may cause heating.

  Testing indicates that diathermy can cause heating of the VNS Therapy System well above temperatures required for tissue destruction. The heating of the VNS Therapy System resulting from diathermy can cause temporary or permanent nerve, tissue, or vascular damage. This damage may result in pain or discomfort, loss of vocal cord function, or even possibly death if there is damage to blood vessels.

  Because diathermy can concentrate or reflect its energy off any size implanted object, the hazard of heating is possible when any portion of the VNS Therapy System remains implanted, including just a small portion of the lead or electrode. Injury or damage can occur during diathermy treatment whether the VNS Therapy System is turned “ON” or “OFF.”

Diathermy is further prohibited because it may also damage the VNS Therapy System components resulting in loss of therapy, requiring additional surgery for system explantation and replacement. All risks associated with surgery or loss of therapy would then be applicable.

Advise your patients to inform all their healthcare professionals that they should not be exposed to diathermy treatment.

1.4 Warnings

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System physician's manuals.

1.4.1 All Devices

- **Use —** This device is a permanent implant. It is only to be used in patients with severe depression who are unresponsive to standard psychiatric management. It should only be prescribed and monitored by physicians who have specific training and expertise in the management of treatment-resistant depression and the use of this device. It should only be implanted by physicians who are trained in surgery of the carotid sheath and have received specific training in the implantation of this device.
- **Not curative —** Physicians should warn patients that VNS Therapy has not been determined to be a cure for depression. Patients should be counseled to understand that individual results will likely vary. Beneficial results might not become evident for months. Most patients will continue to require antidepressant medications and/or electroconvulsive therapy (ECT) in addition to VNS Therapy.
- **Worsening depression/suicidality —** Patients being treated with adjunctive VNS Therapy should be observed closely for clinical worsening and suicidality, especially at the time of VNS Therapy stimulation parameter changes or drug or drug dose changes, including either increases or decreases in the stimulation parameters or concomitant treatments. Consideration should be given to changing the therapeutic regimen of VNS Therapy or concomitant treatments, including possibly discontinuing VNS Therapy or the concomitant therapy, in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of the patient's presenting symptoms.
- **Unapproved uses —** The safety and efficacy of the VNS Therapy System have not been established for uses outside the "Intended Use / Indications" section, including (but not limited to) patients with:
    - Acute suicidal thinking or behavior
    - Cardiac arrhythmias or other abnormalities
    - History of schizophrenia, schizoaffective disorder or delusional disorders
    - History of rapid cycling bipolar disorder
    - History of previous therapeutic brain surgery or CNS injury
    - History of dysautonomias
    - History of respiratory diseases or disorders, including dyspnea and asthma

- History of ulcers (gastric, duodenal, or other)
- History of vasovagal syncope
- Only one vagus nerve
- Other concurrent forms of brain stimulation
- Pre-existing hoarseness
- Progressive neurological diseases other than depression

- **Dysfunctional cardiac conduction systems —** The safety and effectiveness of the VNS Therapy System in patients with predisposed dysfunction of cardiac conduction systems (re-entry pathway) have not been established. Evaluation by a cardiologist is recommended if the family history, patient history, or electrocardiogram suggests an abnormal cardiac conduction pathway. Serum electrolytes, magnesium, and calcium should be documented before implantation. Additionally, postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. Post-implant electrocardiograms and Holter monitoring are recommended if clinically indicated.
- **Bradycardia or asystole during implantation —** It is important to follow recommended implantation procedures and intraoperative product testing described in the *Implantation Procedure* chapter. During the intraoperative System Diagnostics (Lead Test), infrequent incidents of bradycardia and/or asystole have occurred. If asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate is encountered during a System Diagnostics (Lead Test) or during initiation of stimulation, physicians should be prepared to follow guidelines consistent with Advanced Cardiac Life Support (ACLS).

  Additionally, postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. If a patient has experienced asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate during a System Diagnostics (Lead Test) at the time of initial device implantation, the patient should be placed on a cardiac monitor during initiation of stimulation.

  The safety of this therapy has not been systematically established for patients experiencing bradycardia or asystole during VNS Therapy System implantation.
- **External defibrillation or cardioversion (electrical) —** These procedures may damage the generator, and can temporarily or permanently damage the nerve. Attempt to minimize current flowing through the generator and lead system by following these recommendations:
  - Position defibrillation patches or paddles perpendicular to the generator and lead system, and as far from the generator as possible.
  - Use the lowest clinically appropriate energy output (watt-seconds).
  - Confirm generator function after any internal or external defibrillation, or cardioversion treatment.
- 

Magnetic resonance imaging (MRI) — Patients with the VNS Therapy System, or any part of the VNS Therapy System, implanted should have MRI procedures performed **only as described in the *MRI with the VNS Therapy System* instructions for use.** In

some cases, surgery will be required to remove the VNS Therapy System if a scan using a transmit RF body coil is needed.

- **Excessive stimulation —** Excessive stimulation is the combination of an excess duty cycle (i.e. one that occurs when ON time is greater than OFF time) and high frequency stimulation (i.e. stimulation at ≥ 50 Hz). Excessive stimulation has resulted in degenerative nerve damage in laboratory animals. While LivaNova limits the maximum programmable frequency to 30 Hz, it is recommended that you do not stimulate with excess duty cycle.
- **Device manipulation —** Patients who manipulate the generator and lead through the skin (Twiddler's Syndrome) may damage or disconnect the lead from the generator and/or possibly cause damage to the vagus nerve. Patients, parents, and caregivers should be warned against manipulating the generator and lead.
- **Swallowing difficulties —** Difficulty swallowing (dysphagia) may occur with active stimulation, and aspiration may result from the increased swallowing difficulties. Patients with pre-existing swallowing difficulties and those with a history of drooling or hypersalivation are at greater risk for aspiration. Appropriate aspiration precautions should be taken for such patients. Use of the magnet to temporarily stop stimulation while eating may mitigate the risk of aspiration.
- **Dyspnea or shortness of breath —** Dyspnea (shortness of breath) may occur with active VNS Therapy. Any patient with underlying pulmonary disease or insufficiency, such as chronic obstructive pulmonary disease or asthma, may be at increased risk for dyspnea and should have their respiratory status evaluated prior to implantation and monitored following initiation of stimulation.
- **Obstructive sleep apnea —** Patients with obstructive sleep apnea (OSA) may have an increase in apneic events during stimulation. Lowering stimulus frequency or prolonging "OFF" time may prevent exacerbation of OSA. Vagus nerve stimulation may also cause new onset sleep apnea in patients who have not previously been diagnosed with this disorder. It is recommended that patients being considered for VNS Therapy who demonstrate signs or symptoms of OSA, or who are at increased risk for developing OSA, should undergo the appropriate evaluation(s) prior to implantation.
- **Device malfunction —** Device malfunction could cause painful stimulation or direct current stimulation. Either event could cause nerve damage and other associated problems. Patients should be instructed to use the magnet to stop stimulation if they suspect a malfunction, and then to contact their physician immediately for further evaluation. Prompt surgical intervention may be required if a malfunction occurs.

1.4.2 Model 1000 (Serial Numbers <100,000 Only)

Some Model 1000 generators (serial numbers <100,000) report higher impedance values compared to prior models (Models 103-106), due to a change in the timing of the impedance measurement during the diagnostic test pulse. This timing difference will not impact the battery longevity or the ability to safely deliver therapy. However, it may result in an erroneous high impedance warning:

- **Potential erroneous high impedance warning during implantation surgery** — Erroneous high impedance is more likely for replacement generator surgeries compared to new implants due to fibrosis of the lead. Follow troubleshooting steps in

the programming system physician's manuals to resolve common sources of true high impedance (confirm: lead pin insertion, setscrew tension, electrode placement on the nerve, irrigation of the nerve, and generator diagnostics indicative of normal function). If high lead impedance (≥ 5300 Ohms) is still reported, consider lead or generator replacement.

- **Potential erroneous high impedance warning at follow-up or titration visit** — If high lead impedance is observed (≥ 5300 Ohms,) perform a chest and neck x-ray (anteroposterior and lateral views) and contact Technical Support. Surgery is warranted if improper lead pin insertion or lead break is present in the x-ray. For implanted Model 1000 (serial numbers <100,000), advise patients to use the magnet daily to verify that stimulation is felt and report any change in perceived clinical symptoms related to stimulation (e.g., increase in depressive symptoms, painful stimulation, changes in perception of stimulation). In the absence of device-related complications (e.g. magnet stimulation is perceived and there are no changes in clinical symptoms), higher than expected lead impedance is not an indication of generator or lead malfunction. Continue to perform system diagnostics at each visit to monitor for further increases in impedance.

1.5 Precautions

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System physician's manuals.

1.5.1 All Devices

- Unless otherwise specified, all indications, contraindications, and possible complications and adverse events are applicable to all implantable parts of the VNS Therapy System. Possible adverse events specifically related to the lead include migration, dislodgement, breakage, and corrosion.
- **Physician training —** Appropriate physician training is very important.
  - **Prescribing physicians** should be experienced in the diagnosis and treatment of depression and should be familiar with the programming and use of the VNS Therapy System.
  - **Physicians who implant the VNS Therapy System** should be experienced performing surgery in the carotid sheath and should be trained in the surgical technique relating to implantation of the VNS Therapy System.

  Note: See "Physician Training/Information" in the *Implantation Procedure* chapter.
- **Use during pregnancy —** The safety and effectiveness of the VNS Therapy System have not been established for use during pregnancy. There are no adequate and well-controlled studies of VNS Therapy in pregnant women. Reproduction studies have been performed using female rabbits stimulated with the commercially available VNS Therapy System at stimulation dose settings similar to those used for humans. These animal studies have revealed no evidence of impaired fertility or harm to the fetus due to VNS Therapy. Because animal reproduction studies are not always predictive of human response and animal studies cannot address developmental abnormalities, VNS Therapy should be used during pregnancy only if clearly needed. Although the

operating ranges of the VNS Therapy System and fetal monitors are dissimilar and no interaction would be expected, testing has not been performed. Therefore, the potential may exist for interaction between the VNS Therapy System and fetal monitoring systems.

- **Vagus nerve placement —** The VNS Therapy System is indicated for use only in stimulating the left vagus nerve in the neck area inside the carotid sheath. The VNS Therapy System is indicated for use only in stimulating the **left vagus nerve below where the superior and inferior cervical cardiac branches separate from the vagus nerve.** The safety and efficacy of the VNS Therapy System have not been established for stimulation of the right vagus nerve or of any other nerve, muscle, or tissue.
- **Effects on other medical devices —** The VNS Therapy System may affect the operation of other implanted devices, such as cardiac pacemakers and implanted defibrillators. Possible effects include sensing problems and inappropriate device responses. If the patient requires concurrent implantable pacemaker, defibrillator therapy, or other types of stimulators, careful programming of each system may be necessary to optimize the patient's benefit from each device. Furthermore, when the VNS Therapy System and another stimulator are implanted in the same patient, the two stimulators should be placed at least 10 centimeters (4 inches) apart to avoid communication interference. Users should refer to the product labeling for the concurrent device to determine if there are additional precautions that should be observed.
- **Infection control —** It is important to follow infection control procedures. Infections related to any implanted device are difficult to treat and may require that the device be explanted. The patient should be given antibiotics preoperatively. The surgeon should ensure that all instruments are sterile prior to the operation. Frequent irrigation of both incision sites with generous amounts of bacitracin or equivalent solution should be performed prior to closure. To minimize scarring, these incisions should be closed with cosmetic closure techniques. Also, antibiotics should be administered postoperatively at the discretion of the physician. Careful monitoring for site infection as well as the avoidance of manipulation of the surgical site post implant should be stressed.
- **Reversal of lead polarity —** Reversal of lead polarity has been associated with an increased chance of bradycardia in animal studies. It is important that the electrodes are attached to the left vagus nerve in the correct orientation. It is also important to make sure that leads with dual connector pins are correctly inserted (white marker band/serial number to + connection) into the generator's lead receptacle(s).
- **Lead stabilization —** The patient can use a neck brace for the first week to help ensure proper lead stabilization.
- **Programming after surgery —** Do not program the VNS Therapy System to an ON or periodic stimulation treatment for at least 14 days after the initial or replacement implantation. Failure to observe this precaution may result in patient discomfort or adverse events.

- **Vagus nerve damage — Some complications** may be associated with damage to the vagus nerve.
  - Hoarseness may be caused by device malfunction, nerve constriction, or nerve fatigue. Nerve constriction should be apparent within a few days after implantation and may require explantation of the lead. Nerve fatigue usually occurs after intense stimulation parameters have been used, and might not be associated with any other adverse event. If fatigue is suspected, the generator should be turned off for several days until hoarseness subsides.
  - Persistent hoarseness *not* associated with stimulation suggests possible nerve irritation and should be immediately investigated.
  - Trauma to the vagus nerve at the implantation site could result in permanent vocal cord dysfunction.
- **Device Reset —** A reset of the device will program the device OFF (output current = 0 mA).
- **Laryngeal irritation —** Laryngeal irritation may result from stimulation. Patients who smoke may have an increased risk of laryngeal irritation.

1.5.2 Model 100 - 102R Only

- **Battery depletion —** For Model 100, 101, 102, and 102R generators, do not use frequencies of 5 Hz or below for long-term stimulation, because these frequencies generate an electromagnetic trigger signal, which results in excessive battery depletion of the implanted generator. Therefore, use these low frequencies for short periods of time only.
- **Device history loss —** For Model 100, 101, 102, and 102R generators, a reset of the device causes all device history information to be lost. The device history information (e.g., programmed patient initials, implant date, device serial number) should be documented before resetting.

1.5.3 Model 103 and Higher

- **Device reset —** When a Model 103 or subsequent model generator is reset, its stimulation output is disabled (0 mA); however, all settings and device history are preserved. After a successful reset, the generator stimulation output may be re-enabled to resume operation at the previously programmed settings.

1.5.4 Model 1000/1000-D Only

- **Day-Night Programming —** When using the optional Day-Night programming feature:
  - Consider risk and benefits of altering a patient's known efficacious settings before this feature is used or when parameter adjustments are made.
  - Inform your patients about when to expect a setting change (i.e., when Daytime settings transition into Nighttime settings).
  - Assess patient tolerability of the alternate parameter set before the patient leaves the office visit.

- **Time-based Features —** Day-Night Programming does not automatically adjust for Day Light Savings or time zone changes. Tell the patient to follow-up with the physician for reprogramming, if needed.

1.5.5 Lead Evaluation and Connection

- **Do not use a lead other than a VNS Therapy lead —** Use a VNS Therapy dual-pin lead with the dual-receptacle generator or a VNS Therapy single-pin lead with the single-receptacle generator because use of other leads may damage the generator or injure the patient.
- **Lead size —**The lead is available in multiple sizes. Since it is not possible to predict in patients what size lead will be needed, **it is recommended that at least one alternate lead size be available in the operating room**. In addition, backups for leads should be available in the event of compromised sterility or damage induced during surgery.

  Note: For lead size availability, see "Lead Physical Characteristics" in the lead Technical Information chapters.

- **Potential effects of lead breaks —** Lead fractures of the VNS Therapy System may prevent patients from receiving therapy. If a lead fracture is suspected, perform diagnostic testing to evaluate continuity within the system. If diagnostics suggest that a fracture is present, consider turning the generator to zero milliamps (0 mA) of output current. Continuing stimulation with a fractured lead may result in dissolution of the conductor material resulting in adverse events, such as pain, inflammation, and vocal cord dysfunction. The benefits and risks of leaving the generator ON (actively stimulating) when a lead fracture is present should be evaluated and monitored by the medical professional treating the patient.

  Note: For more information on diagnostic testing, see "Troubleshooting" in this manual and in the programming system physician's manuals.

- **Line powered equipment —** Exercise extreme caution if testing the lead using **line-powered equipment** because leakage current can injure the patient.
- **Setscrew —** Do not insert a lead in the generator lead receptacle(s) without first visually **verifying that the setscrew(s) is sufficiently retracted** to allow insertion. Avoid backing the setscrew(s) out further than needed for lead insertion.
- **Hex screwdriver —** Ensure that the hex screwdriver is fully inserted in the setscrew, and then push in on the hex screwdriver and turn it clockwise until it clicks. To avoid damaging (stripping) the setscrew(s) and/or dislodging the setscrew plug(s), insert the hex screwdriver into the center of the setscrew plug, keeping it perpendicular to the generator.

1.5.6 Environmental and Medical Therapy Hazards

Patients should exercise reasonable caution in avoiding devices that generate a strong electric or magnetic field. If a generator ceases operation while in the presence of electromagnetic interference (EMI), moving away from the source may allow it to return to its normal mode of operation.

1.5.6.1 Hospital and medical environments

- **VNS Therapy System operation should always be checked —** Perform device diagnostics after any of the procedures mentioned in this manual. Additional precautions for these procedures are described below.
- **Mammography —** For clear imaging, patients may need to be specially positioned for mammography procedures because of the location of the generator in the chest. (Most routine diagnostic procedures, such as fluoroscopy and radiography, are not expected to affect system operation.)
- **Therapeutic radiation —** This procedure may damage the generator's circuitry. Sources of such radiation include therapeutic radiation, cobalt machines, and linear accelerators. The radiation effect is cumulative, with the total dosage determining the extent of damage. The effects of exposure to such radiation can range from a temporary disturbance to permanent damage, and may not be detectable immediately.
- **Electrosurgery —** Use of electrosurgery [electrocautery or radio frequency (RF) ablation devices] may damage the generator. During the VNS implantation procedure, do not use electrosurgical equipment after the generator has been introduced to the sterile field. When performing other surgical procedures on a patient implanted with a VNS generator, attempt to minimize the current flowing through the generator and lead system by following these precautions:
  - Position the electrosurgery electrodes as far as possible from the generator and lead.
  - Avoid electrode placement that puts the generator or lead in the direct path of current flow or within the part of the body being treated.
  - Confirm that the generator functions as programmed after electrosurgery.
- **Electrostatic Discharge (ESD) —** ESD may damage the generator. Care should be taken when using the hex screwdriver to avoid touching the metal shaft when the screwdriver is engaged with the setscrew of the generator. This shaft can serve as a path to conduct electrostatic discharges into the device circuitry.
- **Extracorporeal shockwave lithotripsy —** This procedure may damage the generator. If therapeutic ultrasound is required, avoid positioning the area of the body where the generator is implanted in the water bath or in any other position that would expose it to ultrasound therapy. If that positioning cannot be avoided, program the generator output to 0 mA for the treatment, and then after therapy, reprogram the generator to the original parameters.
- **Treatment involving electrical currents —** If the patient receives medical treatment for which electric current is passed through the body (such as from a TENS unit), either the generator output should be set to 0 mA or function of the generator should be monitored during initial stages of treatment.
- **Therapeutic ultrasound —** Routine therapeutic ultrasound could damage the generator and may be inadvertently concentrated by the device, causing harm to the patient.

- **Magnetic resonance imaging (MRI) —** An MRI should not be performed using a transmit RF body coil for certain VNS Therapy device configurations or under certain specific conditions. In some cases, heating of the lead caused by the transmit RF body coil during MRI may result in serious injury. Static, gradient, and radio frequency (RF) electromagnetic fields associated with MRI may change the generator settings (i.e., reset parameters) or activate the VNS device if the Normal Mode output remains "ON".

  Note: See the *MRI with the VNS Therapy System* instructions for use for details.

- **Receive RF coils —** Note that certain magnetic resonance (MR) system head coils operate in receive-only mode and require use of the transmit RF body coil. Other MR systems use a transmit/receive RF head coil. Local or surface coils may also be receive-only RF coils that require the transmit RF body coil for MRI. **The use of a receive RF coil does not alter hazards of the transmit RF body coil.**

  Note: See the *MRI with the VNS Therapy System* instructions for use for details.

- **Transmit RF coils —** Exposure of the VNS Therapy System to any transmit RF coil must be avoided. Do not perform MRI scans using any transmit RF coil in the defined exclusion zones.
- **Routine diagnostic procedures —** Most routine diagnostic procedures, such as fluoroscopy and radiography, are not expected to affect system operation.

1.5.6.2 Home occupational environments

- **Not expected to affect the generator —** Properly operating microwave ovens, electrical ignition systems, power transmission lines, theft-prevention devices, and metal detectors are not expected to affect the generator. However, because of their higher energy levels, sources such as transmitting antennas may interfere with the VNS Therapy System. It is suggested that the generator be moved away from equipment—typically at least 1.8 meters (6 feet)—that may be causing interference.

  Caution: The patient should seek medical advice before entering environments that are protected by a warning notice preventing entry by patients implanted with a cardiac pacemaker or defibrillator.

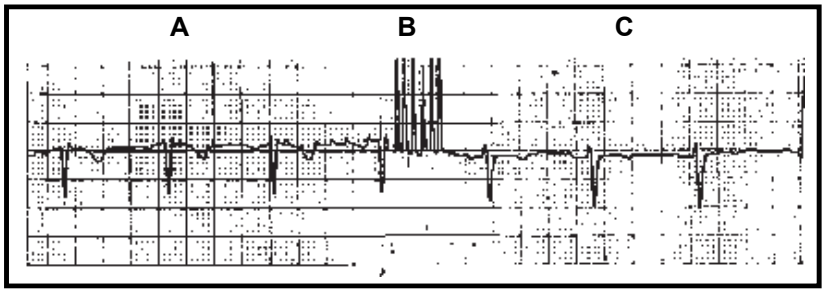
- **Cellular phones —** Based on testing to date, cellular phones have no effect on generator operation.
- **Electronic Article Surveillance (EAS) System tag deactivators —** EAS System tag deactivators can interfere with VNS Therapy when it's operated in proximity of the generator. Potential effects include inhibited pulses. Patients should be cautioned to keep at least 60 centimeters (2 feet) away from EAS System tag deactivators to avoid potential interference.
- **Other Electro-mechanical devices —** Strong magnets, tablet computers and their covers, hair clippers, vibrators, loudspeaker magnets, and other similar electrical or electro-mechanical devices, which have a strong static or pulsing magnetic field, can

cause accidental inhibition of the generator. Patients should be cautioned to keep such devices at least 20 centimeters (8 inches) away from the generator.

1.5.6.3 Generator and EMI effects on other devices

- **Interference during stimulation —** During stimulation, the generator may interfere with devices operating in the 30 kHz to 100 kHz range (e.g., pocket transistor radios and hearing aids). This interference is a theoretical possibility, and no effects on hearing aids have been reported, although the generator can interfere with a transistor radio. No specific testing has been done to date, and no definite information on effects is available.The generator should be moved—typically at least 1.8 meters (6 feet)—away from equipment with which it may be interfering.
- **Interference during programming or interrogation —** Programming or interrogating the generator may momentarily interfere with other sensitive electronic equipment nearby. The generator is not expected to trigger airport metal detectors or theft-protection devices that are further than about 1.8 meters (6 feet).
- **Operation of other implanted devices —** The generator and the VNS Therapy magnet may affect the operation of other implanted devices, such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems and inappropriate generator responses. If the patient requires concurrent implantable pacemaker and/or defibrillator therapy, careful programming of each system is necessary to optimize the patient's benefit from each device.
- **Items affected by strong magnetic fields —** The magnet provided for inhibition of the generator may damage **televisions, computer disks, credit cards, and other items** affected by strong magnetic fields.
- **Effects on ECG monitors —** Generator data communication produces an ECG artifact, an example of which is shown in the ECG tracings in Figure 1:

Figure 1. ECG Artifact Produced by Generator Communication



A Generator Off **B** Programming **C** Generator On

1.5.7 Sterilization, Storage, and Handling

1.5.7.1 Sterilization

- The generator, lead, accessory pack, and tunneler have been sterilized using either hydrogen peroxide (H_2O_2 or HP) gas plasma or ethylene oxide (EO) gas, and are supplied in a sterile pack to permit direct introduction into the operating field. An expiration (or use-before) date and method of sterilization is marked on each package. See Table 1 for sterilization methods.

Table 1. Sterilization Methods

Model	EO	H_2O_2 (HP)
102	x	x
102R	x	x
103	x	x
104	x	x
105	x	x
106	–	x
8103	–	x
1000	–	x
1000-D	–	x
302	x	x
303	x	x
304	x	x
402	x	x
502	x	x

Note: A sterilization process indicator is located on the inner sterile pack and is only used as an internal manufacturing process aid.

- **Do not re-sterilize any VNS Therapy System product —** Return any opened devices to LivaNova.

1.5.7.2 Storage

- **Store the VNS Therapy System** between - 20 °C (- 4 °F) and + 55 °C (+ 131 °F). Temperatures outside this range can damage components.
- **Do not store the VNS Therapy System** where it is exposed to water or other liquids. Moisture can damage the seal integrity of the package materials.
- **Nonpyrogenic —** The implantable portions of the VNS Therapy System are nonpyrogenic.

1.5.7.3 Handling

- **Do not implant a device** if any of the following has occurred:
  - The device has been dropped, because dropping it could damage internal components.
  - The outer or inner storage package has been pierced or altered, because this could have rendered it non-sterile.
  - The expiration (use-before) date has expired, because this can adversely affect the device's longevity and sterility.
- **Do not ultrasonically clean the generator —** Ultrasonically cleaning the generator may damage generator components.
- **Do not reimplant an explanted generator —** The generator and lead are single-use-only devices. **Do not reimplant an explanted generator or lead for any reason**, because sterility, functionality, and reliability cannot be ensured, and infections may occur.
- **Return explanted generators and leads —** Explanted generators and leads are medical waste and should be handled as such according to local laws. Explanted generators and leads should be returned to LivaNova for examination and proper disposal, along with a completed Returned Product Report form. Before returning the generator or lead, disinfect the device components with Betadine®, Cidex® soak, or other similar disinfectant, and double-seal them in a pouch or other container properly labeled with a biohazard warning.
- **Do not incinerate the generator —** The generator contains a sealed chemical battery, and an explosion could result if subjected to incineration or cremation temperatures.

1.6 Education, Training, and Services

LivaNova employs highly trained representatives and engineers located throughout the world to serve you and provide training to prescribers and implanters of LivaNova products. Physicians must contact LivaNova before prescribing or implanting a VNS Therapy System for the first time. In addition to the information provided in this physician's manual, training material includes but is not limited to, surgeon or prescribing physician training slide presentation, surgical video, training block & demo lead, etc. The required training (elements, duration, and frequency) to use LivaNova products may vary depending on the product and physician and can be discussed and arranged with your local LivaNova representative, or you can call or write LivaNova at the appropriate telephone number or address listed in the *Information and Support* chapter of this physician's manual to obtain more information.

2 Depression Information

2.1 Clinical Studies—Safety

Except where noted otherwise, the safety information presented in this section derives from the pivotal (D-02) study. The D-02 study of VNS Therapy consisted of both an acute and a long-term phase to collect data regarding the safety and efficacy of VNS Therapy as an adjunctive treatment for persons with chronic or recurrent treatment-resistant depression.

Note: For intended use/indications, see the *Introduction to the VNS Therapy System* chapter.

2.1.1 Device Performance

The VNS Therapy System performed according to its specifications. Most device issues were communication difficulties resolved by repositioning the programming wand or replacing the programming wand batteries. One high lead impedance occurred requiring replacement; a lead break due to fatigue at the electrode bifurcation was noted. Most device complaints were resolved on the day of initial complaint.

2.1.2 Adverse Events

The number (and percentage) of subjects reporting an adverse event during the 0-3 month period and during the 9-12 month period of the pivotal (D-02) study is depicted in Table 2 for the most commonly reported adverse events. Adverse events were coded using the COSTART 5 dictionary. Note that some subjects may have reported multiple events.

Table 2. Adverse Events Reported During VNS Therapy at 0-3 Months and 9-12 Months (D-02)

Adverse Event	0-3 Months (N=232)	9-12 Months (N=209)
Voice Alteration	135 (58.2%)	113 (54.1%)
Increased Cough	55 (23.7%)	13 (6.2%)
Neck Pain	38 (16.4%)	27 (12.9%)
Dyspnea	33 (14.2%)	34 (16.3%)
Dysphagia	31 (13.4%)	9 (4.3%)
Paresthesia	26 (11.2%)	9 (4.3%)
Laryngismus	23 (9.9%)	10 (4.8%)
Pharyngitis	14 (6.0%)	11 (5.3%)
Nausea	13 (5.6%)	4 (1.9%)
Pain	13 (5.6%)	13 (6.2%)
Headache	12 (5.2%)	8 (3.8%)
Insomnia	10 (4.3%)	2 (1.0%)
Palpitation	9 (3.9%)	6 (2.9%)
Chest Pain	9 (3.9%)	4 (1.9%)
Dyspepsia	8 (3.4%)	4 (1.9%)
Hypertonia	6 (2.6%)	10 (4.8%)
Hypesthesia	6 (2.6%)	2 (1.0%)

Adverse Event	0-3 Months (N=232)	9-12 Months (N=209)
Anxiety	5 (2.2%)	6 (2.9%)
Ear Pain	5 (2.2%)	6 (2.9%)
Eructation	4 (1.7%)	0
Diarrhea	4 (1.7%)	2 (1.0%)
Dizziness	4 (1.7%)	3 (1.4%)
Incision Site Reaction	4 (1.7%)	2 (1.0%)
Asthma	4 (1.7%)	3 (1.4%)
Device Site Reaction	4 (1.7%)	0
Device Site Pain	4 (1.7%)	2 (1.0%)
Migraine Headache	4 (1.7%)	2 (1.0%)

It is important to note that subjects often had comorbid illnesses and almost all study subjects were also receiving antidepressant and other drugs that could have contributed to these events.

2.1.2.1 Discontinuation due to adverse events

In the feasibility (D-01) study, no discontinuations were related to adverse events attributed to VNS Therapy or the implant procedure. By the time all continuing subjects in the pivotal (D-02) study had at least 1 year of VNS Therapy, 3% (8/235) of the subjects had discontinued VNS Therapy for an adverse event-related reason. The reasons for these eight discontinuations included one case each of suicide, implant-related infection necessitating device removal, hoarseness, lightheadedness, post-operative pain, chest and arm pain, sudden death (of unknown cause), and worsening depression (reported by the investigator as an adverse event rather than as lack of efficacy).

2.1.3 Serious Adverse Events (SAEs)

2.1.3.1 SAEs

The SAEs described in this section are based on investigator reports from the pivotal (D-02) study from study initiation through the data cutoff date for submission; the data cutoff date included the entire period of evaluation for subjects who did not complete 12 months of VNS Therapy and included a minimum of 12 months of evaluation during VNS Therapy for all subjects who continued the study for 12 months or longer.

During the pivotal (D-02) study, 12 SAEs were considered related to the implant procedure (wound infection, asystole, bradycardia, syncope, abnormal thinking, vocal cord paralysis, aspiration pneumonia, voice alteration, device site reaction [two reports], acute renal failure, and urinary retention). During the acute phase of the D-02 study, investigators did not report any SAE to be related to stimulation. During the long-term phase of the D-02 study, eight SAEs were considered at least possibly related to stimulation (sudden death of unknown cause, syncope (two reports), dizziness, a manic depressive reaction in a subject with bipolar disorder, hemorrhage GI, paresthesia, and an incident of worsening depression. Table 3 displays all the SAEs reported during the D-02 study prior to the data cutoff date, regardless of relationship to implantation or stimulation.

Table 3. Serious Adverse Events Reported in Study D-02, Regardless of Relationship to Implantation or Stimulation

Event	Acute (N=235)		Long Term (N=233)	
	Number of Events Treatment (N=119) / Sham (N=116)	Number of Subjects	Number of Events	Number of Subjects
Worsening Depression	5/7	11	62	31
Suicide Attempt	0	0	7	6
Syncope	0	0	4	3
Dehydration	1/1	2	1	1
Wound Infection	1/0	1	1	1
Cholecystitis	0/1	1	1	1
Gastrointestinal Disorder	0	0	2	2
Abnormal Thinking	1/0	1	1	1
Convulsion	0	0	2	2
Device Site Reaction	2/0	2	0	0
Pneumonia	0/1	1	0	0
Abdominal Pain	0	0	1	1
Accidental Injury	0	0	1	1
Chest Pain	0	0	1	1
Overdose	0	0	1	1
Peritonitis	0	0	1	1
Sudden Unexplained Death	0	0	1	1
Suicide	1/0	1	0	0
Surgical Procedure	0	0	1	1
Asystole	1/0	1	0	0
Bradycardia	1/0	1	0	0
Cholelithiasis	0	0	1	1
Constipation	0	0	1	1
Myasthenia	0/1	1	0	0
Confusion	1/0	1	0	0
Dizziness	0	0	1	1
Drug Dependence	0	0	1	1
Manic Depression	0	0	1	1
Somnolence	0	0	1	1
Vocal Cord Paralysis	0/1	1	0	0
Breast Cancer	0	0	1	1
Aspiration Pneumonia	1/0	1	0	0
Voice Alteration	0/1	1	0	0
Acute Renal Failure	0/1	1	0	0
Enlarged Uterine Fibroid	0	0	1	1
Urinary Retention	1/0	1	0	0

2.1.3.2 Deaths

Four deaths occurred during the pivotal (D-02) study: one after the subject had given consent, but before the subject was implanted; the second, a suicide; the third, a death of unknown cause; and the fourth, a subject who developed multi-organ failure.

2.1.3.3 Unanticipated adverse device effects

Two events in the pivotal (D-02) study met criteria for an unanticipated adverse device effect (UADE)—see the VNS Therapy *Glossary* document for definition. Both these events were non-specific complications of surgery related to the implant procedure and occurred before stimulation began. One UADE was an episode of acute renal failure thought to be secondary to antibiotic administration, and the other was an episode of altered mental status thought to be due to perioperative narcotic administration.

2.1.4 Safety Considerations Specific to Depressed Patients

Two specific safety concerns in the use of all antidepressant therapies are the precipitation of manic or hypomanic episodes and the possible effect of antidepressant therapy on suicidal ideation and behavior.

2.1.4.1 Antidepressant treatments and manic or hypomanic reaction

Although patients with bipolar disorder experience manic episodes as the cardinal feature of their disorder, effective antidepressant therapies themselves can occasionally precipitate a manic or hypomanic episode. Antidepressant therapies can also occasionally precipitate a manic or hypomanic episode in patients without a prior history of mania who are being treated for a major depressive episode.

2.1.4.1.1. Manic reactions

In the pivotal (D-02) study, six hypomanic or manic reactions were identified according to DSM IV criteria or the Young Mania Rating Scale (YMRS). Five were observed in subjects with a known history of prior hypomanic or manic episodes. One of the events was considered serious and the subject was hospitalized.

2.1.4.2 Suicidal ideation, suicide attempts, suicide, and worsened depression

Suicidal ideation was analyzed by examining the $HRSD_{24}$ Item 3 scores. At 12 months of VNS Therapy, 90% of the subjects in the pivotal (D-02) study showed either improvement (56%) or no change (34%) in their Item 3 scores. During the acute D-02 study, 2.6% of the sham subjects and 1.7% of the stimulation subjects increased their Item 3 score by 2 or more points, indicative of an increase in suicidal ideation. During the long-term D-02 phase, 2.8% of the subjects had an increase in their Item 3 score by at least 2 points at 12 months compared to baseline. In a non-randomized control group of subjects treated with standard antidepressant therapies without VNS Therapy (the D-04 study population), 1.9% of the subjects had an increase of at least 2 points. Based on the occurrence of any increase in Item 3 score from baseline to 12 months, 10% of the D-02 subjects had an increase compared to 11% of the D-04 population. Conversely, 27% of the D-02 subjects decreased their score by at least 2 points at 12 months compared to baseline, whereas only 9% of the D-04 subjects did.

Suicide attempts and completed suicides in the D-02 and D-04 studies are shown in Table 4. As noted above, one subject committed suicide in the acute phase and six attempted suicide during the long-term phase of the D-02 study (N = 235). One of the six subjects noted in the long-term phase attempted suicide twice. Although safety data were not prospectively collected for the D-04 study, the healthcare utilization form documented suicide attempts. Three suicide attempts were reported for the D-04 study through the first year of the study (N=124).

Table 4. Suicide Attempt and Suicide Rates

	Number of Patients	Patient Years	Suicide Attempts/ Patient Years	Suicide/ Patient Years
D-02	235	502	2.4%	0.2%
D-04	124	118	2.5%	0.0%

In the acute phase of the D-02 study, there were 12 reports of worsening depression, 5 in the stimulation group (5 of 119 subjects) and 7 in the sham group (7 of 116 subjects). One of the treatment-group reports occurred prior to stimulation initiation. Following acute phase exit and during the long-term phase of stimulation, 62 events were reported in 31 subjects. The number of episodes of worsening depression per subject ranged from 1 to 6. Although specific rates of worsening depression (and other safety endpoints) were not collected during the D-04 study, "hospitalizations for psychiatric illness," which might be a reasonable surrogate for worsening depression, were recorded. The rate of this event was 0.237 events per patient-year in the D-04 group compared to 0.293 events of worsening depression per patient-year in the D-02 group.

2.1.5 Adverse Event (AE) Relationship to VNS Therapy and Duration of Events

The pivotal (D-02) study investigators determined whether an adverse event (AE) was possibly, probably, or definitely related to implantation of, or stimulation by, the VNS Therapy generator and lead.

2.1.5.1 Adverse events related to implantation

Because all eligible study subjects in the pivotal (D-02) study were implanted with the VNS Therapy™ System device, no control was available to assess whether an adverse event was related to the surgery. Investigators, therefore, determined which adverse events were related to implantation. The events reported as related to implantation and occurring in at least 10% of the subjects who received VNS Therapy System implants in the pivotal (D-02) study were device site pain, device site reaction, incision pain, dysphagia, hypesthesia, pharyngitis, voice alteration, and incision site reaction. The complete list of implantation-related adverse events is shown in Table 5 and Table 6.

Note: Although not seen as part of the pivotal (D-02) study, seroma formation is a potential implantation related adverse event.

Table 5. Implantation-Related Adverse Events Occurring in Greater Than or Equal To 5% of Subjects During the Acute Phase of the Pivotal (D-02) Study

	D-02 Acute Phase Incidence of Surgery-Related AEs (n=235)
Body as a Whole	
Incision Pain	36%
Device Site Pain	23%
Device Site Reaction	14%
Headache	8%
Neck Pain	7%
Pain	7%
Digestive System	
Dysphagia	11%
Nausea	9%
Nervous System	
Hypesthesia	11%
Paresthesia	6%
Respiratory System	
Voice Alteration	33%
Pharyngitis	13%
Dyspnea	9%
Cough Increased	6%
Skin and Appendages	
Incision Site Reaction	29%

Table 6. Implantation-Related Adverse Events Occurring in Less Than 5% of Subjects in Acute Phase - Pivotal (D-02) Study

Body as a Whole
Abdominal Pain, Allergic Reaction, Anaphylactic Reaction, Asthenia, Back Pain, Chest Pain, Chills, Fever, Infection, Injection Site Pain, Neck Rigidity, Photosensitivity Reaction, Surgical Injury, Viral Infection, Wound Infection
Cardiovascular System
Arrhythmia, Asystole, Bradycardia, Hemorrhage, Migraine, Palpitation, Syncope, Tachycardia
Digestive System
Anorexia, Constipation, Diarrhea, Dyspepsia, Flatulence, Gastrointestinal Disorder, Vomiting
Endocrine System
Thyroid Disorder
Hemic and Lymphatic System
Ecchymosis, Lymphadenopathy
Metabolic and Nutritional Disorders
Edema, Hyperglycemia, Peripheral Edema
Musculoskeletal
Arthralgia, Joint Disorder, Myalgia, Myasthenia

Nervous System
Abnormal Dreams, Agitation, Ataxia, Dizziness, Hypertonia, Insomnia, Nervousness, Neuralgia, Neuropathy, Thinking Abnormal, Tremor, Vasodilatation, Vocal Cord Paralysis
Respiratory System
Aspiration Pneumonia, Asthma, Atelectasis, Bronchitis, Hiccup, Hypoxia, Laryngismus, Laryngitis, Lung Disorder, Respiratory Disorder, Rhinitis, Sinusitis, Sputum Increased
Skin and Appendages
Application Site Reaction, Maculopapular Rash, Pruritus, Rash, Sweating
Special Senses
Ear Disorder, Ear Pain, Tinnitus
Urogenital
Acute Kidney Failure, Dysuria, Metrorrhagia, Urinary Retention

2.1.5.2 Duration of implant-related adverse events

As can be seen in Table 7, many of the individual incidences of the most common implantation-related AEs resolved within 30 days. Hypesthesia (generally described as a localized numbness) and voice alteration, however, tended to be more persistent in some individuals. For example, in 17 of 24 reports of implantation-related hypesthesia, the event continued beyond 3 months. Hypesthesia would be an expected side effect of nerve injury during surgery. The persistence of voice alteration in some subjects is difficult to assess because it could represent surgical injury to the innervation of the larynx, but vagus nerve stimulation itself can cause voice alteration.

Table 7. D-02 Acute Phase Duration of Treatment-Emergent Adverse Events Related to Implantation Reported by More Than 10% of Subjects

Body System	Preferred Term	Duration to Resolution of Event in Days by all Implanted Subjects					
		1 – 7 Days	8 – 14 Days	15 – 30 Days	31 – 60 Days	61-90 Days	>90 Days
		Total N = 235 through 30 days, 234 for 31 to 90, 233 for >90 days Number within each box indicates number of subjects whose event resolved within the days shown (i.e., 27 subjects had the event of device site pain resolve within 7 days)					
Body as a Whole	Device Site Pain	27	4	9	9	3	4
	Device Site Reaction	5	5	8	9	2	8
	Incision Pain	28	18	21	10	3	6
Digestive System	Dysphagia	2	5	9	5	2	5
Nervous System	Hypesthesia	0	0	3	2	2	17
Respiratory System	Pharyngitis	10	8	10	2	0	1
	Voice Alteration	11	7	22	17	3	21
Skin and Appendages	Incision Site Reaction	19	16	24	16	2	14

2.1.5.3 Stimulation-related adverse events

Among AEs judged by investigators to be stimulation-related in the D-02 study acute phase treatment group, seven events occurred at a frequency of 10% or greater: voice alteration (55%), cough increased (24%), dyspnea (19%), neck pain (16%), dysphagia (13%), laryngismus (11%), and paresthesia (10%).

Table 8 and Table 9 list stimulation-related adverse events that occurred during the acute phase of the pivotal (D-02) study.

Table 8. Stimulation-Related Adverse Events Occurring in Greater Than or Equal To 5% of Subjects in Treatment Versus Control, Acute Phase - Pivotal (D-02) Study

	D-02 Treatment (n=119)	D-02 Sham-control* (n=116)
Body as a Whole		
Incision Pain	6 (5%)	3 (3%)
Neck Pain	19 (16%)	1 (<1%)
Digestive System		
Dysphagia	15 (13%)	0 (0%)
Nausea	8 (7%)	1 (<1%)
Nervous System		
Paresthesia	12 (10%)	3 (3%)
Respiratory System		
Cough Increased	28 (24%)	2 (2%)
Dyspnea	23 (19%)	2 (2%)
Laryngismus	13 (11%)	0 (0%)
Pharyngitis	9 (8%)	1 (<1%)
Voice Alteration	65 (55%)	3 (3%)

*__Note:__ These subjects were not receiving stimulation during this phase.

Table 9. Stimulation-Related Adverse Events Occurring in Less Than 5% of Subjects in the Treatment Group, Acute Phase - Pivotal (D-02) Study

Body as a Whole
Asthenia, Chest Pain, Device Site Pain, Device Site Reaction, Headache, Neck Rigidity, Pain
Cardiovascular System
Migraine, Palpitation, Postural Hypotension, Syncope, Tachycardia
Digestive System
Anorexia, Constipation, Diarrhea, Dyspepsia, Eructation, Flatulence, Increased Appetite, Vomiting
Metabolic and Nutritional Disorders
Weight Gain
Musculoskeletal
Myalgia, Myasthenia
Nervous System

Abnormal Dreams, Agitation, Depression, Dizziness, Emotional Lability, Hypertonia, Hypesthesia, Insomnia, Manic Reaction, Nervousness, Sleep Disorder, Somnolence, Twitching, Vasodilatation
Respiratory System
Asthma, Hiccup, Respiratory Disorder, Rhinitis
Skin and Appendages
Incision Site Reaction
Special Senses
Ear Pain, Tinnitus
Urogenital
Amenorrhea

2.1.5.4 Stimulation-related events, long-term phase

Table 10 lists stimulation-related adverse events that occurred at an incidence of ≥5% during the pivotal (D-02) study. These adverse events were observed over quarters of stimulation. Note that this table also includes observations after 24 months of treatment. Subjects are counted only once within each preferred descriptive term, e.g., neck pain, nausea, pharyngitis, and time interval. Table 11 lists stimulation-related adverse events that occurred at an incidence of <5% during the long-term phase of the D-02 study.

Table 10. Stimulation-Related Adverse Events Occurring in Greater Than or Equal To 5% of Subjects by Time Intervals After Initiation of Stimulation - Pivotal (D-02) Study

	0-3 Mos. n=232	>3-6 Mos. n=225	>6-9 Mos. n=217	>9-12 Mos. n=209	>12-24 Mos. n=184
Body as a Whole					
Neck Pain	16%	11%	14%	13%	15%
Pain	6%	7%	5%	6%	5%
Headache	5%	4%	4%	3%	3%
Digestive System					
Dysphagia	13%	8%	7%	5%	5%
Nausea	6%	2%	2%	1%	1%
Nervous System					
Paresthesia	11%	7%	3%	4%	4%
Respiratory System					
Voice Alteration	59%	60%	58%	54%	52%
Cough Increased	24%	10%	8%	7%	4%
Dyspnea	14%	16%	15%	16%	14%
Laryngismus	10%	8%	8%	6%	5%
Pharyngitis	6%	4%	4%	5%	4%

Table 11. Stimulation-Related Adverse Events Occurring in Less Than 5% of Subjects, Long-Term Phase - Pivotal (D-02) Study

Body as a Whole
Abdominal Pain, Asthenia, Chest Pain, Device Site Pain, Device Site Reaction, Flu Syndrome, Incision Pain, Neck Rigidity, Sudden Unexplained Death, Viral Infection
Cardiovascular System
Bradycardia, Hypotension, Migraine, Palpitation, Postural Hypotension, Syncope, Tachycardia
Digestive System
Anorexia, Colitis, Constipation, Diarrhea, Dyspepsia, Eructation, Flatulence, Gastritis, Gastrointestinal Disorder, Increased Appetite, Vomiting
Metabolic and Nutritional Disorders
Weight Gain, Weight Loss
Musculoskeletal
Athralgia, Joint Disorder, Myalgia
Nervous System
Abnormal Dreams, Agitation, Amnesia, Anxiety, Confusion, Depression, Dizziness, Dry Mouth, Emotional Lability, Hypertension, Hypertonia, Hypesthesia, Insomnia, Manic Reaction, Manic Depressive Reaction, Nervousness, Sleep Disorder, Somnolence, Speech Disorder, Thinking Abnormal, Tremor, Twitching, Vasodilatation, Vocal Cord Paralysis
Respiratory System
Asthma, Hiccup, Respiratory Disorder, Rhinitis, Stridor
Skin and Appendages
Incision Site Reaction, Sweating
Special Senses
Amblyopia, Deafness, Ear Pain, Eye Pain, Tinnitus
Urogenital
Amenorrhea, Menstrual Disorder

2.1.5.5 Late-emerging adverse events

After the first 3 months of stimulation, the incidence of first-reported (new event types) stimulation-related adverse events did not exceed 1.3% of total study subjects for any event (see Table 12).

Table 12. Incidence of First Reported Stimulation-Related Adverse Events Experienced After 3 Months of VNS Therapy

Body System	COSTART Term	Treatment Group (N=117) N (%)	Delayed Treatment Group (N=116) N (%)	Total (N=233) N (%)
Body as a Whole	Back Pain	1 (<1%)	0	1 (<1%)
	Flu Syndrome	1 (<1%)	0	1 (<1%)
	Sudden Unexpected Death	1 (<1%)	0	1 (<1%)
	Viral Infection	1 (<1%)	0	1 (<1%)
Cardiovascular System	Hypotension	1 (<1%)	0	1 (<1%)
	Syncope	3 (3%)	0	3 (1%)

Body System	COSTART Term	Treatment Group (N=117) N (%)	Delayed Treatment Group (N=116) N (%)	Total (N=233) N (%)
Digestive System	Colitis	2 (2%)	0	2 (<1%)
	Gastritis	2 (2%)	1 (<1%)	3 (1%)
Metabolic and Nutritional Disorders	Weight Gain	1 (<1%)	2 (2%)	3 (1%)
	Weight Loss	1 (<1%)	0	1 (<1%)
Musculoskeletal System	Arthralgia	0	1 (<1%)	1 (<1%)
	Joint Disorder	0	1 (<1%)	1 (<1%)
	Myalgia	0	1 (<1%)	1 (<1%)
Nervous System	Speech Disorder	0	1 (<1%)	1 (<1%)
	Vocal Cord Paralysis	0	1 (<1%)	1 (<1%)
Respiratory System	Stridor	1 (<1%)	0	1 (<1%)
Special Senses	Amblyopia	1 (<1%)	0	1 (<1%)
	Deafness	2 (2%)	0	2 (<1%)

Note: First reported stimulation-related AEs are defined as stimulation-related AEs that were reported after the first 3 months of VNS Therapy and for which no subject reported an AE that coded to that term during the first 3 months.
Note: AEs were coded using the COSTART 5 dictionary.
Note: Subjects were reported only once within each preferred term.
Note: Includes all AEs where relationship to stimulation was recorded as possible, probable, or definite.

2.1.5.6 Duration of stimulation-related events

Subjects who reported adverse events during the first 3 months of stimulation and continued to be observed during the next 9 months were evaluated by 3-month intervals for continuation or resolution of their events. The largest decreases were noted between the first and second quarters of stimulation. The most notable exception was voice alteration. During the first quarter, 135 of 209 subjects (65%) reported voice alteration. Of those 135 subjects, 90 continued to report it during the fourth quarter of stimulation. See Table 13.

Table 13. Duration of Early Stimulation-Related Events Through 1 Year (Study D-02)

	VNS Therapy (N=209)			
	N Reporting Event During First 3 Mos.[1]	N (%) Continuing to Report Event During Succeeding Quarters[2]		
Preferred Term	**0–3 Mos.**	**3-6 Mos.**	**6-9 Mos.**	**9-12 Mos.**
Voice Alteration	135	115 (85%)	101 (75%)	90 (67%)
Cough Increased	55	18 (33%)	15 (27%)	11 (20%)
Neck Pain	38	17 (45%)	19 (50%)	16 (42%)
Dyspnea	35	22 (63%)	18 (51%)	16 (46%)
Dysphagia	31	16 (52%)	10 (32%)	6 (19%)
Paresthesia	26	12 (46%)	6 (23%)	4 (15%)
Laryngismus	23	13 (57%)	9 (39%)	5 (22%)
Pharyngitis	14	3 (21%)	2 (14%)	2 (14%)
Nausea	13	3 (23%)	1 (8%)	2 (15%)

[1]Entries are the number of subjects who experienced the AEs between implantation and 3 months.

[2]Number of subjects who continued to experience the same adverse event between months 3 and 6, months 6 and 9, and months 9 and 12.

Note: Subjects were counted only once within each preferred term and time interval.

2.1.6 Severity of Adverse Events

Investigators rated adverse events as mild, moderate, or severe according to the protocol definitions: mild events were transient and easily tolerated by the subject; moderate events caused discomfort and interrupted usual activities; severe events caused considerable interference with the subject's usual activities.

Most adverse events for the feasibility (D-01) study and pivotal (D-02) study were mild or moderate. Because the pivotal (D-02) study included a sham-control group, further analysis of severity rating was performed. After 3 months of treatment, there were 280 (43%) adverse events that were categorized as mild, 293 (45%) as moderate, and 73 (11%) as severe in the sham-control group. The active VNS Therapy group had 360 (47%) adverse events categorized as mild, 349 (45%) as moderate, and 61 (8%) as severe.

2.1.7 VNS Therapy Continuation Rates

Of the 295 subjects implanted during both the feasibility (D-01) and pivotal studies (D-02), 270 subjects (92%) were still receiving VNS Therapy at 12 months and 242 subjects (82%) were still receiving VNS Therapy at 24 months. This compares to 12- and 24-month continuation rates of 95% and 83%, respectively, for the subjects implanted in the epilepsy preapproval trials.

2.2 Clinical Studies—Effectiveness

2.2.1 Feasibility (D-01) Study

The primary efficacy measure in the open-label feasibility (D-01) study was the percent of subjects responding (response was defined as a 50% or greater improvement in the $HRSD_{28}$ score). Of the 59 subjects with evaluable data, 18 (31%) responded at acute study exit, which

was 12 weeks after implantation. Observation of subjects continued. After 1 year of adjunctive VNS Therapy, 25 of 55 subjects (45%) responded, and after 2 years, 18 of 42 (43%) responded. After 1 and 2 years of treatment, 27% and 21% of the subjects, respectively, were in remission (defined as $HRSD_{28}$ scores less than or equal to 10. Other measures of depressive symptoms (CGI, MADRS, BDI, IDS-SR) and quality of life (MOS-36) supported the $HRSD_{28}$ scores.

2.2.2 Pivotal (D-02) Study

The pivotal (D-02) study of VNS Therapy consisted of both an acute and a long-term phase to collect data regarding the safety and efficacy of VNS Therapy as an adjunctive treatment for persons with chronic or recurrent treatment-resistant depression.

2.2.2.1 Pivotal D-02 study, acute phase

The acute phase was a 12-week (after implantation), double-blind, randomized, parallel-group sham treatment-controlled, multi-center study. Subjects were assigned randomly to either the treatment (stimulation) group or control (sham) group and results of these two groups were compared. All subjects in both groups meeting the eligibility criteria for participation in the study were implanted with the VNS Therapy generator and VNS Therapy lead. The VNS Therapy System remained OFF for 2 weeks after implantation to allow for recovery from surgery. Most subjects in the pivotal (D-02) study were being treated with one or more antidepressant medications at the time of enrollment. Medications were to remain constant at the pre-implant baseline dosages throughout the acute phase for both the treatment and sham-control groups.

Sham Control: Sham-control group subjects were treated the same as the treatment group, except that the output current of the device remained at 0.0 mA so that it did not deliver stimulation during the acute phase.

Treatment Group: Two weeks after implant, stimulation was initiated for the treatment group. Over the next 2 weeks, parameters were adjusted to subject tolerance, then remained constant for the rest of the acute phase (8 weeks). Decreases in stimulation parameters were permitted to accommodate subject tolerance.

2.2.3 Pivotal (D-02) Study, Long-term Phase

All pivotal (D-02) study subjects who completed the acute phase were eligible to continue into the long-term extension phase, during which all subjects received active VNS Therapy. During the first 10 weeks of the extension phase, sham-control subjects (also referred to as the delayed treatment group for the long-term phase), received stimulation parameter adjustments. Weekly or every other week clinic visits and assessments were identical to those experienced by the treatment group during the acute phase. Otherwise, the protocol specified monthly clinic visits for both groups through 12 months of active VNS Therapy. Various assessments, including depression ratings, were performed throughout this period. During the long-term extension phase, investigational site programmers were allowed to adjust stimulation parameters as clinically indicated. Additionally, concomitant antidepressant treatments could be added, removed, or adjusted as clinically indicated.

2.2.3.1 Comparative assessments

Outcomes from a non-randomized comparative study (D-04) were compared with the long-term outcomes in study D-02. D-04 was a long-term, prospective, observational study to

collect data regarding usual standard-of-care for treatment-resistant chronic or recurrent depression in persons who were experiencing a major depressive episode at the time of admission. Clinical (depression assessments) and quality of life outcomes were assessed at baseline, 3, 6, 9, and 12 months.

2.2.3.1.1. Concomitant therapies

Subjects enrolled in the comparative (D-04) study met the same enrollment criteria regarding chronicity or recurrence of depression, previous treatment failures, and severity of depression as subjects in the pivotal (D-02) study. Because the study was observational in nature, the protocol did not specify therapies for the treatment of depression; rather the physician managing the study subject's depression selected therapy according to clinical judgment. Thus antidepressant therapy in the comparative (D-04) study comprised "standard of care" treatment (also known as "treatment as usual"). The entire range of treatment options available for the comparative (D-04) study subjects was also available to the pivotal (D-02) study subjects as concomitant treatment to their VNS Therapy. Thus subjects in both the long-term pivotal (D-02) extension and the comparative (D-04) study received standard-of-care treatment; however, only the pivotal (D-02) study subjects received VNS Therapy.

2.2.3.1.2. Comparison of D-02 and D-04 study populations

The comparative (D-04) study was conducted at 13 investigational sites, 12 of which were also pivotal (D-02) study sites. The similarities in the key inclusion criteria and study sites provide a basis to expect that the demographic and disease characteristics of both groups would be comparable, which was confirmed by the results of the analyses conducted to examine the comparability. The D-04 subjects provided a comparison group for the pivotal (D-02) study subjects at 12 months. See Table 14.

Table 14. Description of Subjects in Pivotal (D-02) and Comparative (D-04) Studies

Parameter	Statistic	D-02 (N=205)	D-04 (N=124)
Age (years)	Mean	46.3	45.5
Male	N (%)	74(36)	39(31)
Female	N (%)	131(64)	85(69)
Caucasian	N (%)	198(97)	111(90)*
African-American	N (%)	3(1)	5(4)
Hispanic	N (%)	3(1)	2(2)
Unipolar	N (%)	185(90)	109(88)
Bipolar	N (%)	20(10)	15(12)
Recurrent	N (%)	161(87)	93(85)
Single Episode	N (%)	24(13)	16(15)
Length of Current MDE (mos)	Mean (S.D.)	49.9(52.1)	68.6(91.5)
# Failed Trials in Current MDE	Mean (S.D.)	3.5(1.3)	3.5(1.3)
Received ECT Lifetime	N(%)	108(53%)	32(26%)*
Received ECT, Current MDE	N(%)	72(35%)	15(12%)*
Duration of Illness (yrs)	Mean (S.D.)	25.5(11.9)	25.8(13.2)

Parameter	Statistic	D-02 (N=205)	D-04 (N=124)
Lifetime episodes of Depression*			
0-2	N(%)	50(24)	31(25)
3-5	N(%)	69(34)	36(29)
6-10	N(%)	56(27)	18(15)
>10	N(%)	19(9)	32(26)
No Suicide Attempts in Lifetime	N(%)	140(68)	80(65)
Treatment induced (hypomania)	N(%)	16(8)	6(5)
Hospitalizations for Depression	Mean (S.D)	2.7(5.4)	2.1(2.9)
ECT Treatment Within past 2 yrs	N(%)	54(26)	19(15)

* $P < 0.05$

This comparison analyzed evaluable populations of 205 adjunctive VNS Therapy subjects (D-02) and 124 usual standard-of-care subjects (D-04). Groups were well matched, with similar demographic, psychiatric, and mood disorder treatment histories. The only relevant significant differences between groups were previous ECT history (with higher usage of ECT found in the D-02 group) and number of lifetime episodes of depression (with a higher percentage of the D-04 group reporting >10 lifetime episodes). These differences were handled within the efficacy analysis by use of a propensity adjustment.

2.2.4 Data Analysis: D-02 and D-04 Studies

2.2.4.1 Pivotal (D-02) study

The primary efficacy variable for both the acute and the long-term phases of the pivotal (D-02) study was the Hamilton Rating Scale for Depression-24 item ($HRSD_{24}$). For the acute-phase analysis, the $HRSD_{24}$ response rate (percentage of subjects with a $\geq$ 50% improvement from baseline to 3 months, acute phase exit) was compared between the treatment and the sham-control groups. For the long-term phase, a linear regression model was used to assess the changes in $HRSD_{24}$ raw scores. Secondary efficacy analyses included within and between-group comparisons of 1) the Inventory of Depressive Symptomatology-Self Report (IDS-SR), 2) the Clinical Global Impressions (CGI), 3) the Montgomery-Asberg Depression Rating Scale (MADRS), and 4) the Medical Outcome Survey 36-Item Short Form Health Survey (MOS SF-36).

2.2.4.2 Comparative (D-04) study

The primary efficacy variable for the D-02 and D-04 comparative analysis was the IDS-SR (raw scores). Multiple assessments with the IDS-SR allowed use of a linear regression model for the analysis. The $HRSD_{24}$ was used as a secondary assessment variable to analyze differences in response rates and raw score changes between subjects in the pivotal (D-02) and comparative (D-04) studies. Subjects in the comparative (D-04) study were assessed with the $HRSD_{24}$ only at baseline and 12 months.

Secondary analyses included IDS-SR average change, IDS-SR response, IDS-SR remission, IDS-SR sustained response, and $HRSD_{24}$ remission. Other secondary analyses included the CGI response.

2.2.4.3 Propensity scores

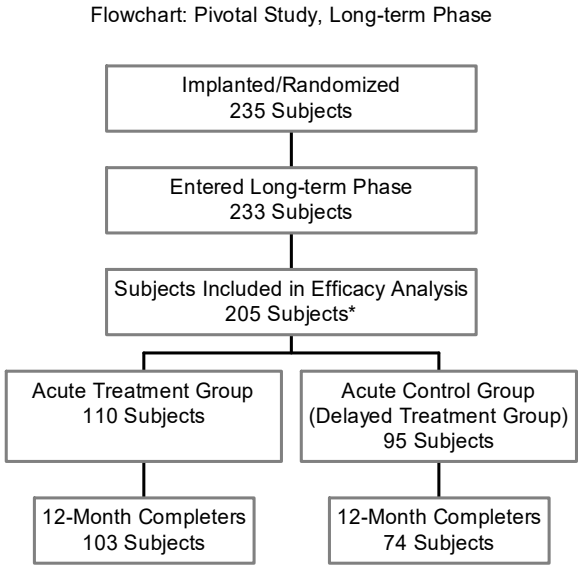
Propensity scores were calculated for the pivotal (D-02) study and comparative (D-04) study groups and used in the linear regression analysis to address the potential impact of baseline differences on differences in outcome between the two groups. Propensity scores provide a scalar summary of the covariate information (e.g., age, number of prior depressive episodes, etc.). They are not limited by the constraints of traditional methods of adjustment, which can only use a limited number of covariates for adjustment.

2.2.4.4 Responder rate

Response was prospectively defined as a ≥ 50% improvement from baseline for the IDS-SR, $HRSD_{24,}$ and MADRS ratings and as a score of much or very much improved for the CGI improvement rating. Remission (complete response) was prospectively defined as an $HRSD_{24}$ score of ≤ 9, a MADRS score of ≤ 10, or an IDS-SR score ≤ 14.

All statistical analyses were performed using the updated SAS version 8.2. All statistical tests were two-sided and performed at the 0.050 level of significance. No adjustments were made for multiple outcome measures.

Figure 2. Pivotal Study, Long-Term



*28 subjects did not qualify for Efficacy Analysis:
- 21 sham-control subjects did not have required $HRSD_{24}$ score ≥ 18 at acute phase exit
- 4 subjects did not have long-term phase efficacy assessments
- 3 subjects did not meet continuation criteria for acute phase

2.2.5 Results: Pivotal Study (D-02)

Figure 2 provides a flow chart of subjects from the acute phase through the long-term phase of the pivotal (D-02) study. Information describing subjects in the pivotal (D-02) and comparative (D-04) studies is presented in Table 14.

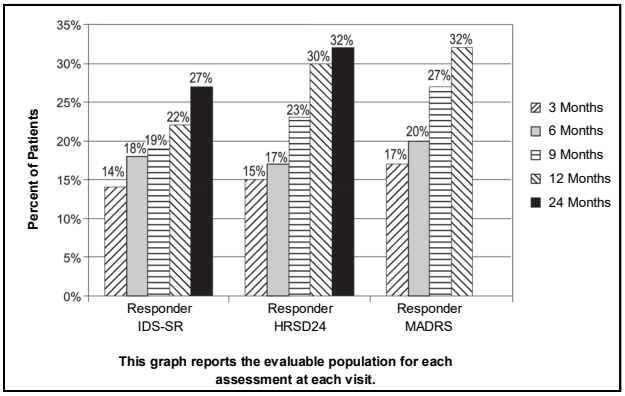
2.2.5.1 Results: acute phase, pivotal (D-02) study

In the primary efficacy measure, $HRSD_{24}$ response rate, (the percentage of subjects achieving a ≥50% improvement in $HRSD_{24}$ total score from baseline to acute phase exit), 15% of the treatment group and 10% of the sham-control group were responders (p=0.238). Analyses using a secondary efficacy parameter, the IDS-SR, did show a statistically significant advantage for VNS Therapy over sham treatment: 17% response versus 7% response (p=0.032) using the last observation carried forward (LOCF) method.

2.2.5.2 Results: long-term phase, pivotal study (D-02)

During long-term adjunctive VNS Therapy, the D-02 subjects exhibited statistically significant and clinically meaningful improvement. The primary analysis found statistically significant improvement from baseline in $HRSD_{24}$ scores averaged over 12 months (p<0.001). Additionally, clinical significance was shown, using the $HRSD_{24}$, IDS-SR, MADRS, and CGI (Figure 3 and Figure 4, evaluable population, and Table 15, 12-month completer population).

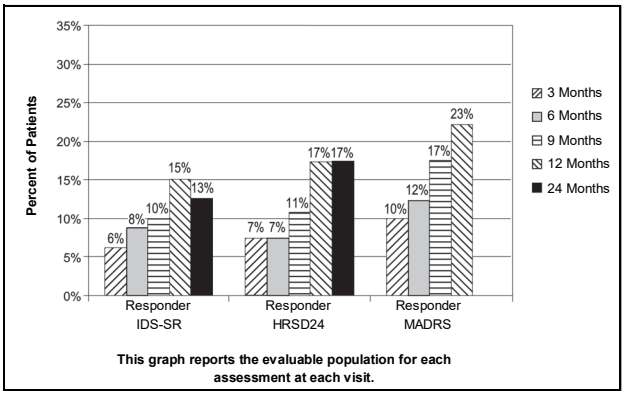
Figure 3. Responder Quarterly Results for D-02 Evaluable Subjects



The number of evaluable subjects in each of the above analyses is as follows:

Mos	IDSSR	HRSD	MADRS
3	203	205	205
6	192	197	197
9	185	186	196
12	180	181	181
24	157	157	N/A

Figure 4. Remitter Quarterly Results for D-02 Evaluable Subjects



The number of evaluable subjects in each of the above analyses is as follows:

Mos	IDSSR	HRSD	MADRS
3	203	205	205
6	192	197	197
9	185	186	196
12	180	181	181
24	157	157	N/A

Table 15. Responders, Remitters, and Percent Change Pivotal (D-02) Study, 12-Month Completer Population

	$HRSD_{24}$[a]	IDS-SR[b]	MADRS[c]
	12-Month Visit	**12-Month Visit**	**12-Month Visit**
Responders – N (%)			
Treatment	34/103 (33%)[2]	25/102 (25%)	34/103 (33%)[2]
Delayed treatment	18/71 (25%)	13/71 (18%)	22/71 (31%)[1]
All 12-Month Completers	52/174[a] (30%)[3]	38/173 (22%)[1]	56/174 (32%)[3]
Remitters – N (%)			
Treatment	19/103 (18%)[2]	16/102 (16%)[1]	25/103 (24%)[2]
Delayed treatment	10/71 (14%)	10/71 (14%)	16/71 (23%)[1]
All 12-Month Completers	29/174 (17%)[2]	26/173 (15%)[2]	41/174 (24%)[3]
Mean Percent Change from Baseline			
Treatment	31.9%[3]	27.8%[3]	32.9%[3]
Delayed treatment	26.5%[3]	17.3%[3]	26.3%[3]
All 12-Month Completers	29.7%[3]	23.5%[3]	30.2%[3]

[1] $p<0.05$; [2] $p<0.01$; [3] $p<0.001$; Response and Remitter used the Exact McNemar's test compared with 3 months; Percent Change used the paired t-test (change from pre-stimulation baseline).

[a] Three subjects did not have 12-month $HRSD_{24}$ assessments. (These 3 subjects did have 11-month assessments.)

[b] One subject did not have a baseline IDS-SR assessment and several others did not have 12-month assessments, which accounts for the varying Ns in the comparison of $HRSD_{24}$ with IDS-SR data.

[c] Two delayed-treatment subjects did not have 12-month MADRS assessments.

2.2.5.3 Quality of life assessment

The observed improvement in depression among subjects in the pivotal (D-02) study long-term phase was supported by improved quality of life as measured by the MOS SF-36. Significant improvement was observed in several of the MOS SF-36 subscales: Vitality, Social Functioning, Role Functioning – Emotional, Mental Health ($p<0.01$).

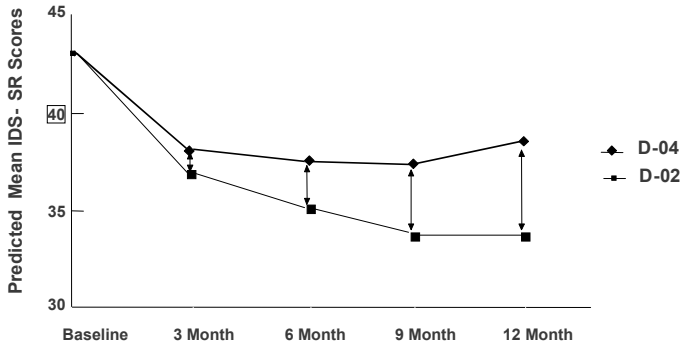
2.2.6 Results: Comparison of D-02 and D-04 Studies

The D-04 study provided a control group of similarly ill subjects who received usual standard-of-care therapies for 12 months but were not implanted with the VNS Therapy device. See Table 14.

2.2.6.1 Primary effectiveness outcome

The primary and secondary analyses comparing subjects treated with VNS Therapy plus usual standard-of-care (pivotal, D-02) with subjects treated with usual standard-of-care alone (comparative, D-04) showed that adjunctive VNS Therapy produced statistically significantly greater improvement in depressive symptoms over 1 year of treatment. The primary efficacy analysis, a repeated measures linear regression analysis of the IDS-SR over 1 year, showed a statistically significant ($p<0.001$ evaluable; $p<0.001$ intent to treat) difference favoring adjunctive VNS Therapy (see Figure 5).

Figure 5. Comparison of IDS-SR Scores of Pivotal (D-02) Versus Comparative (D-04) Study Subjects by Quarter (Repeated Measures Linear Regression Analysis), Evaluable Population



	B/L	3 mos	6 mos	9 mos	12 mos
Mean D-04 Scores	43.0 (N=124)	38.1 (N=120)	37.5 (N=119)	37.3 (N=116)	38.5 (N=112)
Mean D-02 Scores	43.0 (N=201)	36.9 (N=200)	35.1 (N=195)	33.7 (N=183)	33.7 (N=177)
Predicted Mean Difference	0	-1.2	-2.4	-3.6	-4.8
Actual Mean Difference	-0.9	-4.6	-4.1	-5.0	-6.6

2.2.6.2 Secondary analyses

Additionally, the following secondary analyses were statistically significant and showed adjunctive VNS Therapy improved depressive symptoms more than usual standard-of-care alone after 12 months of therapy. See Figure 6 and Figure 7.

Figure 6. Secondary Analyses: Categorical Outcomes at 12 Months (Evaluable Observed Analysis)

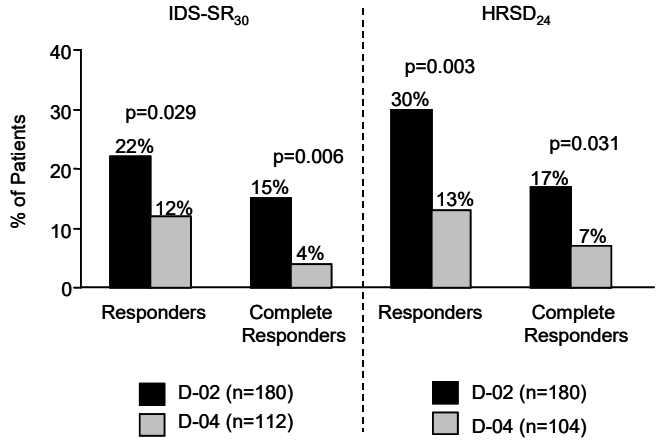
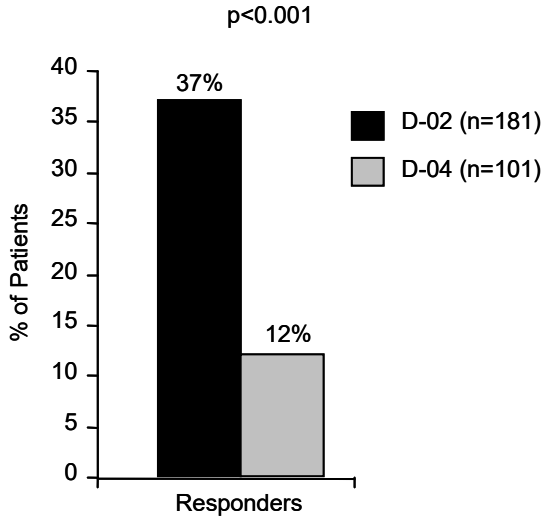


Figure 7. Secondary Analyses: CGI-I Categorical Outcome at 12 Months (Evaluable Observed Analysis)

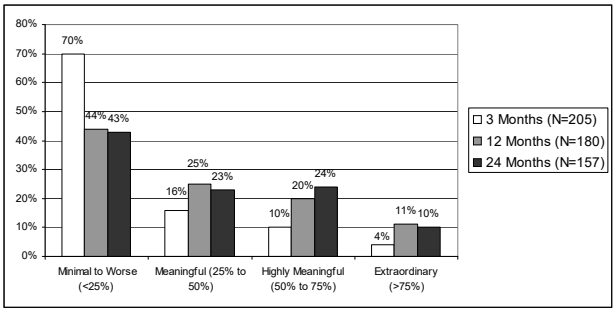


2.2.7 Clinical Benefit Over Time

To explore whether these subjects were receiving benefit that was not fully reflected in the response rates, they were assigned to categories according to "clinical benefit." Clinical benefit was prospectively defined as extraordinary (≥75% improvement in $HRSD_{24}$), highly meaningful (50% to <75%), meaningful (25% to <50%), minimal (0% to <25%), and worsened (less than 0%). This scale is consistent with studies in many chronic illnesses that define less than a 50% improvement as a clinically meaningful response (e.g., schizophrenia, obsessive compulsive disorder).

As shown in Figure 8, clinical benefit increased over time. The percent of subjects realizing at least a meaningful clinical benefit at 12 months was significant when compared to those experiencing a similar benefit after 3 months (Stuart-Maxwell test, p<0.001).

Figure 8. Clinical Benefit After 3, 12, and 24 Months; D-02 Evaluable Population; $HRSD_{24}$



The subjects realizing at least a meaningful clinical benefit after 12 months of adjunctive VNS Therapy included subjects who sustained their 3-month meaningful or greater benefit and those who had minimal to no 3-month benefit and accrued at least a meaningful benefit after 12 months. Of the 56 subjects who had at least a meaningful benefit at 3 months, 41 (73%) continued to have at least a meaningful benefit at 12 months and 34 (61%) of these same 56 subjects had at least the *same* level of clinical benefit after 12 months of adjunctive VNS

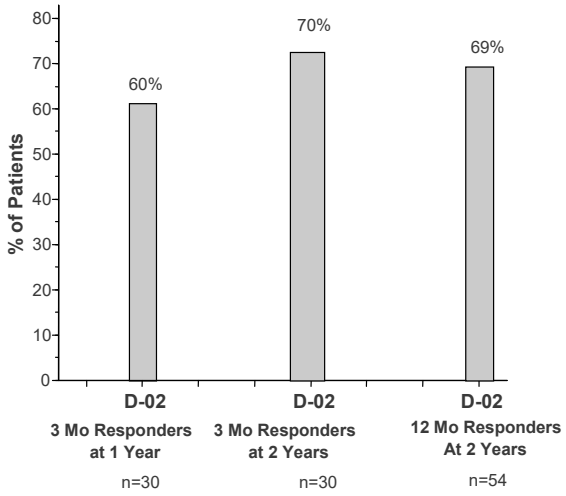
Therapy as they did after 3 months. Of the 118 subjects who realized minimal–to-worse clinical benefit after 3 months of adjunctive VNS Therapy, 56 (47%) had at least a meaningful benefit after 12 months of adjunctive VNS Therapy.

A majority (56%) of evaluable subjects treated with adjunctive VNS Therapy realized at least a meaningful clinical benefit after 12 months of treatment. After 24 months of VNS Therapy, 57% of evaluable subjects realized at least a meaningful clinical benefit.

2.2.8 Maintaining Response (2-Year Data)

An analysis of subjects having an initial ≥50% reduction in HRSD score at the designated "early" visit (3 months or 12 months) and then maintaining at least a ≥40% reduction at the later visit (1 or 2 years), was performed for the D-02 Study. Data are presented below in a bar graph (Figure 9), with each bar showing the percent of subjects that maintained their early response at the later observation.

Figure 9. Maintenance of Adjunctive VNS Therapy Response (% of $HRSD_{24}$ Responders who Maintained Response at 1 and 2 Years)



When IDS data were used instead of HRSD data, similar results were observed (61% of 3-month responders were also responders at 12 months, 57% of 3-month responders were also responders at 24 months, and 85% of 12-month responders were also responders at 24 months). By contrast, no D-04 3-month responder maintained that response at the 12-month observation.

2.2.9 Standard-of-Care Antidepressant Treatments During the Long-term Phase of Study D-02 and During Study D-04

2.2.9.1 Electroconvulsive therapy

Electroconvulsive therapy (ECT) use was similar among the pivotal (D-02) and comparative (D-04) study subjects (7% and 6%, respectively) during the first year of observation.

2.2.9.2 Antidepressant drugs and response

Antidepressant drug use was significantly greater among pivotal (D-02) study subjects who were non-responders and comparative (D-04) study subjects overall than among the pivotal (D-02) study subjects who achieved a response (p<001). During the 12 months, 77% of the

pivotal (D-02) study non-responders and 81% of all comparative (D-04) study subjects either added a new antidepressant treatment or increased an existing antidepressant dose by an antidepressant resistance rating (ARR) level of one or more. By contrast, only 56% of the pivotal (D-02) study subjects who were responders to VNS Therapy either added a new antidepressant treatment or increased an existing antidepressant dose by an antidepressant resistance rating (ARR) level of one or more.

For the evaluable group at 12-months, 61 subjects were responders while 144 subjects were non-responders (N=205). On a percentage basis twice as many pivotal (D-02) study responders had no ARR changes or removed or decreased medications by at least one ARR level or were not taking medications as compared to the non-responders (44% versus 23%, respectively).

2.2.9.3 Medication censoring analyses

Additional medication censoring analyses were performed using the D-02 and the D-02 versus D-04 repeated measures linear regression methods to evaluate further the potential effect of medication changes. This censoring approach used a missing data paradigm to calculate the D-02 results that would have been observed under conditions where no intercurrent changes in medications would have occurred in the D-02 group. The approach censors the D-02 IDS-SR scores after the point at which a subject had a significant medication increase (ARR increase) or ECT treatment, and the last pre-censored score is carried forward and used for subsequent assessment periods. The censoring had the effect of truncating the VNS treatment benefit from 12 months to an average of 7 months. In the D-02 censored analysis, the average $HRSD_{24}$ change from baseline was –0.25 points per month in the repeated measures linear regression ($p<0.001$).

The D-02 censored versus D-04 IDS-SR repeated measures linear regression comparison was an asymmetric comparison of the VNS group treated for 7 months with VNS plus no changes from baseline treatments versus the D-04 group treated for a full 12 months with unlimited standard-of-care treatments (no censoring was performed on the D-04 data). The results of the censoring analysis approached but did not reach statistical significance in the comparison of the D-02 group with the D-04 group ($p = 0.052$; 95% CI -0.37, 0.00) for the evaluable population.

2.2.10 Bibliography

A bibliography of animal, clinical, and mechanism of action studies is available from LivaNova on request.

2.3 Guidelines for Patient Follow Up

During the first few weeks after implantation, the patient should be seen to confirm wound healing and proper generator operation. The generator's output current for both the magnet and the programmed stimulation must be 0 mA for the first 14 days after implantation.

The VNS Therapy System is an adjunctive therapy to existing (prior to device implantation) antidepressant medications. Physicians are strongly encouraged **to keep all antidepressant medications stable for the first three months** of stimulation before attempting to reduce or change a patient's medication.

During initial programming, the output current should be programmed to start at nominal parameters (0 mA) and then be slowly increased in 0.25 mA increments until the patient feels

the stimulation at a comfortable level. Patients who are receiving replacement generators should also be started at nominal parameters, with 0.25 mA-step increases to allow re-accommodation.

At each patient visit, the generator should be interrogated, using the appropriate version of the VNS Therapy programming software. After reprogramming and/or diagnostics testing, data should be printed out and filed. These data can be used for comparison with a patient's own records to evaluate the VNS Therapy System, to confirm proper VNS Therapy System functioning, and to assess the need for reprogramming.

Note: For instructions on printing out data, see the programming system physician's manuals.

The median output current used during the clinical studies was about 1 mA. Other standard treatment settings were 20 Hz, 500 µsec pulse width, 30 sec ON time, and five min OFF time. There are no data to verify that these are optimal parameters.

There is no proven correlation at present between high output current (mAmps) and device effectiveness, nor is there a standard treatment level that needs to be achieved during treatment ramping. VNS Therapy System treatment should not be uncomfortable, nor should it cause bothersome side effects. Patients should be observed for at least 30 minutes after the last stimulation adjustment to make certain that they are comfortable with programmed stimulation.

Although LivaNova recommends adjusting output current as necessary, there are no controlled data at this time to indicate that higher current levels are associated with better efficacy. Patients whose depression is well controlled at follow up should not have their settings changed unless they experience uncomfortable side effects.

The subsequent follow-up schedule and the nature of each examination should be determined by the physician on the basis of patient response to and tolerance of the implant. In all other respects, follow up should be performed in accordance with the standard medical practice for patients with depression.

In the event intolerable adverse events are reported, physicians should always try reducing the output current (mA) as a means of eliminating or reducing the severity of an event. Additionally, physicians should instruct patients or caregivers on the application of the magnet to turn the generator off (output current 0 mA) if an adverse event becomes intolerable.

2.4 Individualization of Treatment

Patients should be started on stimulation at a low current output setting (0.25 mA), and the current should be increased gradually to allow accommodation to the stimulation. For patient comfort, the output current should be increased in 0.25 mA increments until a comfortable tolerance level is reached. Physicians should appreciate that some patients will accommodate to stimulation levels over time and should therefore allow further increases (in 0.25 mA steps) in output current, if needed.

Note: See the programming system physician's manuals.

Table 16 lists the stimulation parameters reported at 12 months of VNS Therapy in the pivotal (D-02) study.

Table 16. Stimulation Parameters at 12 Months of VNS Therapy in the Pivotal (D-02) Study

Stimulation Parameters	Median Value at 12 Months	Range
Output current	1.0	0 to 2.25
Frequency	20 Hz	2 to 30 Hz
Pulse width	500 µsec	130 to 750 µsec
ON time	30 sec	7 to 60 sec
OFF time	5 min	0.3 to 180 min

The magnet output current should be set to 0 mA.

2.5 Patient Counseling Information

In the event of uncomfortable adverse events, continuous stimulation, or other malfunction, the patient must be advised to hold or tape the magnet directly over the implanted generator to prevent additional stimulation. If patients or caregivers find this procedure necessary, they should immediately notify the patient's physician.

3 Technical Information — VNS Therapy Generators

3.1 Detailed Device Description

3.1.1 Physical Characteristics

The titanium case of the VNS Therapy generators are hermetically sealed and leak-rate tested. Specially designed feedthrus using platinum conductors form the electrical connection from the connector blocks to the circuitry through the hermetically sealed enclosure. Table 17 provides physical characteristics for all generator models.

Table 17. Generator Physical Characteristics

	Model 1000/103/8103	Model 106/105/102	Model 104/1000-D	Model 102R
Measurements (Typical) - All dimensions nominal				
Lead receptacle(s)	0.126 in (3.2 mm) (single-pin lead)	0.126 in (3.2 mm) (single-pin lead)	0.2 in (5 mm) (dual-pin lead)	0.2 in (5 mm) (dual-pin lead)
Dimensions	1.8 in x 1.3 in x 0.27 in (45 mm x 32 mm x 6.9 mm)	2.0 in x 2.0 in x 0.27 in (52 mm x 52 mm x 6.9 mm)	1.8 in x 1.6 in x 0.27 in (45 mm x 39 mm x 6.9 mm)	2.0 in x 2.0 in x 0.27 in (52 mm x 58.4 mm x 6.9 mm)
Weight	0.56 oz (16 g)	0.88 oz (25 g)	0.63 oz (17 g)	0.95 oz (27 g)
Connector Retention Strength				
With VNS Therapy lead	> 10 N			
Package Contents				
	Generator Hex Screwdriver			

3.1.2 Biological Compatibility

Materials exposed to the subcutaneous environment are biologically compatible. All of these materials have a long history in medical implants and have been found to be tissue compatible. Table 18 provides a list of component materials for all generator models.

Table 18. Generator Component Materials

Component	Material
Case	Titanium, hermetically sealed
Header	Polyurethane — Tecothane™ TT-1075D-M Thermoplastic
Lead connector blocks	Stainless steel
Setscrew plug	Silicone*

* No component of the VNS Therapy System is made with natural rubber latex.

3.1.3 Power Source

The power source for the VNS Therapy generators is a Wilson Greatbatch Ltd, lithium carbon monofluoride battery. Table 19 contains battery characteristics for each generator model.

Table 19. Battery Characteristics

Model	Battery Manufacturer & Model	Battery Chemistry	Open Circuit Voltage	Maximum Capacity	Self Discharge	Voltage Drop at End of Life (EOL)
Model 103	Wilson Greatbatch Ltd., Model 2183	Lithium carbon monofluoride	3.3 V, open circuit	1 Amp-hour	reduces capacity by <1% per year	gradual drop in voltage at EOL
Model 104						
Model 1000						
Model 1000-D						
Model 8103						
Model 102/102R	Wilson Great-batch Ltd., Model 2075	Lithium carbon monofluoride	3.3 V, open circuit	1.7 Amp-hour	reduces capacity by <1% per year	gradual drop in voltage at EOL
Model 105						
Model 106						

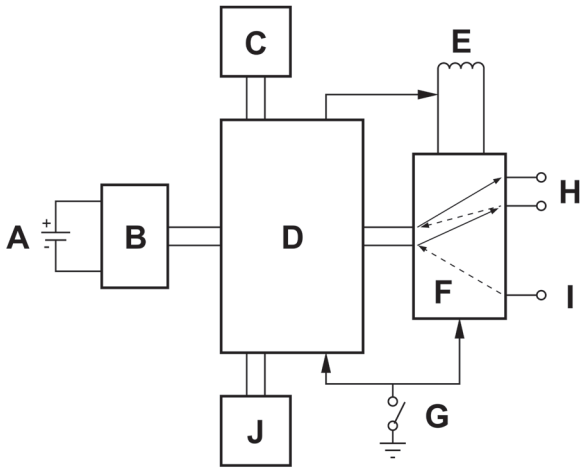
3.1.4 Circuitry

The generator uses complementary metal oxide semiconductor (CMOS) integrated circuits, including a microprocessor. The circuitry is functionally represented in Figure 10.

For descriptive purposes, circuitry of the generator can be divided into the following major functional sections:

Voltage regulators	Regulates the system power supplies
Crystal oscillator	Provides a timing reference
Logic and control	Controls overall generator function; receives and implements programming commands; collects and stores telemetry information, processes sensory input, and controls scheduled and sensory-based therapy outputs
Antenna	Receives programming signals; transmits telemetry information to the programming wand
Reed switch	Provides a mechanism to inhibit the generator's output
Input/Output	Develops and modulates signals delivered to the lead; allows the traditional VNS electrodes to serve as therapy outputs
Accelerometer	Provides information related to patient posture (Model 1000/1000-D)

Figure 10. Generator Circuitry



A Battery

B Voltage Regulator

C Crystal Oscillator

D Logic and Control

E Antenna

F Input/Output

G Reed Switch

H Lead Electrodes

I Titanium Can Connection (Models 106 and 1000/1000-D)

J Accelerometer (Model 1000/1000-D)

3.1.5 Identification

The generator can be identified on an x-ray by the x-ray tag codes provided in Table 20. The serial number and model number of the generator are marked on its titanium case, but do not appear on the x-ray.

The serial number and model number are identified by interrogating the generator with the programming system.

Table 20. X-Ray Tag Codes and Further Identification by Serial Number

Model	Possible X-Ray Tag Codes	Further Identification by Serial Number
Model 1000	LIVN and VNS	N/A
Model 1000-D		
Model 106	CYBX	N/A
Model 105	CYBX	N/A
Model 103	CYB A and VNS A	N/A
Model 104		
Model 8103		
Model 102	CYBX	Serial numbers <1000000
	CYBX-J-XX (XX = year, e.g. 10 for 2010)	
Model 102R	CYBX	Serial numbers ≥1000000
	CYBX-J-XX (XX = year, e.g. 10 for 2010)	

Note: See the programming system physician's manuals for details.

3.2 VNS Therapy System Feature Overview and Compatibility

Table 21 provides a high level description of features and compatibility for the VNS Therapy generators, and their surgical accessories and programming systems.

Table 21. VNS Therapy System Compatibility and Programming Features

Generator	Compatible Lead (Header)	Surgical Accessories	Programming Features	Programming Wand	Programmer
Depression Specific Devices					
Model 8103	Model 302 Model 303 Model 304	Model 502 Model 402	Normal Mode Guided Programming	Model 2000 v1.1	Model 3000 v1.6 and higher
Previously Implanted Generators					
Model 1000	Model 302 Model 303 Model 304	Model 502 Model 402	Normal Mode Magnet Mode AutoStim Mode Guided Programming Low Heart Rate/Prone Scheduled Programming Day-Night Programming	Model 2000 all versions	Model 3000 all versions
Model 1000-D	Dual-pin header for connection to Model 300 leads only			Model 2000 v1.1 and higher	Model 3000 v1.6 and higher
Model 106	Model 302 Model 303 Model 304	Model 502 Model 402	Normal Mode	Model 201	Model 250 v11.x
			Magnet Mode		
			AutoStim Mode		
			Guided Programming	Model 2000 all versions	Model 3000 all versions
Model 105	Model 302 Model 303 Model 304	Model 502 Model 402	Normal Mode	Model 201	Model 250 v11.x
			Magnet Mode		
			Guided Programming	Model 2000 all versions	Model 3000 all versions
Model 102 Model 103	Model 302 Model 303 Model 304	Model 502 Model 402	Normal Mode	Model 201	Model 250 v8.0 through v11.x
			Magnet Mode		
			Guided Programming	Model 2000 all versions	Model 3000 all versions
Model 102R Model 104	Dual-pin header, for connection to Model 300 Leads only	Model 502 Model 402	Normal Mode	Model 201	Model 250 v8.0 through v11.x
			Magnet Mode		
			Guided Programming	Model 2000 all versions	Model 3000 all versions

Note: Although the devices listed in Table 21 are capable of Magnet Mode, AutoStim Mode, and Low Heart Rate/Prone detection these features and modes are not recommended for depression patients.

Note: Normal Mode, Guided Programming (Model 8103 and 1000/1000-D), Scheduled Programming (Model 1000/1000-D) and Day-Night Programming (Model 1000/1000-D) are available for depression patients.

Note: A full description of the programming features in Table 21 can be found in "Features and Modes" section of this chapter.

Note: Model 2000 and Model 3000 are capable of programming all of the features listed in Table 21; however, Guided Programming can only be programmed with Model 2000 and Model 3000.

Note: Guided Programming is not recommended for depression patients implanted with generator models lower than Model 1000/1000-D.

Note: If Guided Programming or Scheduled Programming are used for a depression patient implanted with a Model 1000/1000-D, a Custom Protocol should be entered and selected where both the Magnet Mode and AutoStim Mode Outputs are both 0.0 mA for each desired step.

3.3 Directions for Use

3.3.1 Stimulation Parameters

Generator stimulation parameters and available parameter setting are presented in Table 22 and Table 23.

Table 22. Stimulation Parameters & Available Parameter Settings (Models 1000, 1000-D and 106)

	Model 1000/1000-D	Model 106
Stimulation Parameters		
Output current	0-2.0 mA in 0.125-mA steps (± 0.1 mA or ± 10%; whichever is greater) 2-3.5 mA in 0.25-mA steps (± 0.1 mA or ± 10%; whichever is greater)	
Signal frequency	1, 2, 5, 10, 15, 20, 25, 30 Hz ±6%	
Pulse width	130, 250, 500, 750, 1000 µsec ±10%	
Signal ON time	Normal Mode—7, 14, 21, 30, 60 sec AutoStim Mode—30, 60 sec	Normal Mode—7, 14, 21, 30, 60 sec (+ 7 sec/ -15%) AutoStim Mode—30, 60 sec (+ 15%/ - 7sec)
Signal OFF time	0.2, 0.3, 0.5, 0.8, 1.1, 1.8, 3 min, and 5 to 180 min (5 to 60 in 5-min steps; 60 to 180 in 30-min steps) ± 4.4 sec or ± 1%, whichever is greater	
Reset parameters	Settings are unchanged, but output is disabled (no stimulation)	
Day-Night Programming		
Day-Night Programming	Enabled or Disabled; When enabled, allows user to program the generator to deliver 2 independent sets of stimulation parameters at different times during a 24-hour period.	Not Applicable
Nighttime Period	Time period for which Nighttime Values are active; 1-23 hours in 30 minute increments	Not Applicable

	Model 1000/1000-D	Model 106
Nighttime Values	Programmable parameters for Nighttime stimulation includes: ■ Normal Mode output current ■ Normal Mode frequency ■ Normal Mode pulse width ■ Normal Mode ON time ■ Normal Mode OFF time	Not Applicable
Scheduled Programming Parameters		
Scheduled Programming	Enabled or Disabled When enabled, allows user to schedule automated increases in output current using a protocol of up to 7 steps	Not Applicable
Interval Between Steps	Default value: 14 days; range is from 7 days to 28 days	Not Applicable
Step Values	Programmable parameters for each step of a protocol: First step: All stimulation parameters Subsequent steps: output currents only	Not Applicable
Device History and Diagnostics		
Device History	Patient ID, implant date, model number, serial number, total ON time, total operating time, and manufacturing date. Device settings and stimulation statistics for last 3 office visits. Reference programming system physician's manual for details.	
Device Diagnostics	Patient ID, model ID, serial number, firmware build number, implant date, communication status, output current status, measured current delivered, lead impedance, and battery status indicators (IFI, N EOS, EOS) Reference programming system physician's manual for details.	

Table 23. Stimulation Parameters & Available Parameter Settings (Models 105, 8103/103/104 and 102/102R)

	Model 105	Model 8103/103/104	Model 102/102R
Stimulation Parameters			
Output current	0-3.5 mA in 0.25-mA steps (± 0.1 mA or ± 10%; whichever is greater)	0-3.5 mA in 0.25-mA steps* ±0.25 ≤ 1 mA, ±10% > 1 mA	
Signal frequency	1, 2, 5, 10, 15, 20, 25, 30 Hz ±6%		
Pulse width	130, 250, 500, 750, 1000 µsec ±10%		
Signal ON time	Normal Mode—7, 14, 21, 30, 60 sec (+ 7 sec/ - 15%)	7, 14, 21, 30, 60 sec† ±15% or + 7 sec, whichever is greater	
Signal OFF time	0.2, 0.3, 0.5, 0.8, 1.1, 1.8, 3 min, and 5 to 180 min (5 to 60 in 5-min steps; 60 to 180 in 30-min steps) + 4.4 / - 8.4 sec or ± 1%, whichever is greater		

	Model 105	Model 8103/103/104	Model 102/102R
Reset parameters	Settings are unchanged, but output is disabled (no stimulation)		
Device History and Diagnostics			
Device History	Patient ID, implant date, model number, serial number, total ON time, total operating time, and manufacturing date. Reference programming system physician's manual for details.		Patient code, implant date, model number, and serial number Reference programming system physician's manual for details.
Device Diagnostics	Patient ID, model ID, serial number, implant date, communication status, output current status, measured current delivered, lead impedance, and battery status indicators (IFI, N EOS, EOS) Reference programming system physician's manual for details.		Status messages for programming, telemetry, N EOS, output current, lead impedance, DC-DC converter value, programmed amplitude, and device treatment status Reference programming system physician's manual for details.

* For output currents ≤ 1 mA, the tolerance is ± 0.25mA. Maximum output is 12.5 ± 2.5 V with the exception of 10 Hz, 7 seconds On Time, in which case the maximum output is 4.4 V and 0.25 mA tolerance. This 0.25 mA tolerance also applies to 15 Hz, 7 seconds On Time, 0.5mA output current.

† For Signal ON time > 7 sec, there is no ramp-down at 15 Hz with 0.5 mA and at 10 Hz with 0.5-1.75 or 2.75 mA. For Signal ON time at 30 sec, actual ON time is 40 sec for 10 Hz with 0.25 mA and 38 sec for 15 Hz with 0.25 mA.

3.3.2 Communicating with the VNS Therapy System

3.3.2.1 Programming system

A compatible VNS Therapy programming system is required to communicate with and program the generator. A programming system consists of a programming wand, and a compatible computer running the programming software.

Note: For more information, such as the proper placement of the wand, connection of the wand to the computer, and use of the programming system, see the programming system physician's manuals.

3.3.2.2 Communication

The generator "listens" for a communication signal from the programming wand. Communication usually initiates between 1 and 4 seconds (between 3 and 10 seconds for Model 102/102R), but may be prolonged or interrupted in the presence of electromagnetic interference (EMI). Depending on the type and amount of information being transferred between the generator and the programming wand, complete communication may take up to one minute. Downloading additional information may take more time.

The generator listens for and implements interrogations, parameter programming instructions, requests for diagnostics testing, and device history inquiries.

In response, the generator transmits information on the stimulation parameter settings, changes its parameter settings, responds to requests for diagnostics testing, and provides device histories, respectively. Each time these data are transmitted by the generator, they are saved by the programming software to a database.

Note: For details on viewing generator information on a programming computer, see the programming system physician's manuals.

In addition to the programming system, a magnet can be used for one-way communication to the generator by activating a reed switch in the electronic circuitry. The magnet can be used to initiate stimulation, temporarily inhibit stimulation.

3.3.3 Features and Modes

3.3.3.1 Normal Mode

After the generator has been programmed, stimulation will repeat in accordance with the programmed ON and OFF cycle (Normal Mode) until the generator receives communication from the programming system, or is inhibited with the magnet. Immediately after successful programming, the generator delivers a programmed stimulation that enables the programmer to evaluate patient response. If programming is performed during stimulation, stimulation will be terminated; after programming, stimulation will begin using the revised settings.

3.3.3.2 Day-Night Programming (Model 1000/1000-D)

Caution: Time-based features (e.g., Scheduled Programming, Day-Night Programming) do not automatically adjust for Day Light Savings or time zone changes. Tell the patient to follow-up with the physician for reprogramming if needed.

Day-Night Programming is an optional feature that allows the generator to deliver 2 independent sets of therapy parameters at different times during a 24-hour period. The physician specifies what parameters will change, and a time period during the 24-hours when the alternate parameter set should be active. After the Day-Night program has been defined, the generator will alternate between the 2 independent parameter sets on a daily basis. This feature provides the physician the ability to further customize the delivery of VNS Therapy to accommodate to each individual patient's needs after a target level has been established for the patient.

As with any therapy setting change, the risk and benefits of altering a patient's known efficacious settings should be considered when making adjustments. Inform your patients about when to expect a setting change (i.e. when Daytime settings transition into Nighttime settings). In addition, patient tolerability of the alternate parameter set should be assessed prior to the patient leaving the office visit.

Note: For additional information on use of the feature, refer to the programming system physician's manuals.

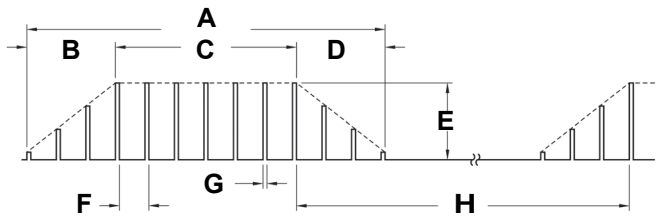
3.3.4 Stimulation Parameters, Duty Cycle, and Impacts on Battery Life

3.3.4.1 Programmable parameters

A graphic representation of stimulation (Figure 11) depicts the relationship of the programmable parameters. Each parameter can be independently programmed, thereby offering multiple setting combinations from which the physician may select optimal stimulation for the patient.

Figure 11 shows that the output pulse can be varied both by amplitude (output current) and duration (pulse width). The number of output pulses delivered per second determines the frequency.

Figure 11. Stimulation



A Stimulation Time

B Ramp Up (2 sec.)

C On Time

D Ramp Down (2 sec.)

E Output Current

F 1/Signal Frequency

G Pulse Width

H Off Time

Note: Frequencies <10 Hz do not ramp

3.3.4.2 Duty cycle

The percentage of time the generator is stimulating is called a "duty cycle." A duty cycle is calculated by dividing the stimulation time (programmed Normal Mode ON time plus, if frequency is ≥ 10 Hz, 2 seconds of ramp-up time and 2 seconds of ramp-down time) by the sum of the ON and OFF times. The various parameter settings for stimulation are listed in "Stimulation Parameters".

Warning: Excessive stimulation is the combination of an excess duty cycle (i.e. one that occurs when ON time is greater than OFF time) and high frequency stimulation (i.e. stimulation at ≥ 50 Hz). Excessive stimulation has resulted in degenerative nerve damage in laboratory animals. While LivaNova limits the maximum programmable frequency to 30 Hz, it is recommended that you do not stimulate with excess duty cycle.

Table 24 shows duty cycles for typical ON time and OFF time settings.

Table 24. Duty Cycles for Various ON and OFF Time Settings

	OFF Time (min)								
	0.2	0.3	0.5	0.8	1.1	1.8	3	5	10
ON Time (sec)	**Duty Cycles* (% ON Time)**								
7	58	44	30	20	15	10	6	4	2
14	69	56	41	29	23	15	9	6	3
21	76	64	49	36	29	19	12	8	4
30	81	71	57	44	35	25	16	10	5
60	89	82	71	59	51	38	27	18	10

* A duty cycle is calculated by dividing stimulation time (programmed ON time plus 2 seconds of ramp-up time and 2 seconds of ramp-down time) by the sum of the ON time and the OFF time.

* The duty cycles in gray are not recommended as they represent parameter combinations with ON Time > OFF Time.

3.3.4.3 Parameter settings and battery life

When selecting a combination of parameter settings for stimulation, the physician should also consider that some combinations would decrease battery life faster than others. Additional features will also decrease the battery life.

Note: See "Generator Battery Longevity".

3.3.5 VNS Therapy Magnets

The magnet is used to temporarily inhibit stimulation and to reset the generator (in combination with the programming system).

3.3.5.1 Inhibit generator output with the magnet

Application of the magnet during stimulation will inhibit the output. In addition, holding the magnet in place will terminate any ongoing Normal Mode stimulation. Table 25 provides the amount of time the magnet should be held in place to terminate Normal Mode stimulation for each generator model. After the magnet is removed, Normal Mode operation will resume stimulation after one complete OFF time has elapsed.

Table 25. Amount of Time Magnet is Held in Place to Terminate Normal Mode Stimulation

Generator	Amount of Time
Model 1000/1000-D	10 sec.
Model 106	5 sec.
Model 105	65 sec.
Model 8103/103/104	
Model 102/102R	

Caution: If stimulation becomes painful, the patient should be instructed to stop the stimulation with the magnet.

In the unlikely event of continuous stimulation or other malfunction, the patient must be advised to apply the magnet, secure it in place, and immediately notify their physician.

Note: See "Adverse Events" in the *Depression Information* chapter.

3.3.5.2 Reset the microprocessor with the magnet and the programming system

The VNS Therapy System allows the generator microprocessor to be reset in the event of a malfunction. A reset is necessary only in the rare case of microprocessor memory malfunction, which might be caused by conditions described in the *Introduction to the VNS Therapy System* chapter. A reset of the microprocessor may be appropriate when the generator and the programming wand are unable to communicate.

Caution: *Generator reset*— When a Model 102/102R generator is reset, all device history information is lost, and the reset parameters (0 mA, 10 Hz; 500 µsec; ON time, 30 seconds; OFF time, 60 minutes) are internally programmed. Resetting the generator turns the device off (output current = 0 mA). After a successful reset, the generator stimulation output may be re-enabled to resume operation at the previously programmed settings and optional features reactivated.

Caution: *Generator reset*— When generator models higher than Model 103 are reset, optional features (such as Day-Night Programming) and stimulation output are disabled (0 mA); however, all settings and device history are preserved. After a successful reset, the generator stimulation output may be re-enabled to resume operation at the previously programmed settings and optional features reactivated.

For suggestions in solving communication difficulties, see "Troubleshooting" in the programming system physician's manuals.

For instructions on how to reset the microprocessor, see the programming system physician's manuals. It is recommended, except in cases of a medical emergency, that the physician consult a LivaNova technical representative before a reset is performed.

3.3.6 Effects of the daily reset of the internal clock (Model 102/102R)

The Model 102 and 102R generators contain an internal clock that rolls over (i.e., restarts) every 24 hours. This daily rollover of the internal clock is a normal device function. Every time the clock restarts, a stimulation cycle beginning with the programmed ON time is delivered. Patients may notice a shorter OFF time between the last stimulation cycle just prior to the clock restart and the first stimulation cycle after the clock restart.

Note: The time that the clock restarts each day corresponds with the time of day the most recent programming event occurred. Holding the magnet over the generator for an extended period of time will put all timekeeping functions on hold and will delay the time that the internal clock rolls over each day.

Some patients may be more sensitive to this shorter OFF time and may exhibit common stimulation related side effects (e.g. coughing, voice changes). These side effects will only occur once a day at the time of the daily clock restart. In the rare reported instances in which side effects occurred with the daily clock restart, it was noted that the most common programmed duty cycle was 30 seconds ON and 3 minutes OFF along with a high output current (> 2 mA).

Note: For a complete list of side effects, see "Adverse Events" in the *Depression Information* chapter.

As with any normal side effect, adjusting settings for tolerability (i.e., decreasing pulse width, signal frequency, and/or output current) has been shown to be successful in resolving stimulation related side effects associated with the 24-hour rollover event. However, since this 24-hour rollover event is directly related to the programmed ON and OFF times, adjusting the duty cycle may be a better option. Optimizing the patient's benefit from therapy should be considered when making the decision as to which parameter should be adjusted. For example, if the patient is responding well clinically at a particular output current, adjusting a different parameter or duty cycle may be considered. Table 26 shows several ON and OFF time combinations that may be better options when trying to resolve stimulation related side effects associated with the daily clock restart.

Table 26. ON/OFF Time — Options for Optimizing Therapy for Patients Affected by the Internal Clock Cycle

ON Time (sec)	OFF Time (min)
7	0.3
14	0.5
21	0.5
7	0.8
14	1.1
30	1.1
60	1.1
30	1.8
7	3.0
14	3.0
60	5.0
14	10.0

Note: For a comprehensive list of duty cycle settings, see Table 24.

3.3.7 Device History

The generator device history consists of the generator serial number, model number, patient code, implantation date, and other information pertinent to diagnostic and programming events. Use the programming system to access and view device history information.

3.3.8 Device Diagnostics

Information from device diagnostic tests can help the physician determine whether the:

- Generator output current is being delivered at the programmed value
- Lead impedance is within an acceptable range
- Generator battery is at a sufficient level

Note: For details on available diagnostic tests, see the programming system physician’s manuals.

3.3.8.1 System Diagnostics test

The System Diagnostics evaluates the lead impedance of the VNS Therapy System, as well as the generator's ability to deliver the programmed Normal Mode stimulation. Depending on the generator model and programmed Normal Mode output current, different test pulses may be conducted during the test (see Table 27). The programming software will report the lead impedance and whether the programmed stimulus was delivered.

Table 27. System Diagnostics

Normal Mode Output Current	System Diagnostics Behavior		
	M102/102R	M103-106 & 8103	M1000/1000-D
0 mA	1 mA, 500 µsec for approximately 14 seconds	1 mA, 500 µsec for approximately 14 seconds	Delivery of programmed output for approximately 4 seconds, followed by one brief pulse at 0.25 mA for less than 130 µsec.*
>0 mA		One brief pulse at 0.25 mA for 130 µsec, followed by delivery of programmed output for the duration of the programmed ON time.	

*Minor differences in the system diagnostics test exist for M1000 with serial numbers <100,000. Refer to the *Introduction to the VNS Therapy System* chapter for more information.

Note: Once programmed ON, lead impedance measurement readings are automatically performed once every 24 hours for Model 103 and higher generators.

3.3.8.2 Reasons for high or low lead impedance readings

Possible causes of high lead impedance readings are thought to include:

- Lead discontinuity
- Lead disconnection from the generator
- Fibrosis between the nerve and the electrode
- Electrode detachment from the nerve
- Defective generator

Possible causes of low lead impedance readings are thought to include:

- Short-circuit condition within the lead
- Defective generator

3.3.8.3 High lead impedance: possible implications

High lead impedance (≥ 5300 Ohms), in the absence of other device-related complications, is not an indication of a lead or generator malfunction. High lead impedance in combination with the patient's failure to feel even the maximum output stimulus may indicate a lead wire fracture or other type of electrical discontinuity in the lead. Patients experiencing high lead impedance, no sensation of maximum output stimulation, and an increase in depressive symptoms should be further evaluated for possible lead replacement.

Note: For additional instructions on how to perform the System Diagnostics, see the programming system physician's manuals.

Note: To troubleshoot high or low impedance see "Troubleshooting" in the programming system physician's manuals.

For Models 102 and 102R use Table 28 to find the DC-DC Converter Code displayed by the System Diagnostics (Lead Test) screen to determine an estimate of lead impedance in kOhms. The use of Table 28 with the DC-DC Converter Code from diagnostic screens other than the System Diagnostics (Lead Test) and Generator Diagnostics (Pre-Implant Test) is not appropriate, unless the generator output parameters are the values indicated in the tables. High lead impedance is defined as any DC-DC Converter Code greater than or equal to four with 1 mA of diagnostic current.

Table 28. DC-DC Converter Codes and Lead Impedance (Models 102 and 102R)

DC-DC Converter Code[1]	Estimated Lead Impedance[2] 1 mA, 500 msec
0	≤ 1.7 kOhms
1	1.8-2.8 kOhms
2	2.9-4.0 kOhms
3	4.1-5.2 kOhms
4	5.3-6.5 kOhms
5	6.6-7.7 kOhms
6	7.8-8.9 kOhms
7	≥ 9 kOhms

[1] DC-DC Converter Codes are displayed during System Diagnostics (Lead Test).

[2] Tolerance is ± 10 percent.

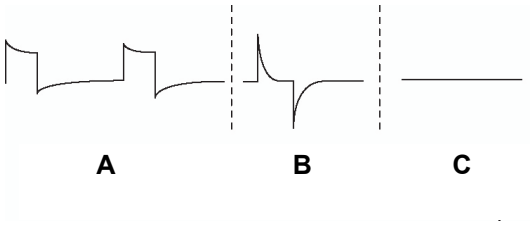
3.3.8.4 Low lead Impedance: possible implications

Low lead impedance (≤ 600 Ohms for Model 103 and higher or DC-DC Converter Code of "0" for Models 102 and 102R) likely indicates the existence of a short-circuit condition, although an impedance value of greater than 600 Ohms does not exclude the possibility. A significant decrease in DC-DC Converter Code value for Model 102/102R on the System Diagnostics (e.g., "3" to "1") from prior System Diagnostics may also indicate a lead problem. A sudden decrease in impedance value in combination with device-related complications (e.g., increase in depressive symptoms or painful stimulation; patient perception of feeling erratic, limited, no stimulation) may also indicate a short-circuit condition in the lead.

3.3.8.5 Stimulus waveform analysis

Either evoked potential monitoring equipment or an oscilloscope can be used to analyze the stimulus waveform from the neck for verification of an electrical discontinuity. A differentiated waveform with narrowed pulses or no waveform at all can confirm a discontinuity. Figure 12 shows characteristic waveforms obtained from skin electrodes for a lead that is intact and for a lead that has a fracture in one or both wires. In addition, lead discontinuities can sometimes be identified on x-ray of the implant site.

Figure 12. Typical Waveforms Obtained from Skin Electrodes



A Intact Lead

B One Broken Lead Wire

C Two Broken Lead Wires or No Output

3.3.9 Delivery of Programmed Output Current

3.3.9.1 LOW as output current (or LIMIT for Model 102/102R)

If the diagnostic tests indicate LOW or LIMIT output current, the generator may not be delivering the programmed output current. Reasons for failure to deliver the programmed output current include high programmed output current and high lead impedance. The maximum deliverable output current, according to Ohm's Law, equals the maximum output voltage (approximately 12 V) divided by the lead impedance.

3.3.9.2 Reprogram to a lower current

If the generator is failing to deliver the programmed output current, the physician can reprogram the device to a lower output current and attempt to compensate for the decrease in delivered energy by widening the pulse width. For example, if the diagnostics read LOW or LIMIT for a generator programmed at 2.5 mA, 30 Hz, 500 µsec with 30 seconds ON time, then the parameters may be changed by lowering the output current to 2 mA and widening the pulse width to 750 µsec.

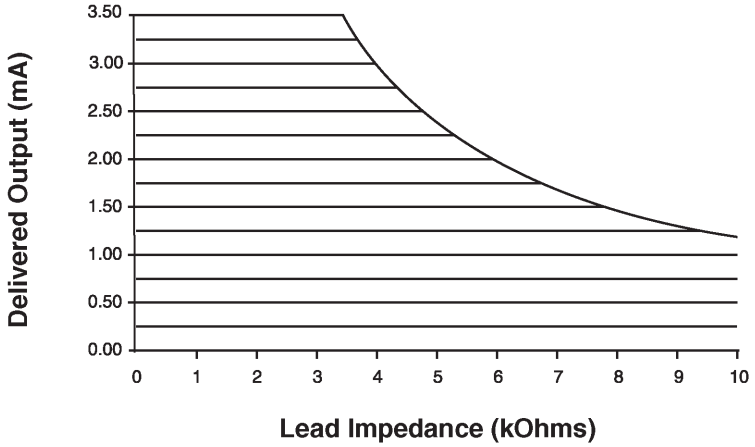
3.3.10 Charge Delivered Per Pulse

3.3.10.1 Output current x pulse width = charge delivered per pulse

The charge delivered per pulse is the most important parameter in evaluating stimulation output. It is defined as a microcoulomb (µC), which is the product of current and time—that is, the output current (mA) multiplied by the pulse width (msec). Figure 13 shows the relationship of delivered output current (mA) to lead impedance for a 1000 µsec pulse with output currents from 0 to 3.5 mA.

⚠ **Caution: For Model 102/102R, do not use frequencies of 5 Hz or below for long-term stimulation.** Because these frequencies generate an electromagnetic trigger signal, their use results in excessive battery depletion of the implanted generator and, therefore, should be used for short periods of time only.

Figure 13. Relationship of Delivered Output Current to Lead Impedance



3.3.11 Generator Battery Longevity

3.3.11.1 Battery longevity and programmed setting choices

The anticipated longevity of the generator battery varies, depending on the choice of programmed settings. Higher output currents, frequencies, pulse widths, and duty cycles generally deplete the battery over a shorter period of time than lower settings. Generally, the increase in battery depletion rate is proportional to the increase in the programmed setting.

⚠ **Caution:** *Undeliverable output currents*— Programming the generator to a high output current that cannot be delivered due to a high lead impedance may disproportionately increase the battery depletion rate and should be avoided.

Other factors, such as lead impedance or use of optional features also affect the anticipated battery longevity. The anticipated battery longevity decreases as lead impedance increases. Although 1.5 k to 3 kOhms may be a typical lead impedance at implantation, the impedance may increase to 3 k to 5 kOhms during the life of the implant.

The *Appendices* chapter provides estimated battery lifetimes or all VNS Therapy generators under a variety of stimulation conditions. Because of the number of possible parameter combinations, it is impractical to provide the projected life for all possible combinations. The tables should not be used to predict battery end of service (EOS), but they give some indication of the effect of various parameter changes on battery life and can be used to assist in the selection of parameter settings. They also indicate that battery life can be maximized at low duty cycles and low frequencies (e.g., 20 Hz) for stimulation.

ⓘ **Note**: For more information, see the programming system physician's manuals.

3.3.11.2 Battery status indicators

The programming software displays a battery indicator similar to an indicator that may be found in cell phones. The visual indicator illustrates the approximate remaining battery capacity.

The programming software will display warning messages after an interrogation or programming of the generator if the battery has been depleted to a level where action is recommended due to approaching or reaching End of Service (EOS). Please refer to the VNS

Therapy programming system physician's manuals for additional information on these indicators.

⚠ **Caution:** *Battery evaluation at cold temperatures*—Low storage temperatures may affect the battery status indicators. In such cases, the battery status indicators should be re-evaluated using the System Diagnostics or Generator Diagnostics after the generator has been at room or body temperature for 30 minutes.

3.3.12 Generator Replacement

All VNS Therapy generators eventually require surgical replacement as a result of battery depletion. Generator replacement does not, of itself, require lead replacement unless a lead discontinuity is suspected. Generator replacement or removal requires dissection to the generator's pocket, with care being taken not to damage or cut the lead. The entire surgical procedure generally requires about 1 hour.

3.3.12.1 Signs of End of Service

The most common reason for the absence of stimulation is battery depletion, although there may be other reasons. When end of service (EOS) occurs, the generator will disable stimulation and no output will be delivered. If the generator is not explanted or replaced at EOS, the battery voltage will continue to gradually decrease and communication with the generator may not be possible.

⚠ **Caution:** Generator EOS may result in increased frequency, intensity, or duration of signs and symptoms of the patient's disorder, in some cases to levels greater than those reported before stimulation.

3.3.12.2 Replacement Based on Battery Status Indicators

The generators and the programming system have battery status indicators (see "Battery status indicators"). These indicators provide warnings that a generator battery should be monitored more frequently, is nearing EOS, or has reached EOS. Once these warning messages appear, see recommendations in the programming system physician's manuals.

⚠ **Caution:** *Prompt generator replacement***—**LivaNova recommends prompt replacement of the generator at or before EOS. Prompt replacement may help minimize any possible relapse.

⚠ **Caution**: *Explanted generator*—A generator explanted for any reason should not be reimplanted. An explanted generator should be returned to LivaNova. For instructions on returning an explanted generator, see the *Introduction to the VNS Therapy System* chapter.

4 Technical Information — Leads

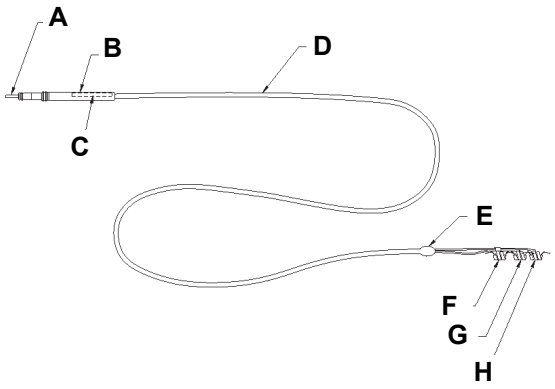
4.1 Detailed Device Description

4.1.1 Physical Characteristics

The VNS Therapy leads are bifurcated at one end and have a single connector pin at the other end, as shown in Figure 14 and Figure 15.

The lead, which delivers the electrical signal from the generator to the vagus nerve, is insulated with silicone. It is available in two sizes (2.0 and 3.0 mm electrode inner diameter) to ensure optimal electrode fit on different size nerves. The lead has two helical electrodes and an anchor tether, which are coiled around the left vagus nerve. The connector end of the lead is tunneled subcutaneously to the generator pocket. Table 29 provides physical characteristics for all lead models.

Figure 14. Model 302 and 304 Lead



A Connector Pin

B Lead Connector

C Model/Serial Number Tag

D Lead Body

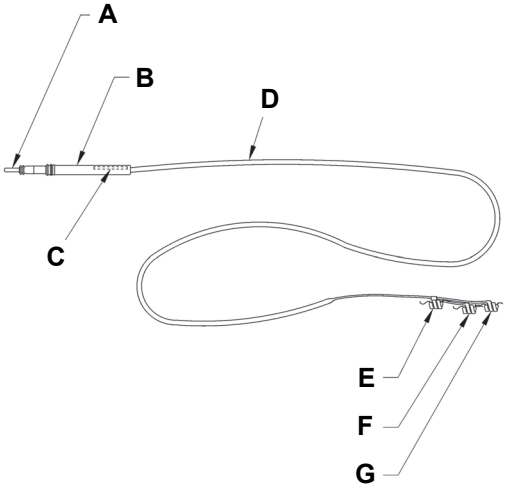
E Electrode Bifurcation

F Anchor Tether

G Electrode (+) (White Suture)

H Electrode (-) (Green Suture)

Figure 15. Model 303 Lead



A Connector Pin

B Lead Connector

C Model/Serial Number Tag

D Lead Body

E Anchor Tether

F Electrode (+) (White Suture)

G Electrode (-) (Green Suture)

Table 29. Lead Physical Characteristics

	Model 302	Model 303	Model 304
Measurements (Typical) - All dimensions nominal			
Lead Connector Diameter	3.2 mm (0.127 in)		
Connector Pin Diameter	1.27 mm (0.05 in)		
Connector Ring Diameter	2.67 mm (0.105 in)		
Lead Body Diameter	2 mm (0.08 in)		
Lead Body Conductor coil construction	Helical, quadfilar	Helical, trifilar	Helical, quadfilar
Overall Lead Body Length	43 cm (17 in)		
Lead Resistance (connector pin/ring to electrode)	120 to 180 Ohms	180 to 250 Ohms	120 to 180 Ohms
Electrodes and Anchor Tether Separation	8 mm (0.31 in) center to center		
Inner Diameter of Helix	2 mm (0.08 in) inner diameter		
	3 mm (0.12 in) inner diameter		
Tie-down Dimensions	5.7 mm x 7.7 mm (0.22 in x 0.30 in)		
Connector Assembly			
Lead connector	One (1)		
Connector Retention Strength			
With VNS Therapy generator	> 10 N		
Package Contents			
	Lead 4 tie-downs		

Integrity information about the lead can be obtained using the Programming System. The software includes a System Diagnostics (Lead Test) feature that can be used to assess lead impedance.

4.1.2 Biological Compatibility

Materials exposed to the subcutaneous environment are biologically compatible. All of these materials have a long history in medical implants and have been found to be tissue compatible. Table 30 provides a list of component materials for all lead models.

Table 30. Lead Component Materials

Component	Material
Lead Connector	Silicone*
Connector Pin	300 series Stainless Steel
Connector Ring	300 series Stainless Steel
Lead Body Insulation	Silicone*
Lead Body Conductor	MP-35N alloy
Helical	Silicone elastomer*
Electrode Conductor	Platinum/Iridium alloy
Sutures	Polyester
Tie-downs	Radiopaque silicone*

* No component of the VNS Therapy System is made with natural rubber latex.

4.1.3 VNS Therapy System Lead Compatibility

The VNS Therapy leads are compatible with the VNS Therapy single-receptacle generators and the VNS Therapy System.

4.2 Lead Lifespan and Replacement

The lead lifespan is undetermined at this time. A lead would require replacement if a lead fracture were suspected, accompanied by increased symptoms (e.g., seizure frequency). Events that can shorten the life expectancy of the lead are as follows:

- Blunt trauma to the neck and/or any area of the body beneath which the lead is implanted
- Patient's twisting or picking at either the implanted lead or pulse generator
- Improper surgical implantation of the VNS Therapy System, including (but not limited to) providing an inadequate strain relief loop, placing sutures directly on the lead body, not using the tie-downs, and suturing to muscle

⚠ **Caution: Lead replacement or removal due to lack of efficacy** is a medical judgment based on the patient's desires and health status, and must be carefully weighed against the known and unknown risks of surgery. At present, there are no known long-term hazards or risks associated with leaving the lead implanted, beyond those already mentioned in this physician's manual.

5 Implantation Procedure

5.1 Physician Training / Information

All programming should be by or under the supervision of a physician familiar with the use and operation of the programming system.

Physicians who implant the VNS Therapy System should be thoroughly familiar with all associated training materials:

- Product labeling for the generator, lead, programming system, and accessories (magnet, tunneler, and accessory pack), and patient labeling
- Electrode practice fixture—a device used to practice placing the helices around the left vagus nerve

Note: If further assistance is needed, contact Technical Support.

5.2 VNS Therapy Devices and Surgical Materials

5.2.1 New Implants

For new implants, the following devices are needed for surgery:

- 2 generator (1 primary and 1 back-up)
- 2 leads (1 primary and 1 back-up)

5.2.2 Replacement Implants

For replacement implants, the following devices are needed for surgery:

- 1 replacement generator and/or lead
- At least 1 back-up generator and/or lead

5.2.3 Other LivaNova Products

- 1 tunneler
- 1 accessory pack (resistors, hex screwdriver, tie downs)
- 1 programming system (non-sterile)

Note: Remember to use proper technique for introducing non-sterile items into a sterile field.

5.2.4 Surgical Materials

Note: The materials and equipment listed below are not provided by LivaNova.

The following is a list of additional materials typically used during the VNS Therapy implantation procedure:

All Generators

- Sterile Laser Arm Bag or equivalent (required)
- Vessel loops and/or silicone sheet for manipulation of the vagus nerve (suggested but optional)

5.2.5 To Open the Sterile Pack

Caution: The sterile lead pack should only be opened after exposing the vagus nerve and selecting the VNS Therapy lead helical that best fits.

Caution: Do not open the sales pack if it has been exposed to extreme temperatures or if there is any indication of external damage or damage to the package seal. Instead, return it unopened to LivaNova.

Before the sterile pack is opened, it should be examined carefully for evidence of damage or compromised sterility. If the outer sales pack or inner sterile pack has been opened or damaged, LivaNova cannot guarantee sterility of the contents, and it should not be used. An opened or damaged product should be returned to LivaNova.

To open the sterile pack, do the following:

1. Grasp the tab, and peel back the outer cover.
2. Observing sterile technique, lift out the sterile inner tray.
3. Grasp the inner tray's tab, and carefully peel off the inner cover to expose the contents without dropping them.

5.3 Recommendations for Implantation

In general, implantation of the VNS Therapy System is similar to accepted practice for implantation of a cardiac pacemaker, with the exception of the placement of the helices and the subcutaneous routing of the lead body. The surgical approach and techniques will vary with the preference of the surgeon.To ensure correct lead placement, this chapter of the physician's manual provides recommendations for implantation, order of placement of the helical electrodes, and the anchor tether and other essential steps.

Caution: To maximize system performance and minimize possible mechanical damage to the nerve or lead, **pay careful attention to helical placement and lead routing.**

Critical to the long-term success of the implant are proper techniques both for the attachment of the electrodes and the anchor tether to the left vagus nerve, and for the provision of adequate strain relief below and above the sternocleidomastoid muscle. For general placement of the generator and lead, see Figure 16.

It is recommended that the lead body be coiled and placed in the chest pocket to the side of the generator.

Adequate exposure of the vagus nerve (> 3 cm) facilitates placement of the helices on the nerve. Stretching the nerve or allowing it to dry during implantation may result in temporary swelling of the nerve. Constriction of the nerve or other nerve damage may result in vocal cord dysfunction.

It is recommended that output of the generator and performance of the implanted system be tested at the time of implantation. Although an oscilloscope can be used for measurements, it is recommended that the use of the appropriate version of the programming software and wand (placed in a sterile drape) be used for routine system verification.

After the electrode is placed on the nerve, test the electrode-nerve interface impedance by connecting the lead directly to the generator and performing a System Diagnostics (Lead Test). If required, a separate resistor assembly from the accessory pack can be used while performing the optional Generator Diagnostics (Pre-Implant Test).

Note: See "Test the VNS Therapy System".

5.3.1 Before Surgery and Outside of the Sterile Field

5.3.1.1 Interrogate the device

To ensure proper device communication, interrogate the device while still in the sterile pack. For a detailed explanation, see the programming system physician's manuals.

Caution: (For 103 and subsequent models only) If interrogating a generator that has been exposed to low temperatures within the last 24 hours, low battery status indicator(s) may be displayed. See "Troubleshooting" in the programming system physician's manuals.

5.3.1.2 Program patient data

Program the patient identification and implant date into the generator. For a detailed explanation, see the programming system physician's manuals.

5.3.2 Implantation Procedure Overview

Caution: This procedural overview is not a substitute for the complete implantation procedure. See detailed steps that follow.

The following overview summarizes the implantation procedure:

1. Expose the left carotid sheath and left vagus nerve.
2. Create a pocket in the chest for the generator.
3. Choose the correct size lead.
4. Tunnel the lead subcutaneously from the neck to the generator pocket in the chest.
5. Attach the electrodes and anchor tether to the left vagus nerve.
6. Secure the lead parallel to the nerve.
7. Form the strain relief bend and strain relief loop.
8. Connect the lead to the generator.
9. Verify that the connector pin is fully inserted, and tighten the setscrew.
10. Perform the System Diagnostics (Lead Test).

11. Place the generator in the chest pocket, with the extra coiled lead to the side of the generator, not behind it.
12. Secure the generator to fascia; do not place sutures directly around or on the lead.
13. Perform the second System Diagnostics (Lead Test).
14. Interrogate the generator to verify current is 0 mA.
15. Irrigate the incision site with bacitracin or other solution.
16. Close the incisions.

5.3.3 Prepare for Surgery

The surgeon should ensure that the generator, lead, and tunneler are compatible.

It is recommended that the patient be given antibiotics preoperatively and that both incision sites be irrigated frequently with generous amounts of bacitracin or equivalent solution prior to closure. (These incisions should be closed with cosmetic closure techniques to minimize scarring.) Also, antibiotics should be administered postoperatively at the discretion of the physician.

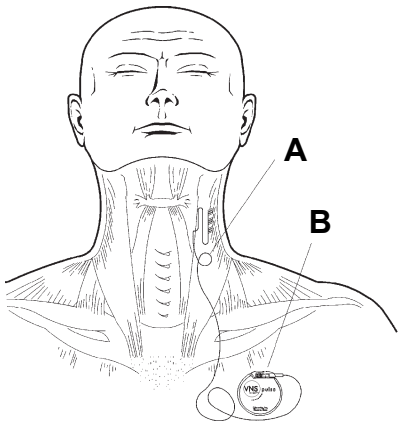
⚠ **Caution**: **Infections related to any implanted device are difficult to treat,** and explantation of the VNS Therapy System may be required.

5.4 Lead and Pocket Location

The generator is usually implanted just below the clavicle in a subcutaneous pocket in the left upper chest. Try to place the generator at rib 4 or above, so the patient can have the maximum flexibility for MRI post-operatively. See *MRI with the VNS Therapy System* instructions for use for details.

Suggested placement for the lead is the area of the left vagus nerve half-way between the clavicle and the mastoid process, with the lead subcutaneously tunneled between the incision site in the neck and the pocket formed in the upper chest (see Figure 16). It is recommended that both the lead body and the generator be positioned on the left side of the body. The VNS Therapy tunneler is recommended for subcutaneous routing of the lead.

Figure 16.Placement of Generator and Lead



A VNS Therapy Lead

B VNS Therapy Generator

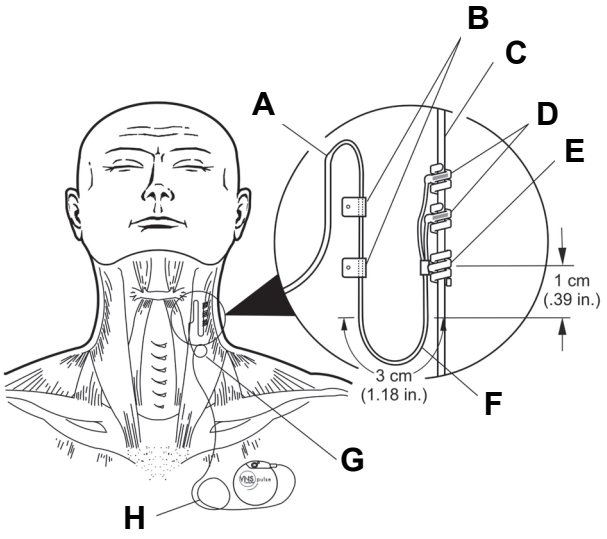
5.5 Begin the Procedure

While the specific surgical approach and techniques for implanting the lead will vary with the implant surgeon, the following detailed instructions are provided for guidance:

1. After administering appropriate anesthesia to the patient, expose the left carotid sheath as it extends along the anterior border of the sternocleidomastoid muscle.
2. Locate and expose *at least 3 centimeters (1.18 inches)* of the left vagus nerve. The recommended stimulation site is a 3-cm section of the vagus nerve, approximately half-way up between the clavicle and the mastoid process, where it is clear of branches (below where the superior and inferior cervical cardiac branches separate from the vagus nerve—see Figure 17 and Figure 19). The nerve usually lies in a posterior groove between the carotid artery and internal jugular vein.

⚠ **Caution: Avoid letting the vagus nerve become dry** during surgery, because dehydration of the nerve can result in nerve damage and swelling.

Figure 17. Electrode Placement



A Lead
B Tie-Downs
C Vagus Nerve
D Helical Electrodes
E Anchor Tether
F Strain Relief Bend
G Strain Relief Loop
H Coiled Extra Lead

3. Create a subcutaneous pocket in the chest below the clavicle for the generator. The pocket depth should not be deeper than 1 inch beneath the skin. It is not recommended to implant the generator below muscle. Doing so may contribute to communication difficulties once implanted.

ⓘ **Note**: It is preferable to place the subcutaneous pocket along the axillary border, at or above rib 4.

5.6 Implant the Lead

To implant the lead, follow these steps:

5.6.1 Choose a Lead

1. Choose the appropriately sized lead (2.0 or 3.0 mm electrode inner diameter) carefully. It should fit snugly without constricting the nerve. The lead (2.0 mm/.08 in) should accommodate most nerves.

Caution: The lead is available in multiple sizes. Since it is not possible to predict in patients what size lead will be needed, **It is recommended that at least one alternate lead size be available in the operating room.** In addition, backups for leads should be available in the event of compromised sterility or damage induced during surgery.

Note: For lead size availability, see "Product Specifications" in the lead-specific Technical Information chapters.

Caution: Do not expose the lead to dust or other similar particulates, because its silicone insulation can attract particulate matter.

Caution: Do not soak the lead in saline or similar solution before implanting it, because this may cause the insulated portions of the connector pin to swell and become difficult to insert into the generator.

5.6.2 Pass the Tunneler and Lead

The tunneler is used to tunnel the lead connector and lead body subcutaneously between the neck incision site and the generator in the chest pocket.

Note: A detailed description of the tunneling tool can be found in the *Tunneler Directions for Use*.

Caution: To maximize system performance and minimize possible mechanical damage to the nerve or lead, pay careful attention to lead routing, lead stabilization, and electrode placement.

Caution: Never route the lead through muscle.

If necessary, the tunneler can be manually shaped to help direct it through the body.

Caution: Do not manually shape the tunneler **more than 25 degrees** because doing so may cause the sleeve to bend or kink.

To pass the tunneler, do the following:

1. Place the bullet-tip end of the tunneler through the neck incision and tunnel subcutaneously toward the chest incision, exerting force on the handle end and directing the tunneler as necessary.

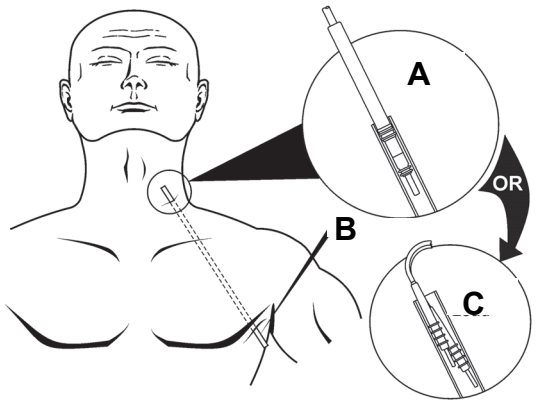
   As an alternative, the lead connector and lead body can be tunneled subcutaneously from the neck incision site to the generator in the chest pocket *after placement of the*

electrodes and anchor tether on the nerve, and placement of strain relief with the tie-downs. (See "Place the Electrodes" and "Provide Strain Relief", respectively.)

2. After the bullet tip has passed from one incision site to the other, unscrew the bullet and withdraw the shaft from the sleeve, leaving the sleeve extended through both incisions (see Figure 18).

Figure 18. Position of Sleeve and Lead Connector(s)

Insert the lead into the sleeve at the neck incision until secure



A Single-Pin Lead

B Tunneler Sleeve

C Dual-Pin Lead

3. With the sleeve in place between the two incisions, carefully insert the lead connector(s) inside the end of the sleeve at the neck incision. For a dual-pin lead, the second connector will form a slight compression fit between the first lead connector tubing and the inside of the sleeve (see Figure 18).
4. Carefully pull the sleeve, along with the lead connector(s), from the chest incision end until the lead connector(s) completely exit(s) the chest incision.
5. Remove the lead connector(s) from the sleeve, leaving the electrode array at the neck incision site.
6. Discard the tunneler after use.

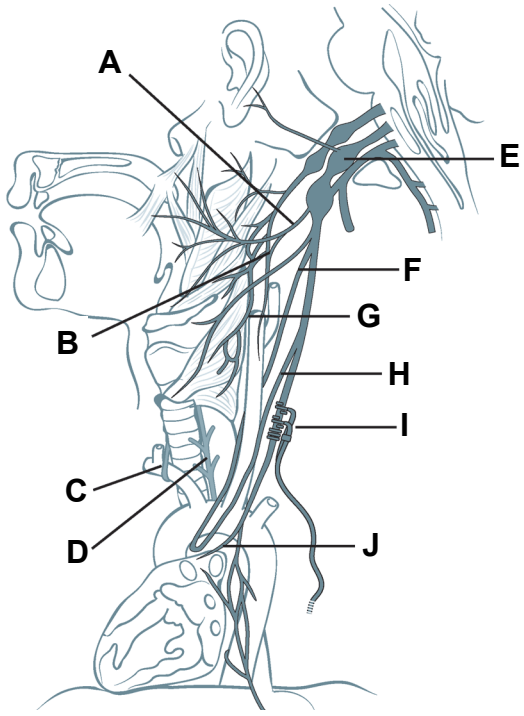
5.6.3 Place the Electrodes

5.6.3.1 Anatomy

It is very important that the surgeon implanting the VNS Therapy System be familiar with vagus nerve anatomy, particularly the cardiac branches. The lead electrodes must not be placed on either the superior or the inferior cervical cardiac branches. **Place the lead below where the superior and inferior cardiac branches separate from the vagus nerve.** Stimulation of either of these two branches during the System Diagnostics (Lead Test) may cause **bradycardia and/or asystole.** Careful dissection laterally on the vagus nerve should aid the physician in determining proper electrode placement. In most but not all patients, the main vagus nerve is the largest of the three nerves. Figure 19 shows the correct anatomical placement of the helices.

⚠ **Caution:** Attachment of lead electrodes must not involve the superior cervical cardiac branch or the inferior cervical cardiac branch of the vagus nerve. Place the electrodes *below* where these two branches separate from the vagus nerve.

Figure 19. Vagus Nerve Anatomy and Placement of the Lead



A Pharyngeal Branch of Vagus Nerve

B Communicating Branch of Vagus Nerve to Carotid Sinus Branch of Glossopharyngeal Nerve

C Right Recurrent Laryngeal Nerve

D Left Recurrent Laryngeal Nerve

E Left Vagus Nerve

F Superior Cervical Cardiac Branch of Vagus Nerve

G Superior Laryngeal Nerve

H Inferior Cervical Cardiac Branch of Vagus Nerve

I Lead Electrode Location

J Thoracic Cardiac Branch of Vagus Nerve

⚠ **Caution**: Excessive manipulation of the vagus nerve during placement of the lead can result in noticeable post-operative hoarseness. Under most circumstances, this condition will resolve without additional medical intervention within three to four weeks, depending on the degree of stress applied to the nerve during surgery. It is not recommended that stimulation treatment be initiated until this condition has resolved, since it could aggravate the condition.

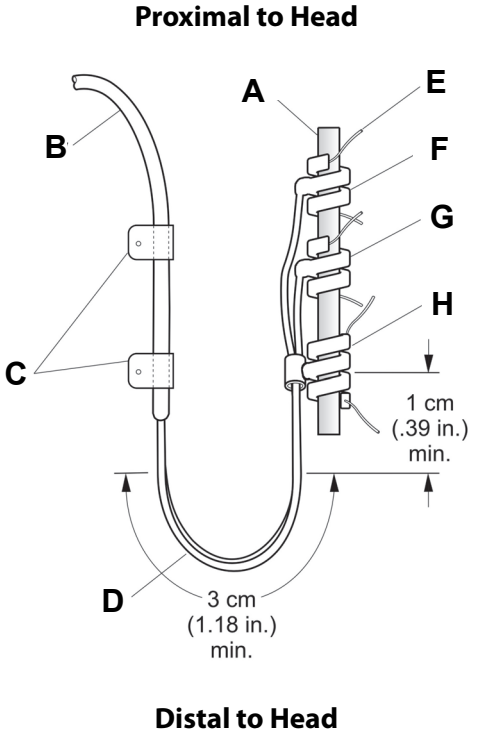
5.6.3.2 Electrode Polarity

The helical electrodes and anchor tether are coiled around the nerve, beginning with the electrode that is farthest from the lead bifurcation (with a green suture embedded in the helical material). This electrode should be nearest (proximal to) the patient's head.

⚠ **Caution: The lead and helical electrodes are very delicate**; be careful not to stretch, pinch, or crush them when using forceps, and not to over-straighten or stretch the helices when coiling them around the nerve, because doing so may damage the electrode or tether. Use soft rubber vessel loops to raise, or lift, the nerve, if necessary.

Depending on the surgeon's preference, the helices can alternately be placed by putting the anchor tether on first (distal to head), next placing the electrode closest to the lead bifurcation (with white suture), and then placing the electrode farthest from the lead bifurcation (with green suture). The polarity of stimulation does not change (see Figure 20).

Figure 20. Electrode Polarity



A Vagus Nerve

B Lead Body

C Tie-Downs

D Strain Relief Bend

E Suture

F Electrode [Green Suture (-)]

G Electrode [White Suture (+)]

H Anchor Tether (Green Suture)

5.6.3.3 Place the helicals around the nerve

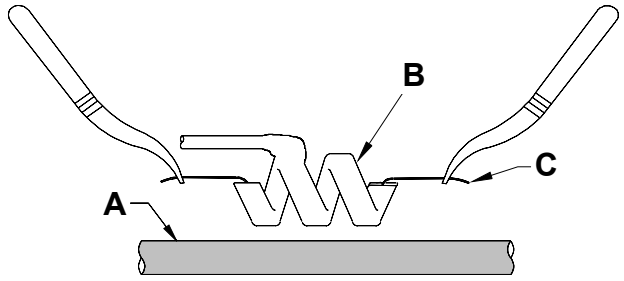
The helicals can be placed on the nerve as described below. As an alternative, each helical can be placed underneath the nerve before it is spread. A silicone sheet may be useful to separate the nerve from tissue during the procedure.

1. Locate the first helical (with green suture)
2. With forceps, gently pull each end of the helical, using the attached sutures to spread the helical (see Figure 21).

⚠ **Caution:** The suture may become dislodged from the helical if product labeling is not followed (i.e., grasping the elastomer and suture to manipulate the helical onto the nerve).

⚠ **Caution:** Do not place sutures directly on the lead body. Doing so may result in insulation damage or wire failure, causing premature failure of the lead.

Figure 21. Spread the Helical



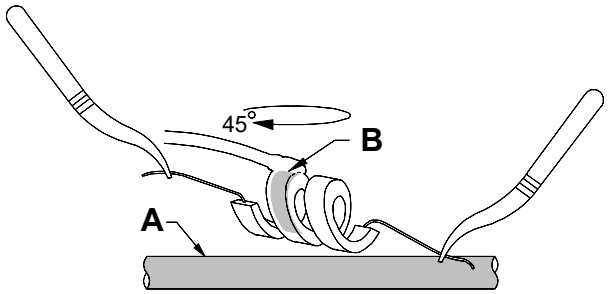
A Nerve

B Helical

C Suture

3. Spread the open helical directly above and parallel to the exposed nerve and turn the helical clockwise at a 45 degree angle to the nerve (see Figure 22).

Figure 22. Turn the Helical

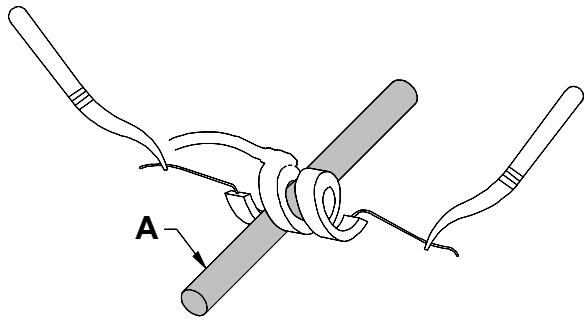


A Nerve

B Metal Ribbon

4. Place the turn of the helical where the lead wire connects to the helical (the section with the metal ribbon) onto the nerve (see Figure 23).

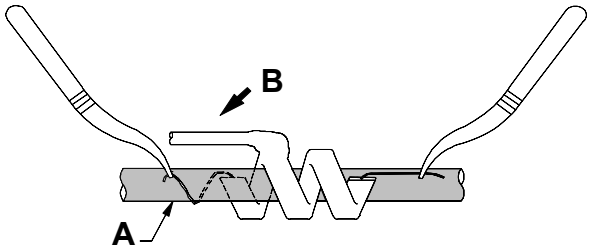
Figure 23. Placement of the Turn



A Nerve

5. Pass the *distal* suture portion of the helical under the nerve and back around so that it encircles the nerve (see Figure 24 and Figure 25).

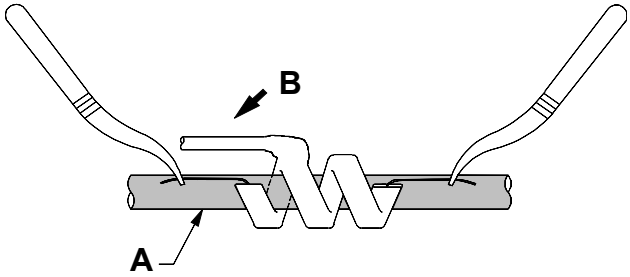
Figure 24. Initial Placement of the Distal Portion of the Helical



A Nerve

B Distal to Head

Figure 25. Helical Placement After Distal Portion Encircles the Nerve

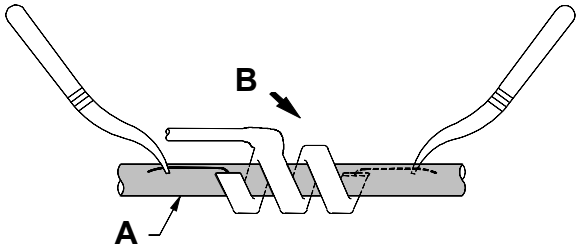


A Nerve

B Distal to Head

6. Pass the *proximal* suture portion of the helical under the nerve and back around so that it encircles the nerve (see Figure 26).

Figure 26. Placement of the Proximal Portion of the Helical



A Nerve

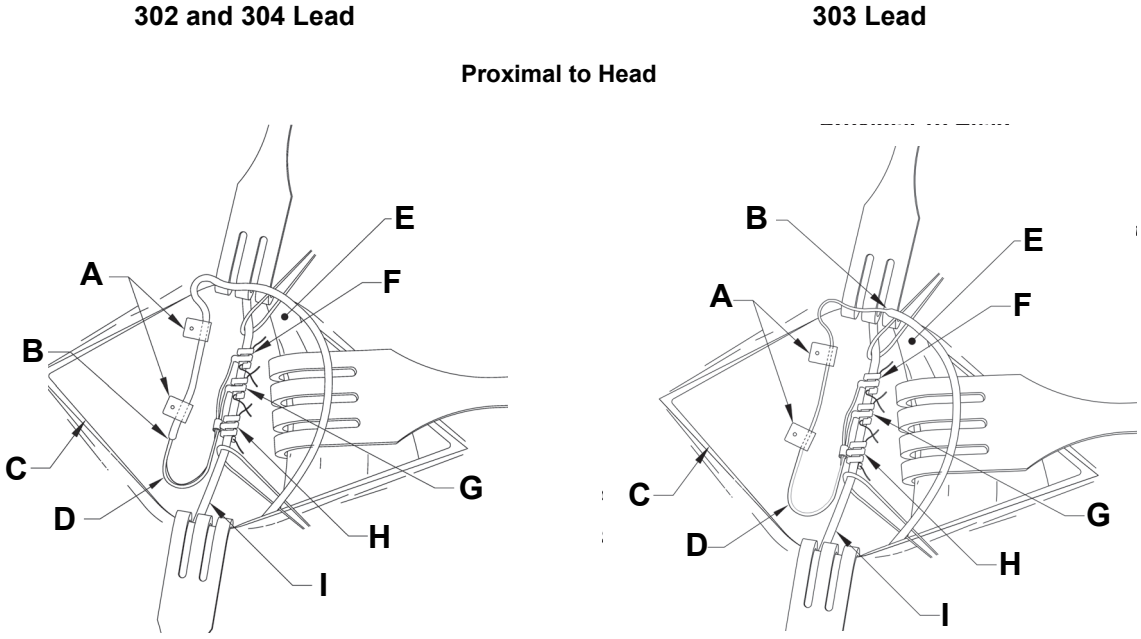
B Proximal to Head

7. Locate the middle helical (with white suture) and repeat steps 2-6.
8. Locate the third helical (with green suture) and repeat steps 2-6.
9. Verify all three helices have been coiled around the nerve, the lead body exits each helical in the same direction, and that the two lead bodies are aligned parallel to each other and to the nerve. The correct placement of the two helical electrodes and anchor tether is shown in Figure 27.

⚠ **Caution:** Sutures that are part of the lead (embedded in the helices of the electrodes and anchor tether) are meant to assist in helical placement around the vagus nerve. These sutures should not be tied to each other or around the nerve, since this may cause nerve damage.

⚠ **Caution: Proper techniques** for attaching the electrodes and the anchor tether to the left vagus nerve are critical to the long-term success of the implant.

Figure 27. Placement of Electrodes and Anchor Tether



A Sutured Tie-Downs

B Lead Transition

C Neck Incision

D Strain Relief Bend

E Sternocleidomastoid Muscle

F Electrode Farthest From Lead Transition [Green Suture (-)]

G Electrode [White Suture (+)]

H Anchor Tether (Green Suture)

I Vagus Nerve

⚠ **Caution:** Never suture the lead or lead body to muscle tissue.

⚠ **Caution:** Always use the tie-downs.

5.6.4 Provide Strain Relief

⚠ **Caution: Proper techniques** for providing adequate strain relief below and above the sternocleidomastoid muscle are critical to the long-term success of the implant.

⚠ **Caution: The lead wire has a potential for fracture** if the recommended strain relief is not provided as described.

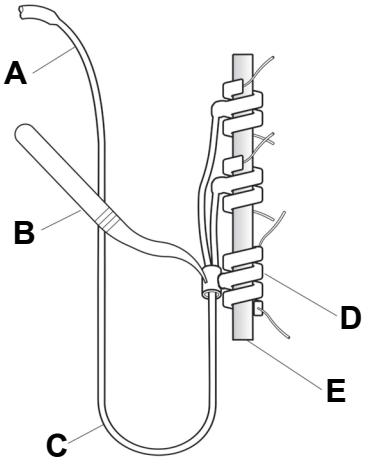
After attaching the two electrodes and the anchor tether, form a strain relief bend and a strain relief loop in the lead to provide adequate slack and allow for neck movement.

5.6.4.1 Form the strain relief bend

To form the *strain relief bend* [see Figure 17, Figure 28 (303 only), and Figure 29], do the following:

1. Form the lead body into a 3-cm (1.18 in) strain relief bend with at least 1 cm (.39 in) of lead routed parallel to the nerve. [303 lead only—Pay careful attention to the previously placed anchor tether and electrodes so they do not come unattached. Slight pressure may be placed against the anchor tether with a surgical instrument to ensure support to the anchor tether while the strain relief bend is being formed (see Figure 28).] The parallel portion can be placed in a pocket formed adjacent to the anchor tether.

Figure 28. (*303 Lead only*) Use of Surgical Tool (e.g., forceps) to Support Anchor Tether During Strain Relief Formation



A Lead

B Surgical Tool

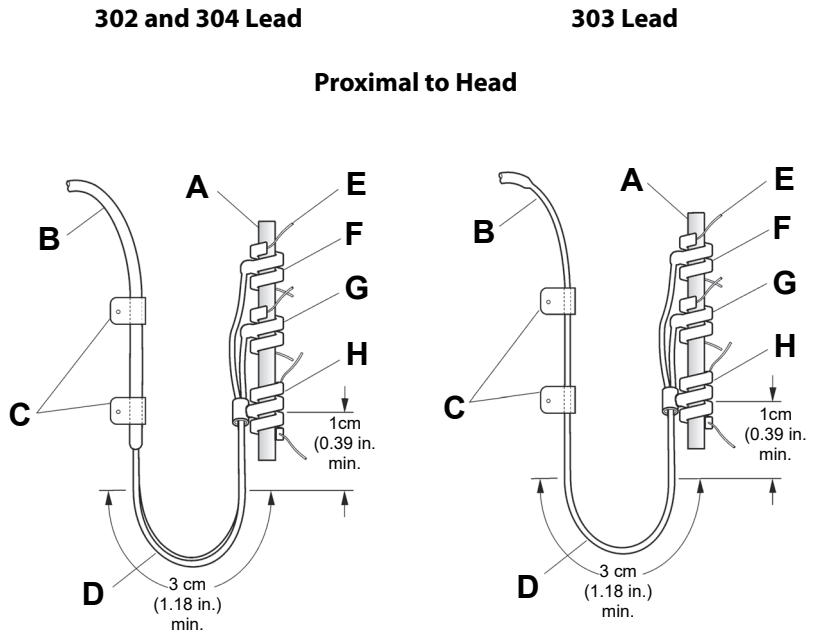
C Strain Relief Bend

D Anchor Tether (Green Suture)

E Vagus Nerve

2. Loosely attach the 3-cm strain relief bend to the adjacent fascia with tie-downs before routing the lead over the muscle. The first tie-down should be positioned laterally to the anchor tether (see Figure 29). Four (or more) tie-downs are provided in the lead sales pack.

Figure 29. Use of Tie-downs in Electrode Placement



A Vagus Nerve	E Suture
B Lead Body	F Electrode [Green Suture (-)]
C Tie Downs	G Electrode [White Suture (+)]
D Strain Relief Bend	H Anchor Tether (Green Suture)

⚠ **Caution:** Sutures that are part of the lead coil are meant to assist in electrode placement around the left vagus nerve. These sutures should *not* be tied to each other since this may cause nerve damage (see Figure 29).

⚠ **Caution: The lead and its electrodes are very delicate,** and care should be taken not to over stretch or crush the helices.

5.6.4.2 Form the strain relief loop

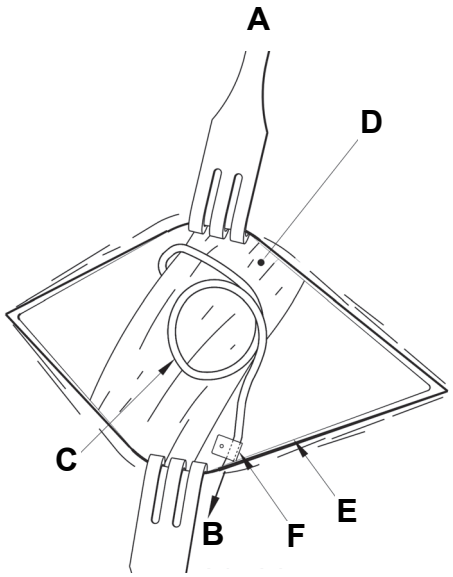
To form the *strain relief loop* (see Figure 30), do the following above the sternocleidomastoid muscle:

1. In the neck, form the lead into a large subcutaneous loop.
2. Loosely attach it to fascia with a tie-down before routing the lead over the clavicle. This strain relief loop should be large enough to provide several inches/centimeters of lead extension when the neck is turned to its maximum stretched positions.

⚠ **Caution: Leave enough extra lead** on both sides of the clavicle to prevent the tension over the clavicle from damaging the lead.

⚠ **Caution:** Placing the sutures directly on the lead body may result in insulation damage or wire failure, causing premature failure of the lead. Use only supplied tie-downs to secure the lead.

Figure 30. Strain Relief Loop



A Proximal To Head

B To Clavicle

C Strain Relief Loop

D Sternocleidomastoid Muscle

E Neck Incision

F Tie-Down

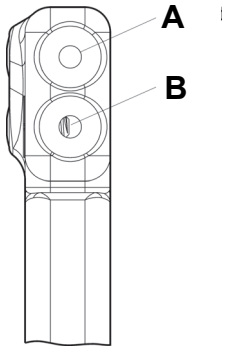
5.7 Connect the Lead to the Generator

⚠ **Caution**: Do not use electrosurgical equipment after the generator has been introduced to the sterile field. Exposure to this equipment may damage the generator.

To connect the lead directly to the generator:

1. Look inside the generator lead receptacle(s) to verify that no obstruction exists and that the setscrew(s) has been backed out adequately to allow full insertion of the connector pin(s). Avoid backing the setscrew(s) out further than needed for lead insertion (see Figure 31). The figure is intended to show the contrast between a blocked and a clear receptacle, and applies to single or dual pin headers.

Figure 31. Generator Receptacle and Setscrew



A Receptacle Hole Clear

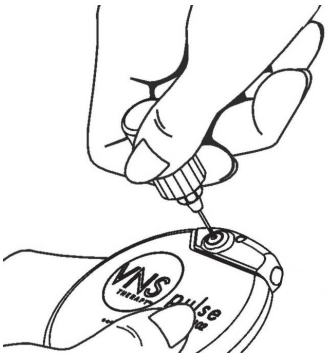
B Setscrew Visible (Manually back out)

2. Keep the hex screwdriver perpendicular to the generator. Insert the hex screwdriver through the center of the setscrew plug(s) to vent back pressure accumulated during lead insertion (see Figure 32).

   ⚠ **Caution:** In the steps below, **always push down on the hex screwdriver while turning it clockwise until it clicks** (begins ratcheting) while ensuring that it is fully inserted in the setscrew. Also, the hex screwdriver must be inserted into the center of the silicone rubber setscrew plug and kept perpendicular to the generator to avoid stripping the setscrew and/or dislodging the setscrew plug.

   ⚠ **Caution:** When using the hex screwdriver, grasp it by the handle only, as shown in Figure 32. Do not grasp any other portion of the hex screwdriver during use, as this may affect its proper function. Touching the metal shaft while the hex screwdriver is engaged with the setscrew can conduct an electrostatic discharge into the device circuitry and may damage the generator.

Figure 32. Hex Screwdriver Position



3. When using a **single-receptacle** generator and VNS Therapy single-pin lead, insert the lead connector pin fully into the generator header. To allow escape of the back pressure created by insertion, leave the tip of the hex screwdriver in the slit in the setscrew plug.

   When using a **dual-receptacle** generator and VNS Therapy dual-pin lead, insert the lead connector pins fully into the appropriate lead receptacles in the generator header. To allow escape of the back pressure created by insertion, leave the tip of the hex screwdriver in the slit in the setscrew plug of the connector being inserted. Insert the lead connector with the white marker band and with the embedded model number and serial number tag into the lead receptacle labeled "+" [see the Dual-Receptacle generator portion of Figure 33]. The remaining lead connector is inserted into the remaining lead receptacle.

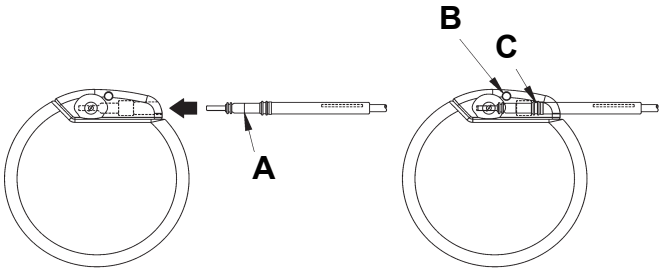
   ⚠ **Caution:** To avoid backing the setscrew out completely when loosening, during surgery, use no more than two counterclockwise turns.

   ⚠ **Caution: Reversal of lead polarity has been associated with an increased chance of bradycardia** in animal studies. It is important to make sure that the lead connector pins in the VNS Therapy dual-pin lead are correctly inserted (white marker band to + connection) into the generator dual receptacles.

Figure 33. Lead Connector(s) Prior to Insertion and Fully Inserted

Single-Receptacle Generator

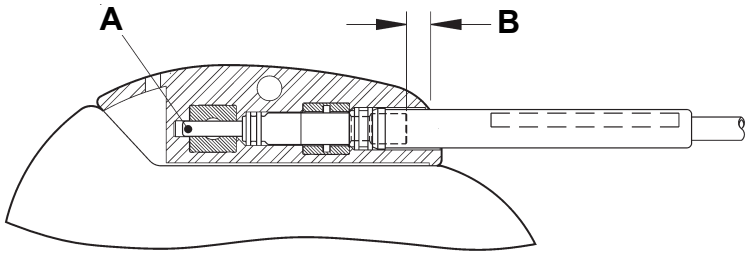
Prior to Insertion **Fully Inserted**



A Lead

B Suture Hole - Always suture to fascia

C Insert fully

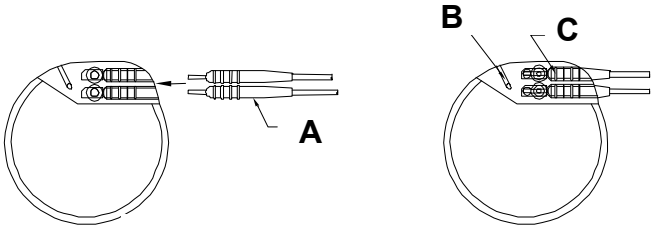


A End of connector pin should be visible in cavity

B Be sure end of connector ring is inside of lead receptacle

Dual-Receptacle Generator

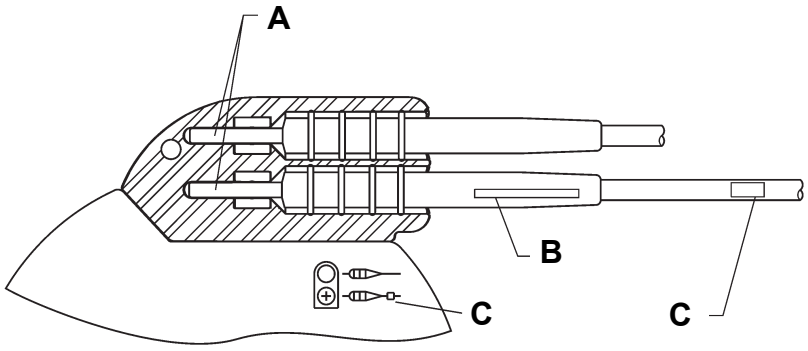
Prior to Insertion **Fully Inserted**



A Lead

B Suture Hole - Always suture to fascia

C Insert fully



A Make sure connector pins are fully inserted

B Serial Number Tag

C White Marker Band

4. With the hex screwdriver still inserted through the setscrew plug, verify that the connector pin is fully inserted. The pin should be visible in the area at the back end of the setscrew connector block. If it is not, remove the pin. To loosen the setscrew, engage the hex screwdriver into the setscrew, and turn it counterclockwise until the connector pin can be fully inserted. Avoid backing the setscrew out further than needed for lead insertion. If using the dual-receptacle generator, repeat this procedure for each setscrew.
5. After verifying that the connector pin(s) has been fully inserted, tighten each setscrew by engaging the setscrew with the hex screwdriver and turning the hex screwdriver clockwise until it begins to click. Always push in on the hex screwdriver while turning it to ensure that the hex screwdriver is fully inserted in the setscrew.

⚠ **Caution:** It is important to do the following:

- Ensure that the lead receptacle(s) is clean and free of obstruction.
- Carefully insert the lead connector pin(s) into the lead receptacle(s) without bending the lead connector(s).
- Visually inspect that the connector pin(s) is clean and completely inserted.
- **Electrical connection to the generator is not established until the setscrew(s) is completely tightened with the hex screwdriver.** Failure to make a good connection can result in HIGH impedance during a System Diagnostics (Lead Test) or erratic stimulation at varying intensity due to rapid, unpredictable changes in lead impedance, which is expected to adversely affect device effectiveness and may have serious safety consequences.
- Gently grasp and pull on lead connector boot(s) (the thick section of the lead) to verify the lead is properly secured inside the lead receptacle(s). Do not pull on lead body (thin section) or use excessive pull force, because doing so may cause lead damage.

5.8 Test the VNS Therapy System

The System Diagnostics (Lead Test), which should be conducted first, is performed with the lead and the generator connected. Thus, if the System Diagnostics (Lead Test) is successful, both components are working properly. However, if the System Diagnostics (Lead Test) fails, either of the two components could be defective, or there may not be a good electrical connection between the generator and the lead connector pin(s). If a defective component is suspected, disconnect the lead and perform the optional Generator Diagnostics (Pre-Implant Test), using the resistor assembly supplied with the accessory pack.

ⓘ **Note:** The programming wand should be placed into a sterile laser arm bag or equivalent (not provided by LivaNova) in order to introduce the programming wand into the sterile field. See the programming system physician's manuals for more information.

⚠ **Caution:** During the intraoperative System Diagnostics (Lead Test), infrequent incidents of bradycardia and/or asystole have occurred. If asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate is encountered during a System Diagnostics (Lead Test) or during initiation of stimulation, physicians should be prepared to follow guidelines consistent with Advanced Cardiac Life Support (ACLS).

Additionally, postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. If a patient has experienced asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate during a System Diagnostics (Lead Test) at the time of initial device implantation, the patient should be placed on a cardiac monitor during initiation of stimulation.

The safety of this therapy has not been systematically established for patients experiencing bradycardia or asystole during VNS Therapy System implantation.

5.8.1 System Diagnostics (Lead Test)

The System Diagnostics is performed intraoperatively when the lead and the generator are connected. The test checks the connection between the lead, generator, and the nerve. Depending on the generator model and programmed Normal Mode output current, different test pulses may be conducted during the test (see Table 31).

Table 31. System Diagnostics (Lead Test)

Normal Mode Output Current	System Diagnostics Behavior		
	M102/102R	M103-106 & 8103	M1000/1000-D
0 mA	1 mA, 500 µsec for approximately 14 seconds	1 mA, 500 µsec for approximately 14 seconds	Delivery of programmed output for approximately 4 seconds, followed by one brief pulse at 0.25 mA for less than 130 µsec.*
>0 mA		One brief pulse at 0.25 mA, 130 µsec, followed by delivery of programmed output for the duration of the programmed ON time.	

*Minor differences in the system diagnostics test exist for M1000 with serial numbers <100,000. Refer to the *Introduction to the VNS Therapy System* chapter for more information

ⓘ **Note**: Once programmed ON, lead impedance measurement readings are automatically performed once every 24 hours for Model 103 and higher generators.

To ensure proper system connection and functionality, perform the test and assess the following:

- Model 102/102R: Verify that the lead impedance status is "OK".

  ⓘ **Note:** See the programming system physician's manuals for lead impedance details.

- Model 103-1000-D and 8103: Verify that System Diagnostics is successful (output current and lead impedance are "OK").

If lead impedance status is not "OK" for Model 102/102R, or if the System Diagnostics fails for Model 103-1000-D and 8103 (output current "LOW" or lead impedance "HIGH" or "LOW") see "Troubleshooting" in the programming system physician's manuals.

⚠ **Caution**: Electrical connection between the generator and the lead connector pin(s) may be at fault.

5.8.2 Generator Diagnostics (Pre-Implant Test)

The optional Generator Diagnostics is performed when the test resistor is attached to the generator in cases of troubleshooting. When the System Diagnostics fails (lead impedance "HIGH" or "LOW"), the Generator Diagnostics can be used to determine whether the lead or the generator is causing the problem. The Generator Diagnostics is performed with the test resistor that is included in the accessory pack. This test will verify that the generator is functioning properly, independent of the lead.

To connect the test resistor to the generator, perform these steps:

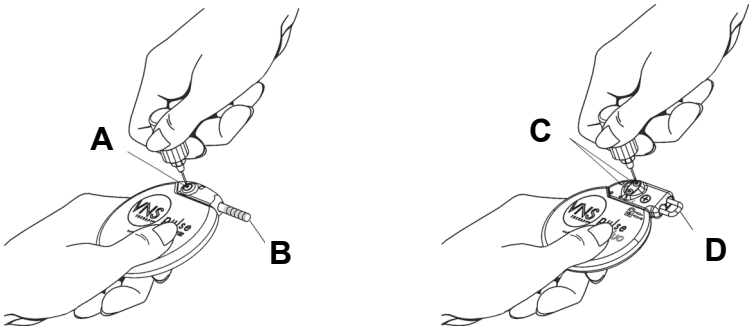
1. Remove the lead connector pin(s) from the lead receptacles by inserting the hex screwdriver through the center of the setscrew plug(s) and loosening the setscrew(s). Avoid backing out the setscrew(s) more than necessary to remove the lead. No more than a half-turn should be required to remove the lead.
2. Insert the connector pin(s) of the resistor assembly into the lead receptacle(s). Be careful while inserting the test resistor pin(s) into the lead receptacle(s). If binding or significant resistance is felt, remove the test resistor, inspect it, and clean it if necessary. Without the use of excessive force, reinsert the test resistor.

   ⓘ **Note:** Fully insert the hex screwdriver into the setscrew and push in on the hex screwdriver whenever the setscrew(s) is being tightened or loosened.

3. When the resistor assembly is in place, tighten the setscrew(s) until the hex screwdriver begins to click (see Figure 34). Again, always push in on the hex screwdriver while turning it to ensure that the hex screwdriver is fully inserted in the setscrew.

Figure 34. Connect the Resistor Assembly

Single-Receptacle Generator **Dual-Receptacle Generator**



A Setscrew Plug

B Resistor Assembly

C Setscrew Plugs (2)

D Resistor Assembly

4. Perform the Generator Diagnostics (Pre-Implant Test).
   - If the Generator Diagnostics (Pre-Implant Test) is successful (lead impedance "OK"), the generator is working properly.
   - If the Generator Diagnostics fails (lead impedance "HIGH" or "LOW"), see "Troubleshooting" in the programming system physician's manuals.
   - If the component is damaged, contact LivaNova and return the item (following the disinfection procedure described in the "Precautions" section of the *Introduction to the VNS Therapy System* chapter), along with a completed Returned Product Form.

Note: See the programming system physician's manuals for details.

5.8.3 Optional Monitoring

Optional physiologic monitoring of VNS Therapy System operation may be done if surgery is performed under local anesthesia. Monitor the patient's voice for signs of hoarseness while gradually increasing the generator output current. After performing the System Diagnostics and obtaining successful results, reset the current to 0 mA.

5.9 Complete the Implantation Procedure

Caution: Do not place the lead slack under the generator, because doing so could result in insulation failure and system malfunction.

Caution: This suturing is important to stabilize the generator and to prevent manipulation by the patient, which could damage the lead wires.

Caution: Do not place the sutures directly around the body of the lead; this could result in insulation failure and system malfunction, and possible lead breakage.

After the testing has been completed, finish the implantation procedure:

1. Place the generator in the chest pocket, coiling the remaining slack of the lead and placing it to the side of the generator. The generator can be placed with either side facing outward.
2. Secure the generator by placing a suture through the suture hole and attaching it to fascia (not to muscle).
3. Perform the second System Diagnostics and verify lead impedance status remains "OK."
4. Interrogate the generator to verify that Normal Mode, Magnet Mode and AutoStim Mode (*Models 106, 1000 and 1000-D generators*) output is 0 mA.
   - Output current: 0 mA
   - Magnet current: 0 mA
   - AutoStim current: 0 mA

Caution: Do not program the generator to an ON or periodic stimulation treatment for at least 14 days after the initial or replacement implantation. Failure to observe this precaution may result in patient discomfort or adverse events.

5. Irrigation of both incision sites with generous amounts of bacitracin or equivalent solution before closure is recommended.
6. Close the surgical incisions. Use cosmetic closure techniques to minimize scarring.
7. Administer antibiotics postoperatively (at the discretion of the physician).

A neck brace can be used by the patient for the first week to help ensure proper lead stabilization.

5.10 Post Implant Patient Identification and Registration Form

5.10.1 Implant Warranty and Registration Form

Included with the generator is an Implant Warranty and Registration form that *must* be completed and the top, white copy returned to LivaNova. Give a copy of this form to the patient or caregiver.

This information, as required by government agencies, becomes part of the LivaNova registry of implantees and is used as a permanent record of implant recipient information.

5.10.2 Patient Magnet Kit

Give the patient a Patient Magnet kit, which contains magnets, accessories, and other patient materials.

5.10.3 Patient Implant Card

The implant card contains information about the patient's VNS Therapy System. Give the card(s) to the patient and/or caregiver after the implant and tell them to complete it with their device information (if not already included), the patient's name, or other identifying information (e.g. patient number) and their treating physician's name and phone number. Tell them to carry it with them at all times.

6 Revision / Replacement / Removal Procedure

6.1 Introduction

Revision, replacement, or removal of the VNS Therapy System or any component of the system may be desired for several reasons:

- Replacement of the generator may be required due to pending End-of-Service (EOS) of the generator or if EOS has been reached and the generator cannot communicate or provide therapy.
- Revision/replacement of the lead may be necessary if a broken or damaged lead is suspected, based on diagnostic testing or x-ray evaluation.
- Removal of the VNS Therapy System may be required in cases of infection or for certain medical procedures (e.g., MRI) contraindicated by the labeling (see the *Introduction to the VNS Therapy System* chapter).

Note: Return explanted or opened and unused component(s) of the VNS Therapy System to the company. A Return Product Kit is available from Technical Support.

The following instructions are intended to be general guidelines. If you have questions about the procedures, contact Technical Support.

6.2 VNS Therapy Components and Surgical Materials

The following materials should be available before performing a revision of any component of the VNS Therapy System.

6.2.1 Dual-Receptacle Generator Replacement

- Primary and backup dual-receptacle generators
- Two backup single-receptacle generators

6.2.2 Single-Receptacle Generator Replacement

- Primary and backup single-receptacle generators

6.2.3 Other Necessary VNS Therapy Components and Surgical Materials

- Primary and backup single-pin leads

  Note: Revision surgeries involving dual-pin leads require the availability of a new single-pin lead, and both single-receptacle and dual-receptacle generators.

- Tunneler
- Accessory pack
- Programming system
- Sterile laser arm bag or equivalent (not provided by LivaNova)
- Soft vessel loops or silicone sheet (not provided by LivaNova)

6.3 VNS Therapy System Revisions

For all revision surgeries, the patient should consent pre-operatively to receiving a new generator and new lead in case either is damaged during the revision surgery.

6.3.1 Procedure — Replacement of the Generator

6.3.1.1 Pre-operative steps

1. Use the programming system to interrogate the existing generator and perform System Diagnostics (Lead Test) before the patient enters the OR.

   Note: For detailed information about Systems Diagnostics, see "Test the VNS Therapy System" in the *Implantation Procedure* chapter.

2. It is recommended that the surgeon review an x-ray of the generator to determine the routing of the lead. This helps to avoid inadvertent damage to the lead during dissection to remove the generator.
3. If System Diagnostics results indicate "HIGH" or "LOW" lead impedance or the x-ray review shows a gross discontinuity in the lead [lead break or pin(s) disconnected], proceed to "Procedure — Replacement of the VNS Therapy Lead".
4. If System Diagnostics results indicate "OK" lead impedance, use the programming system, outside the sterile field in the OR, to interrogate the replacement generator. This ensures clear communication.

   Note: If possible, try to place the replacement generator at rib 4 or above, so the patient can have the maximum flexibility for MRI post-operatively. See *MRI with the VNS Therapy System* instructions for use for details.

5. Program the patient data into the new generator.

6.3.1.2 Intra-operative steps

Caution: Do not use electrosurgical equipment after the new generator has been introduced to the sterile field. Exposure to this equipment may damage the generator.

1. With the lead pin(s) still connected, remove the existing generator from the pocket.
2. Open the new generator sales pack. Use the hex screwdriver to disconnect the existing generator from the implanted lead. Remove the lead connector pin(s) from the lead receptacles by inserting the hex screwdriver through the center of the setscrew plug(s) and loosening the setscrew(s). Avoid backing out the setscrew(s) more than necessary to remove the lead. No more than half a turn should be required to remove the lead.

   Caution: When using the hex screwdriver, grasp it by the handle only. Touching the metal shaft while the hex screwdriver is engaged with the setscrew can conduct an electrostatic discharge into the device circuitry and may damage the generator.

   Note: Extraneous pocket space left behind from the replacement of a larger generator with a smaller generator may increase the likelihood of certain adverse events (e.g., seroma, device manipulation, and device migration).

Note: Replacement of a smaller generator with a larger generator may require enlargement of the generator pocket during surgery. Physicians should assess the potential impact to post-surgical recovery time and likelihood of temporary patient discomfort due to surgical alteration of the generator pocket.

3. Connect the replacement generator to the lead following the steps in the "Connect the Lead to the Generator" section in the *Implantation Procedure* chapter and complete the remainder of the implantation procedure.

6.3.2 Procedure — Replacement of the VNS Therapy Lead

Note: Consult the prescribing physician before the surgery to determine parameter settings following placement of the new generator.

6.3.2.1 Pre-operative steps

1. Use the programming system to interrogate the existing generator and perform System Diagnostics (Lead Test) before the patient enters the OR. It is recommended that the surgeon review x-rays to confirm the existence of a lead discontinuity [lead break or pin(s) disconnected], if possible.
2. If System Diagnostics results indicate "OK" lead impedance, there is no gross discontinuity in the lead from the x-ray review, and a short-circuit condition is not suspected, the implanted lead is functioning properly. Reassess proceeding with surgery or, if replacement of the generator is still desired, proceed to "Procedure — Replacement of the Generator".
3. If System Diagnostic results indicate "HIGH" or "LOW" lead impedance or a gross lead discontinuity is observed, surgical intervention is required. Use the programming system, outside the sterile field in the OR, to interrogate all potential replacement generators. This ensures clear device communication.
4. Proceed to "Intra-operative steps" below.

6.3.2.2 Intra-operative steps

Note: For complete troubleshooting steps, see "Troubleshooting" in the programming system physician's manuals.

6.3.2.2.1. "HIGH" lead impedance on System Diagnostics

If "HIGH" lead impedance is reported, perform the following steps:

1. With lead pin(s) still connected, remove the existing generator from the pocket.
2. Open the accessory pack and remove the hex screwdriver and test resistor.
3. Remove the lead connector pin(s) from the lead receptacle(s) by inserting the hex screwdriver through the center of the setscrew plug(s) and loosening the setscrew(s). Avoid backing out the setscrew(s) more than necessary to remove the lead. No more than a half turn should be required to remove the lead.
4. If foreign material (e.g., blood) is observed in the generator receptacle(s), flush the receptacle(s) with saline to remove the foreign material. Drain the excess fluid from the receptacle(s). Do not place any object (other than the connector pin) into the receptacle. Use saline to clean the lead connector pin(s), then wipe dry.

5. Re-insert the existing lead connector pin(s) into the existing generator following proper lead insertion techniques.

   Note: For proper lead insertion techniques, see "Connect the Lead to the Generator" in the *Implantation Procedure* chapter.

   Caution: Visually inspect that the connector pin(s) is clean and completely inserted.

6. Introduce the programming system into the sterile field with a sterile laser arm bag (or equivalent) and perform an interrogation followed by System Diagnostics.
7. Record System Diagnostics results.

   - If the results indicate "OK" lead impedance, the previous "HIGH" lead impedance was resolved and the system appears to be functioning properly. Assess replacement of the generator.

     If replacement of the generator is not desired, verify that all relevant steps outlined in "Test the VNS Therapy System" section of the *Implantation Procedure* chapter have been completed. Finish the procedure by following the steps in "Complete the Implantation Procedure" section in the *Implantation Procedure* chapter.

     If replacement of the generator is desired, open a new compatible generator sales pack. Connect the replacement generator to the lead following the steps in the "Connect the Lead to the Generator" section in the *Implantation Procedure* chapter and complete the remainder of the implantation procedure. Ensure appropriate patient data has been programmed into the new generator.

     Note: The prescribing physician will program the stimulation parameters post-operatively based on the patient's tolerance to the stimulation.

   - If System Diagnostics results continue to report "HIGH" lead impedance, perform Generator Diagnostics (Pre-Implant Test) with the test resistor assembly from the accessory pack to verify that the generator is functioning properly, independent of the lead. To perform Generator Diagnostics, follow the steps in "Generator Diagnostics (Pre-Implant Test)" below.

6.3.2.2.2. "LOW" lead impedance on System Diagnostics

Note: For complete troubleshooting steps see "Troubleshooting" in the programming system physician's manuals.

If System Diagnostics report "LOW" lead impedance, perform Generator Diagnostics (Pre-Implant Test) with the test resistor assembly from the accessory pack to verify that the generator is functioning properly, independent of the lead.

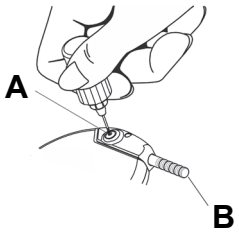
To perform Generator Diagnostics (Pre-Implant Test), follow the steps in "Generator Diagnostics (Pre-Implant Test)" below.

6.3.2.3 Generator Diagnostics (Pre-Implant Test)

1. Insert the connector pin(s) of the resistor assembly into the lead receptacle(s). Be careful while inserting the test resistor pin(s) into the lead receptacle(s). If binding or significant resistance is felt, remove the test resistor, inspect it, and clean it if necessary. Without the use of excessive force, reinsert the test resistor.
2. When the resistor assembly is in place, tighten the setscrew(s) until the hex screwdriver begins to click (see Figure 35). Always push in on the hex screwdriver while turning it to ensure that the hex screwdriver is fully inserted in the setscrew.

Figure 35. Connect the Resistor Assembly

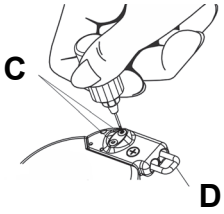
Single-Pin Receptacle



A Setscrew Plug

B Resistor Assembly

Dual-Pin Receptacle



C Setscrew Plugs (2)

D Resistor Assembly

3. Perform Generator Diagnostics (Pre-Implant Test).

Note: For details, see the programming system physician's manuals.

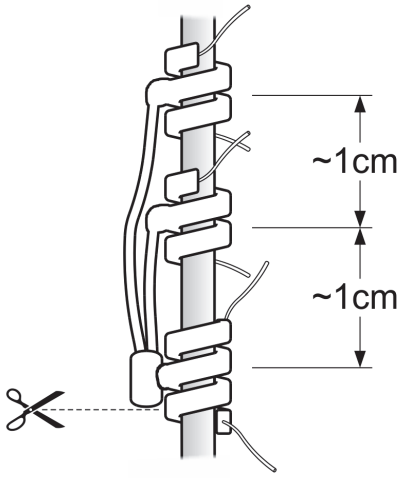
- If Generator Diagnostics results indicate "HIGH" or "LOW" lead impedance, call Technical Support.
- If Generator Diagnostics results indicate "OK" lead impedance, the implanted lead should be replaced and Generator replacement assessed.

6.3.2.4 Remove existing helices and lead

⚠ **Caution:** Lead replacement or removal is a medical judgment that must be carefully weighed against the known and unknown risks of surgery. At present there are no known long-term hazards or risks associated with leaving the lead implanted, beyond those mentioned in this physician's manual.

1. Open the neck incision and locate the vagus nerve/helices interface.
2. Assess the degree of fibrotic encapsulation to determine if the entire lead can be removed safely.
   - If removal of the existing helices can be accomplished, the new helices may be placed in the same location.
   - If complete removal of the helices from the nerve is not possible, transect as much of the lead as possible. With ≤ 2 cm of the lead remaining (see Figure 36) a full body MRI using the body coil to transmit RF is allowable. (See the *MRI with the VNS Therapy System* instructions for use for details.).
   - If it is not possible to leave ≤ 2 cm, then MRI can still be performed for brain or extremity imaging with the appropriate type of T/R coil. (See the *MRI with the VNS Therapy System* instructions for use for details.).

Figure 36. Transected Lead (≤ 2 cm)



3. The replacement helices can be placed above or below the existing helices if they must remain.

6.3.2.5 Complete the procedure

Complete the remainder of the implant procedure per the *Implantation Procedure* chapter, starting with the steps in the "Implant the lead" section. Pay particular attention to all cautions and warnings regarding the cardiac branches.

ⓘ **Note**: The prescribing physician will program the stimulation parameters post-operatively after the recommended 2-week recovery period to allow the nerve to heal.

6.4 Removal of the VNS Therapy System

If removal is medically necessary, LivaNova recommends removing as much of the VNS Therapy System as can be safely accomplished:

- Assess the degree of fibrotic in-growth in and around the helices.
- Remove the entire system, if possible.
- If fibrotic encapsulation hinders safe removal of the entire system, transect as much of the lead wire as possible (see Figure 36).
- Removal of the generator alone does not alter the hazards associated with certain MRI procedures.

  Note: For detailed information, see the *MRI with the VNS Therapy System* instructions for use.

- Diathermy procedures are contraindicated for patients with any portion of the VNS Therapy System remaining in the body.

  Note: For detailed information regarding the use of diathermy with VNS, see the *Introduction to the VNS Therapy System* chapter.

7 Troubleshooting

7.1 Model 102 and 102R

7.1.1 "Patient Cannot Feel Stimulation" at Follow-up Visit (Models 102-102R)

A patient may not feel stimulation if any of the following situations exist:

- Patient has become accustomed to the programmed setting
- Device is approaching its end of service (EOS)
- "High" lead impedance
- Short-circuit condition within the lead
- Generator issue

To determine the cause of the situation, perform the following steps:

4. Interrogate the generator.
5. Perform a System Diagnostics (Lead Test) and record the results.

IF…	*THEN…*
Model 250 version 11.0 software and below: If the DC-DC Converter Code is "0" or there has been a significant decrease in DC-DC Converter Code value (e.g., "3" to "1") in respect to prior System Diagnostics **Model 3000 version 1.0 software and above:** If the impedance is ≤ 1700 Ohms or if there has been a sudden change in impedance range (e.g., 4100-5200 Ohms to 1800-2800) in respect to prior System Diagnostics	A short-circuit condition may be present within the lead and the patient may not be receiving the intended therapy. For more information, see "Short-circuit conditions within the lead" in the*102/102R Technical Information* chapter.
Model 250 version 11.0 software and below: If the DC-DC Converter Code is not "0", there has been no significant decrease in DC-DC Converter Code value (e.g., "3" to "1") in respect to prior System Diagnostics, and the System Diagnostics test indicates the lead impedance is "OK" **Model 3000 version 1.0 software and above:** If System Diagnostics test indicates the lead impedance is OK	The system is functioning properly and the patient could have become accustomed to the settings, as do many patients.
If the System Diagnostics test indicates the lead impedance is "High".	See "Troubleshooting" in the programming system physician's manuals.

⚠ **Caution:** For the System Diagnostics (Lead Test), the software automatically programs the generator to 1 mA, 500 µsec, and 20 Hz. Patients whose generator output current is normally *less* than these values may experience increased sensation, coughing, a flushed face, or other effects. For a complete list of possible adverse events, see "Potential Adverse Events" in the indication-specific information chapters.

6. Perform a Normal Mode Diagnostics test and record the results.

IF…	***THEN…***
The Normal Mode Diagnostics test indicates the Output Current is "LIMIT"	The generator cannot deliver programmed output. Consider reducing output current or frequency and widening the pulse width.
The Normal Mode Diagnostics test indicates the Output Current is "OK"	The generator can deliver the programmed output current. **Note**: To obtain accurate information from the device diagnostics, the generator must be programmed to a **minimum** of 0.75 mA, 15 Hz, and **at least** 30 seconds ON time.
The Normal Mode Diagnostics test indicates "HIGH" lead impedance	See the "Troubleshooting" in the programming system physician's manuals.

7. If further assistance is needed, call Technical Support.

7.2 Model 103, 104, 105, 106, 1000, 1000-D and 8103

7.2.1 "Patient Cannot Feel Stimulation" at Follow-up Visit (Models 103-106, 1000/1000-D and 8013)

A patient may not feel stimulation under any of these conditions:

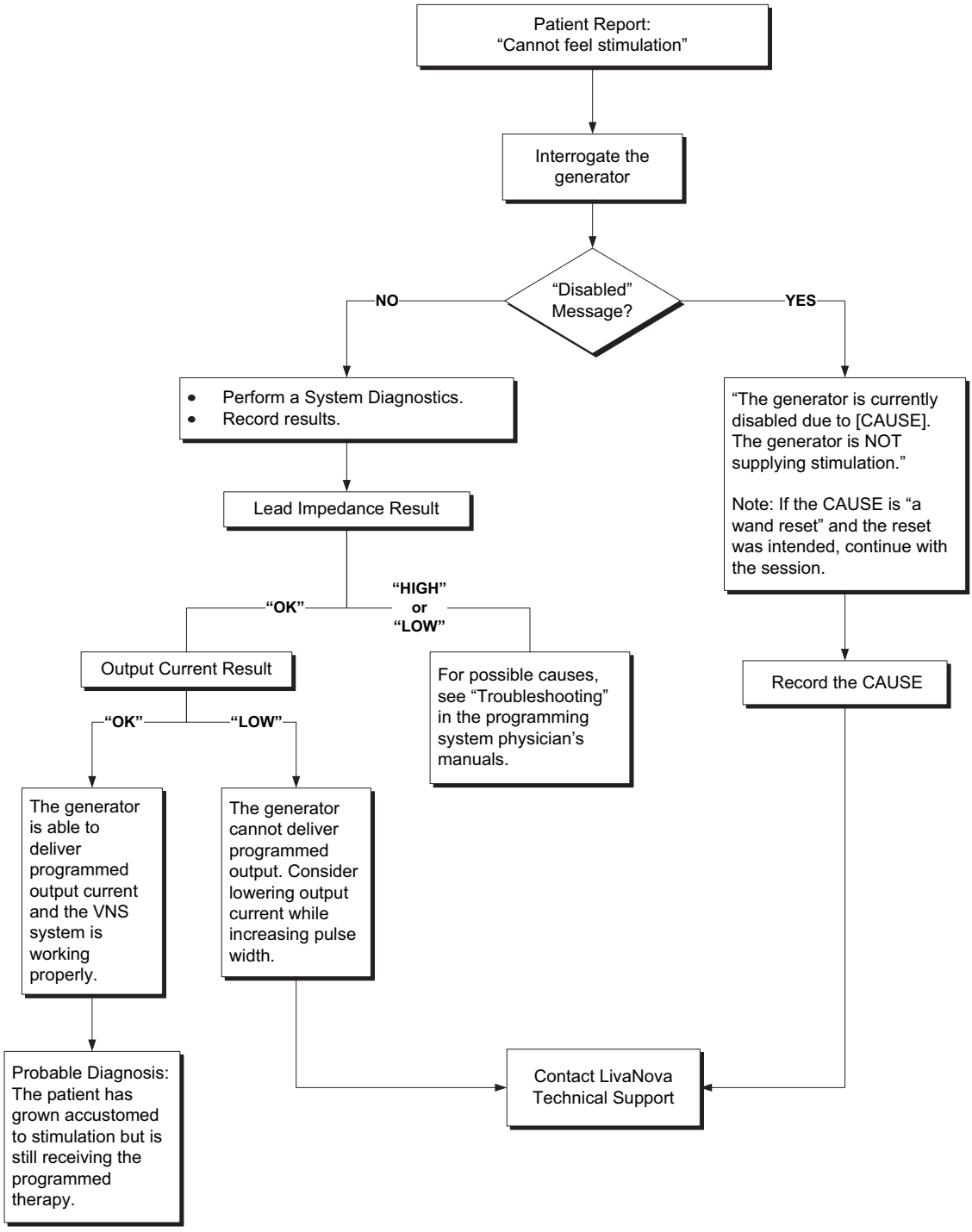
- Patient has become accustomed to the programmed setting
- Generator battery at end of service (EOS)
- "High" lead impedance
- Defective generator
- Disabled generator
- Short-circuit condition within the lead

To determine the cause of the condition, perform these steps (see Figure 37):

1. Interrogate the generator.
   - If the following message appears, call Technical Support: "The generator is currently disabled due to [CAUSE]". The generator is NOT supplying stimulation.

     Note: If the CAUSE is "a wand reset" and the reset was intended, continue with the session.
2. Perform a System Diagnostics and record the results.
   - If the output current reports "OK" and lead impedance reports "OK," then the generator is able to deliver the programmed therapy and the patient may have become accustomed to the stimulation, as do many patients.
   - If the output current reports "OK" and lead impedance reports "LOW" (≤ 600 Ohms), then there is a possibility of a short-circuit condition within the lead. See "Troubleshooting" in the programming system physician's manuals.
   - If the output current reports "LOW" and lead impedance reports "OK," then the generator cannot deliver programmed output due to increased impedance. Consider lowering the output current while increasing pulse width.
   - If the output current reports "LOW" and lead impedance reports "HIGH" (≥ 5300 Ohms), see "Troubleshooting" in the programming system physician's manuals.
3. For further assistance, call Technical Support.

Figure 37. "Patient Cannot Feel Stimulation" at Follow-Up Visit (Models 103-106, 1000/1000-D and 8103)



8 Limited Replacement Warranty

LivaNova USA, Inc. warrants the VNS Therapy generator and lead against any defects due to faulty material or workmanship for a period of two (2) years from the date of implantation. This warranty applies only to the original purchaser of the VNS Therapy generator and lead and the patient implanted with it. This Limited Replacement Warranty also applies only when the product is used in accordance with the product's physician's manual and excludes damage due to improper handling, defacing, accident (including dropping), or misuse. This product is not warranted when used or implanted by a person(s) not trained in or familiar with the VNS Therapy System and Programming System physician's manuals. This Limited Replacement Warranty is not a representation that any one VNS Therapy generator or lead will last the entire time of the Limited Replacement Warranty.

In no event shall LivaNova USA, Inc. be liable for any special, incidental, indirect, or consequential damages based on the failure of the device to function within normal tolerances, or resulting from damage to the device by external forces, whether the claim is based on warranty, contract, tort, or otherwise, or in connection with the purchase, use, or surgical implantation of this device or associated components or costs over and above the original purchase price from LivaNova USA, Inc.

To qualify for the Limited Replacement Warranty, the following conditions must be met:

1. A properly completed Implant and Warranty Registration form for both the VNS Therapy generator and the VNS Therapy lead must be returned to LivaNova USA, Inc. within sixty (60) days of device implantation;
2. The battery in the VNS Therapy generator cannot have been depleted as a result of programming to unusually high output currents, pulse widths, or duty cycles, which will cause a high energy/current drain;
3. The VNS Therapy lead cannot have been cut or damaged due to excessive handling or abuse during surgical implantation;
4. The product must have been used and prescribed in accordance with the VNS Therapy System and Programming System physician's manuals;
5. The VNS Therapy generator or lead must have been implanted prior to its "Expiration Date;"
6. The defective VNS Therapy generator or lead must be returned to LivaNova USA, Inc. with an accompanying Authorization number, available from Technical Support at 1 (866) 882-8804 (U.S. and Canada) or +1 (281) 228-7330 (Worldwide), and confirmed defective by the Quality Assurance Department; and
7. All returned VNS Therapy generators and leads shall become the property of LivaNova USA, Inc.

> ⚠ **Caution: Return explanted generators and leads** to LivaNova USA, Inc. for examination and proper disposal, along with a completed Returned Product Report form. Before returning the lead, disinfect the device components with Betadine®, Cidex® soak, or another similar disinfectant, and double-seal them in a pouch or other container properly labeled with a biohazard warning.

If the VNS Therapy generator or lead becomes defective within the warranty period, contact LivaNova USA, Inc. Customer Service for a no-cost replacement. LivaNova USA, Inc. reserves the right to replace a defective product with the most comparable product currently available.

Returned biohazardous product should be clearly identified as such on the outside surface of the package.

No implied warranty, including, but not limited to, any implied warranty of merchantability or fitness for a particular purpose, shall extend beyond the period specified above. This replacement warranty shall be the exclusive remedy available to any person. No person has any authority to bind LivaNova USA, Inc. to any representation, condition, or warranty except this Limited Replacement Warranty.

While this warranty gives you specific legal rights, you may also have other rights that vary from state to state or that encroach upon the above.

9 Appendices

9.1 Appendix A - Model 102/102R Battery Longevity and Programmed Setting Choices

9.1.1 Nominal Longevity Estimates from Beginning of Life (BOL) to End of Service (EOS)

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	10	130	2	15.3	11.3	9.5
1	10	130	3	15.1	11.1	9.2
1	10	130	5	14.8	10.5	8.7
1	10	130	7	14.4	9.8	8.0
1	10	500	2	14.2	9.6	7.7
1	10	500	3	13.8	8.9	7.1
1	10	500	5	13.0	7.9	6.1
1	10	500	7	12.4	7.3	5.6
1	10	1000	2	12.8	7.6	5.9
1	10	1000	3	12.2	6.9	5.3
1	10	1000	5	10.9	5.7	4.2
1	10	1000	7	10.3	5.2	3.8
1	20	130	2	14.2	9.5	7.6
1	20	130	3	13.8	9.0	7.2
1	20	130	5	13.4	8.5	6.7
1	20	130	7	12.7	7.6	5.9
1	20	500	2	12.3	7.1	5.4
1	20	500	3	11.7	6.5	4.9
1	20	500	5	10.6	5.5	4.0
1	20	500	7	10.0	4.9	3.6
1	20	1000	2	10.3	5.2	3.8
1	20	1000	3	9.6	4.6	3.3
1	20	1000	5	8.2	3.6	2.6
1	20	1000	7	7.5	3.2	2.3
1	30	130	2	13.1	8.1	6.3
1	30	130	3	12.7	7.6	5.9
1	30	130	5	12.2	7.0	5.3
1	30	130	7	11.4	6.2	4.6
1	30	500	2	10.9	5.7	4.2
1	30	500	3	10.2	5.1	3.7
1	30	500	5	9.0	4.2	3.0
1	30	500	7	8.3	3.7	2.6
1	30	1000	2	8.7	3.9	2.8

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	30	1000	3	7.9	3.5	2.4
1	30	1000	5	6.6	2.7	1.8
1	30	1000	7	5.9	2.3	1.6
1.5	10	130	2	14.7	10.3	8.4
1.5	10	130	3	14.4	9.8	7.9
1.5	10	130	5	13.7	8.8	7.0
1.5	10	130	7	13.8	8.9	7.1
1.5	10	500	2	12.4	7.3	5.6
1.5	10	500	3	12.0	6.7	5.1
1.5	10	500	5	10.9	5.7	4.3
1.5	10	500	7	11.2	6.0	4.5
1.5	10	1000	2	10.3	5.2	3.8
1.5	10	1000	3	9.6	4.6	3.3
1.5	10	1000	5	8.4	3.8	2.7
1.5	10	1000	7	8.9	4.1	2.9
1.5	20	130	2	13.1	8.0	6.2
1.5	20	130	3	12.6	7.5	5.8
1.5	20	130	5	11.8	6.5	4.9
1.5	20	130	7	11.8	6.6	5.0
1.5	20	500	2	10.0	5.0	3.6
1.5	20	500	3	9.4	4.5	3.2
1.5	20	500	5	8.2	3.7	2.6
1.5	20	500	7	8.6	3.9	2.8
1.5	20	1000	2	7.5	3.2	2.2
1.5	20	1000	3	6.8	2.8	2.0
1.5	20	1000	5	5.7	2.2	1.5
1.5	20	1000	7	6.2	2.4	1.7
1.5	30	130	2	11.8	6.5	4.9
1.5	30	130	3	11.3	6.1	4.5
1.5	30	130	5	10.3	5.2	3.8
1.5	30	130	7	10.4	5.3	3.9
1.5	30	500	2	8.4	3.8	2.7
1.5	30	500	3	7.7	3.3	2.4
1.5	30	500	5	6.6	2.7	1.9
1.5	30	500	7	7.0	2.9	2.0
1.5	30	1000	2	5.9	2.3	1.6
1.5	30	1000	3	5.3	2.0	1.4
1.5	30	1000	5	4.3	1.6	1.1
1.5	30	1000	7	4.7	1.8	1.2
2	10	130	2	14.1	9.4	7.5
2	10	130	3	13.5	8.5	6.7

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
2	10	130	5	13.5	8.5	6.7
2	10	130	7	13.7	8.8	7.0
2	10	500	2	11.2	6.0	4.4
2	10	500	3	10.1	5.0	3.6
2	10	500	5	10.5	5.4	3.9
2	10	500	7	11.1	5.9	4.3
2	10	1000	2	8.4	3.8	2.7
2	10	1000	3	7.4	3.1	2.2
2	10	1000	5	7.9	3.5	2.4
2	10	1000	7	8.6	3.9	2.8
2	20	130	2	12.2	7.0	5.3
2	20	130	3	11.3	6.0	4.5
2	20	130	5	11.4	6.2	4.6
2	20	130	7	11.7	6.5	4.9
2	20	500	2	8.4	3.8	2.7
2	20	500	3	7.3	3.1	2.2
2	20	500	5	7.8	3.4	2.4
2	20	500	7	8.4	3.8	2.7
2	20	1000	2	5.5	2.1	1.5
2	20	1000	3	4.8	1.8	1.2
2	20	1000	5	5.3	2.0	1.4
2	20	1000	7	5.9	2.3	1.6
2	30	130	2	10.8	5.6	4.1
2	30	130	3	9.7	4.7	3.4
2	30	130	5	9.9	4.9	3.5
2	30	130	7	10.2	5.1	3.8
2	30	500	2	6.8	2.8	1.9
2	30	500	3	5.7	2.2	1.5
2	30	500	5	6.2	2.5	1.7
2	30	500	7	6.8	2.8	1.9
2	30	1000	2	4.0	1.4	1.0
2	30	1000	3	3.6	1.3	0.8
2	30	1000	5	4.0	1.4	1.0
2	30	1000	7	4.6	1.7	1.1
3.5	10	130	2	12.6	7.5	5.7
3.5	10	130	3	12.9	7.8	6.0
3.5	10	130	5	13.3	8.3	6.5
3.5	10	130	7	13.5	8.6	6.8
3.5	10	500	2	8.6	3.9	2.8
3.5	10	500	3	9.2	4.4	3.1
3.5	10	500	5	10.1	5.0	3.7

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
3.5	10	500	7	10.8	5.6	4.1
3.5	10	1000	2	5.8	2.3	1.6
3.5	10	1000	3	6.5	2.6	1.8
3.5	10	1000	5	7.5	3.2	2.3
3.5	10	1000	7	8.3	3.7	2.6
3.5	20	130	2	10.2	5.1	3.8
3.5	20	130	3	10.6	5.5	4.0
3.5	20	130	5	11.1	5.9	4.4
3.5	20	130	7	11.5	6.3	4.7
3.5	20	500	2	5.9	2.3	1.6
3.5	20	500	3	6.5	2.6	1.8
3.5	20	500	5	7.4	3.1	2.2
3.5	20	500	7	8.1	3.5	2.5
3.5	20	1000	2	3.6	1.3	0.9
3.5	20	1000	3	4.1	1.5	1.0
3.5	20	1000	5	5.0	1.9	1.3
3.5	20	1000	7	5.6	2.2	1.5
3.5	30	130	2	8.6	3.9	2.8
3.5	30	130	3	9.0	4.2	3.0
3.5	30	130	5	9.6	4.6	3.3
3.5	30	130	7	10.0	4.9	3.6
3.5	30	500	2	4.5	1.7	1.1
3.5	30	500	3	5.0	1.9	1.3
3.5	30	500	5	5.8	2.3	1.6
3.5	30	500	7	6.5	2.6	1.8
3.5	30	1000	2	2.7	0.9	0.6
3.5	30	1000	3	3.0	1.0	0.7
3.5	30	1000	5	3.7	1.3	0.9
3.5	30	1000	7	4.3	1.6	1.1

9.1.2 Worst Case Longevity Estimates from Beginning of Life (BOL) to Near End of Service (N EOS)

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	10	130	2	9.3	7.1	6.0
1	10	130	3	9.3	7.2	6.1
1	10	130	5	8.8	6.2	5.1
1	10	130	7	8.8	6.2	5.0
1	10	500	2	9.1	6.8	5.7
1	10	500	3	8.9	6.4	5.2
1	10	500	5	8.2	5.3	4.2
1	10	500	7	8.0	5.0	3.9
1	10	1000	2	8.3	5.4	4.3
1	10	1000	3	8.0	5.1	4.0
1	10	1000	5	7.2	4.1	3.1
1	10	1000	7	6.8	3.7	2.8
1	20	130	2	9.1	6.7	5.6
1	20	130	3	8.9	6.4	5.3
1	20	130	5	8.6	5.9	4.8
1	20	130	7	8.2	5.3	4.2
1	20	500	2	8.2	5.2	4.2
1	20	500	3	7.8	4.8	3.7
1	20	500	5	6.9	3.8	2.8
1	20	500	7	6.7	3.6	2.7
1	20	1000	2	6.9	3.7	2.8
1	20	1000	3	6.6	3.5	2.6
1	20	1000	5	5.7	2.8	2.0
1	20	1000	7	5.2	2.4	1.7
1	30	130	2	8.6	5.9	4.7
1	30	130	3	8.4	5.6	4.4
1	30	130	5	8.0	5.0	3.9
1	30	130	7	7.5	4.5	3.4
1	30	500	2	7.4	4.3	3.3
1	30	500	3	7.0	3.9	2.9
1	30	500	5	6.1	3.0	2.2
1	30	500	7	5.7	2.8	2.0
1	30	1000	2	5.8	2.8	2.0
1	30	1000	3	5.6	2.7	1.9
1	30	1000	5	4.7	2.1	1.5
1	30	1000	7	4.1	1.7	1.2
1.5	10	130	2	9.2	6.9	5.9
1.5	10	130	3	8.9	6.5	5.4

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1.5	10	130	5	8.3	5.4	4.3
1.5	10	130	7	8.3	5.5	4.4
1.5	10	500	2	7.9	4.9	3.8
1.5	10	500	3	7.8	4.8	3.7
1.5	10	500	5	7.1	4.0	3.0
1.5	10	500	7	7.2	4.1	3.1
1.5	10	1000	2	7.0	3.9	2.9
1.5	10	1000	3	6.6	3.5	2.6
1.5	10	1000	5	5.8	2.8	2.0
1.5	10	1000	7	6.0	3.0	2.2
1.5	20	130	2	8.5	5.7	4.6
1.5	20	130	3	8.2	5.3	4.2
1.5	20	130	5	7.6	4.5	3.5
1.5	20	130	7	7.6	4.6	3.5
1.5	20	500	2	6.9	3.8	2.8
1.5	20	500	3	6.5	3.4	2.5
1.5	20	500	5	5.7	2.7	2.0
1.5	20	500	7	5.9	2.9	2.1
1.5	20	1000	2	5.3	2.5	1.8
1.5	20	1000	3	4.9	2.2	1.5
1.5	20	1000	5	4.2	1.7	1.2
1.5	20	1000	7	4.5	1.9	1.3
1.5	30	130	2	7.8	4.8	3.8
1.5	30	130	3	7.5	4.5	3.4
1.5	30	130	5	6.9	3.7	2.8
1.5	30	130	7	6.9	3.8	2.8
1.5	30	500	2	5.9	2.9	2.1
1.5	30	500	3	5.5	2.6	1.9
1.5	30	500	5	4.8	2.1	1.5
1.5	30	500	7	5.0	2.2	1.6
1.5	30	1000	2	4.3	1.8	1.3
1.5	30	1000	3	3.9	1.6	1.1
1.5	30	1000	5	3.3	1.2	0.8
1.5	30	1000	7	3.5	1.4	1.0
2	10	130	2	8.8	6.3	5.2
2	10	130	3	8.0	5.0	4.0
2	10	130	5	8.2	5.3	4.2
2	10	130	7	8.3	5.5	4.4
2	10	500	2	7.4	4.3	3.3
2	10	500	3	6.6	3.5	2.6
2	10	500	5	6.9	3.7	2.8

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
2	10	500	7	7.2	4.0	3.1
2	10	1000	2	5.6	2.6	1.9
2	10	1000	3	5.1	2.3	1.7
2	10	1000	5	5.5	2.6	1.9
2	10	1000	7	5.9	2.9	2.1
2	20	130	2	8.0	5.0	3.9
2	20	130	3	7.3	4.2	3.2
2	20	130	5	7.4	4.3	3.3
2	20	130	7	7.6	4.5	3.4
2	20	500	2	5.8	2.8	2.0
2	20	500	3	5.2	2.3	1.7
2	20	500	5	5.4	2.5	1.8
2	20	500	7	5.8	2.8	2.0
2	20	1000	2	3.7	1.4	1.0
2	20	1000	3	3.6	1.4	1.0
2	20	1000	5	3.9	1.6	1.1
2	20	1000	7	4.3	1.8	1.3
2	30	130	2	7.3	4.1	3.1
2	30	130	3	6.5	3.4	2.5
2	30	130	5	6.7	3.5	2.6
2	30	130	7	6.8	3.7	2.8
2	30	500	2	4.7	2.1	1.5
2	30	500	3	4.2	1.7	1.2
2	30	500	5	4.5	1.9	1.3
2	30	500	7	4.9	2.1	1.5
2	30	1000	2	2.9	1.0	0.7
2	30	1000	3	2.7	1.0	0.7
2	30	1000	5	3.1	1.1	0.8
2	30	1000	7	3.4	1.3	0.9
3.5	10	130	2	7.9	4.9	3.8
3.5	10	130	3	8.0	5.1	4.0
3.5	10	130	5	8.2	5.3	4.2
3.5	10	130	7	8.3	5.5	4.4
3.5	10	500	2	5.9	2.9	2.1
3.5	10	500	3	6.2	3.1	2.3
3.5	10	500	5	6.7	3.6	2.7
3.5	10	500	7	7.0	3.9	2.9
3.5	10	1000	2	4.2	1.8	1.2
3.5	10	1000	3	4.6	2.0	1.4
3.5	10	1000	5	5.2	2.4	1.7
3.5	10	1000	7	5.7	2.7	2.0

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Estimated Battery Life (Years)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
3.5	20	130	2	6.8	3.7	2.7
3.5	20	130	3	7.0	3.9	2.9
3.5	20	130	5	7.3	4.2	3.2
3.5	20	130	7	7.4	4.4	3.3
3.5	20	500	2	4.3	1.8	1.3
3.5	20	500	3	4.7	2.0	1.4
3.5	20	500	5	5.2	2.4	1.7
3.5	20	500	7	5.6	2.7	1.9
3.5	20	1000	2	2.8	1.0	0.7
3.5	20	1000	3	3.1	1.2	0.8
3.5	20	1000	5	3.7	1.5	1.0
3.5	20	1000	7	4.1	1.7	1.2
3.5	30	130	2	6.0	2.9	2.1
3.5	30	130	3	6.2	3.1	2.3
3.5	30	130	5	6.5	3.4	2.5
3.5	30	130	7	6.7	3.6	2.7
3.5	30	500	2	3.4	1.3	0.9
3.5	30	500	3	3.7	1.5	1.0
3.5	30	500	5	4.3	1.8	1.2
3.5	30	500	7	4.7	2.0	1.4
3.5	30	1000	2	2.1	0.7	0.5
3.5	30	1000	3	2.4	0.8	0.6
3.5	30	1000	5	2.9	1.1	0.7
3.5	30	1000	7	3.2	1.2	0.8

9.1.3 Estimated Battery Life - Nominal N EOS to EOS Time Estimates

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	10	130	2	9.4	6.7	5.5
1	10	130	3	9.3	6.5	5.3
1	10	130	5	9.1	6.2	5.0
1	10	130	7	8.8	5.8	4.6
1	10	500	2	8.7	5.6	4.4
1	10	500	3	8.4	5.2	4.1
1	10	500	5	7.9	4.6	3.5
1	10	500	7	7.5	4.2	3.2
1	10	1000	2	7.7	4.4	3.4
1	10	1000	3	7.3	4.0	3.1
1	10	1000	5	6.5	3.3	2.5
1	10	1000	7	6.2	3.0	2.2
1	20	130	2	8.6	5.5	4.4
1	20	130	3	8.4	5.3	4.1
1	20	130	5	8.2	4.9	3.8
1	20	130	7	7.7	4.4	3.4
1	20	500	2	7.4	4.1	3.1
1	20	500	3	7.0	3.8	2.8
1	20	500	5	6.3	3.2	2.3
1	20	500	7	5.9	2.9	2.1
1	20	1000	2	6.2	3.0	2.2
1	20	1000	3	5.7	2.7	2.0
1	20	1000	5	4.8	2.1	1.5
1	20	1000	7	4.4	1.9	1.4
1	30	130	2	8.0	4.7	3.6
1	30	130	3	7.7	4.4	3.4
1	30	130	5	7.4	4.1	3.1
1	30	130	7	6.9	3.6	2.7
1	30	500	2	6.5	3.3	2.4
1	30	500	3	6.1	3.0	2.2
1	30	500	5	5.3	2.4	1.8
1	30	500	7	4.9	2.2	1.6
1	30	1000	2	5.1	2.3	1.7
1	30	1000	3	4.7	2.0	1.5
1	30	1000	5	3.9	1.6	1.1
1	30	1000	7	3.3	1.3	0.9
1.5	10	130	2	9.0	6.0	4.9
1.5	10	130	3	8.8	5.7	4.6
1.5	10	130	5	8.4	5.2	4.0

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1.5	10	130	7	8.4	5.2	4.1
1.5	10	500	2	7.5	4.2	3.2
1.5	10	500	3	7.2	3.9	3.0
1.5	10	500	5	6.6	3.3	2.5
1.5	10	500	7	6.7	3.5	2.6
1.5	10	1000	2	6.1	3.0	2.2
1.5	10	1000	3	5.7	2.7	2.0
1.5	10	1000	5	5.0	2.2	1.6
1.5	10	1000	7	5.3	2.4	1.7
1.5	20	130	2	7.9	4.7	3.6
1.5	20	130	3	7.6	4.4	3.3
1.5	20	130	5	7.1	3.8	2.8
1.5	20	130	7	7.1	3.8	2.9
1.5	20	500	2	6.0	2.9	2.1
1.5	20	500	3	5.6	2.6	1.9
1.5	20	500	5	4.9	2.2	1.6
1.5	20	500	7	5.1	2.3	1.7
1.5	20	1000	2	4.4	1.9	1.4
1.5	20	1000	3	4.0	1.7	1.2
1.5	20	1000	5	3.1	1.3	0.9
1.5	20	1000	7	3.6	1.5	1.1
1.5	30	130	2	7.1	3.8	2.9
1.5	30	130	3	6.8	3.5	2.6
1.5	30	130	5	6.1	3.0	2.2
1.5	30	130	7	6.2	3.1	2.3
1.5	30	500	2	5.0	2.2	1.6
1.5	30	500	3	4.6	2.0	1.4
1.5	30	500	5	3.9	1.6	1.2
1.5	30	500	7	4.1	1.7	1.2
1.5	30	1000	2	3.2	1.3	0.9
1.5	30	1000	3	2.9	1.1	0.8
1.5	30	1000	5	2.4	0.9	0.7
1.5	30	1000	7	2.6	1.0	0.7
2	10	130	2	8.6	5.5	4.3
2	10	130	3	8.2	5.0	3.9
2	10	130	5	8.2	5.0	3.9
2	10	130	7	8.3	5.1	4.0
2	10	500	2	6.7	3.5	2.6
2	10	500	3	6.0	2.9	2.1
2	10	500	5	6.3	3.1	2.3
2	10	500	7	6.6	3.4	2.5

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
2	10	1000	2	5.0	2.2	1.6
2	10	1000	3	4.3	1.8	1.3
2	10	1000	5	4.7	2.0	1.5
2	10	1000	7	5.1	2.3	1.7
2	20	130	2	7.4	4.1	3.1
2	20	130	3	6.8	3.5	2.6
2	20	130	5	6.9	3.6	2.7
2	20	130	7	7.0	3.8	2.8
2	20	500	2	5.0	2.2	1.6
2	20	500	3	4.3	1.8	1.3
2	20	500	5	4.6	2.0	1.4
2	20	500	7	5.0	2.2	1.6
2	20	1000	2	3.0	1.2	0.9
2	20	1000	3	2.6	1.0	0.7
2	20	1000	5	2.9	1.2	0.8
2	20	1000	7	3.3	1.3	0.9
2	30	130	2	6.4	3.2	2.4
2	30	130	3	5.8	2.8	2.0
2	30	130	5	5.9	2.8	2.1
2	30	130	7	6.1	3.0	2.2
2	30	500	2	4.0	1.7	1.2
2	30	500	3	3.2	1.3	0.9
2	30	500	5	3.6	1.5	1.1
2	30	500	7	4.0	1.7	1.2
2	30	1000	2	2.2	0.9	0.6
2	30	1000	3	2.0	0.8	0.6
2	30	1000	5	2.2	0.9	0.6
2	30	1000	7	2.5	1.0	0.7
3.5	10	130	2	7.6	4.3	3.3
3.5	10	130	3	7.8	4.5	3.5
3.5	10	130	5	8.1	4.8	3.7
3.5	10	130	7	8.2	5.0	3.9
3.5	10	500	2	5.1	2.3	1.7
3.5	10	500	3	5.5	2.5	1.8
3.5	10	500	5	6.0	2.9	2.1
3.5	10	500	7	6.4	3.2	2.4
3.5	10	1000	2	3.2	1.3	0.9
3.5	10	1000	3	3.8	1.6	1.1
3.5	10	1000	5	4.4	1.9	1.4
3.5	10	1000	7	4.9	2.2	1.6
3.5	20	130	2	6.1	3.0	2.2

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Nominal Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
3.5	20	130	3	6.3	3.2	2.3
3.5	20	130	5	6.7	3.4	2.6
3.5	20	130	7	6.9	3.6	2.7
3.5	20	500	2	3.3	1.3	0.9
3.5	20	500	3	3.8	1.6	1.1
3.5	20	500	5	4.3	1.9	1.3
3.5	20	500	7	4.8	2.1	1.5
3.5	20	1000	2	2.0	0.8	0.6
3.5	20	1000	3	2.3	0.9	0.6
3.5	20	1000	5	2.7	1.1	0.8
3.5	20	1000	7	3.1	1.2	0.9
3.5	30	130	2	5.1	2.3	1.7
3.5	30	130	3	5.4	2.5	1.8
3.5	30	130	5	5.7	2.7	2.0
3.5	30	130	7	6.0	2.9	2.1
3.5	30	500	2	2.5	1.0	0.7
3.5	30	500	3	2.8	1.1	0.8
3.5	30	500	5	3.2	1.3	0.9
3.5	30	500	7	3.8	1.6	1.1
3.5	30	1000	2	1.5	0.6	0.4
3.5	30	1000	3	1.7	0.7	0.5
3.5	30	1000	5	2.1	0.8	0.6
3.5	30	1000	7	2.4	0.9	0.7

9.1.4 Estimated Battery Life - Worst Case N EOS to EOS Time Estimates

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1	10	130	2	7.7	5.6	4.7
1	10	130	3	7.8	5.7	4.8
1	10	130	5	7.2	4.9	4.0
1	10	130	7	7.2	4.9	3.9
1	10	500	2	7.6	5.4	4.4
1	10	500	3	7.3	5.0	4.1
1	10	500	5	6.7	4.2	3.3
1	10	500	7	6.5	3.9	3.0
1	10	1000	2	6.8	4.2	3.3
1	10	1000	3	6.6	4.0	3.1
1	10	1000	5	5.9	3.2	2.4
1	10	1000	7	5.5	2.9	2.2
1	20	130	2	7.5	5.3	4.4
1	20	130	3	7.4	5.1	4.1
1	20	130	5	7.1	4.7	3.7
1	20	130	7	6.7	4.1	3.2
1	20	500	2	6.7	4.1	3.2
1	20	500	3	6.4	3.8	2.9
1	20	500	5	5.6	3.0	2.2
1	20	500	7	5.4	2.8	2.1
1	20	1000	2	5.6	2.9	2.2
1	20	1000	3	5.3	2.8	2.1
1	20	1000	5	4.6	2.2	1.6
1	20	1000	7	4.1	1.9	1.4
1	30	130	2	7.1	4.6	3.7
1	30	130	3	6.9	4.4	3.5
1	30	130	5	6.5	3.9	3.0
1	30	130	7	6.1	3.5	2.7
1	30	500	2	6.0	3.4	2.6
1	30	500	3	5.7	3.0	2.3
1	30	500	5	4.9	2.4	1.8
1	30	500	7	4.6	2.2	1.6
1	30	1000	2	4.6	2.2	1.6
1	30	1000	3	4.5	2.1	1.6
1	30	1000	5	3.8	1.7	1.2
1	30	1000	7	3.1	1.3	0.9
1.5	10	130	2	7.6	5.5	4.6
1.5	10	130	3	7.4	5.1	4.2
1.5	10	130	5	6.8	4.3	3.4

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
1.5	10	130	7	6.8	4.3	3.4
1.5	10	500	2	6.4	3.8	3.0
1.5	10	500	3	6.4	3.8	2.9
1.5	10	500	5	5.7	3.1	2.3
1.5	10	500	7	5.9	3.3	2.5
1.5	10	1000	2	5.6	3.0	2.3
1.5	10	1000	3	5.3	2.7	2.0
1.5	10	1000	5	4.6	2.2	1.6
1.5	10	1000	7	4.8	2.4	1.7
1.5	20	130	2	7.0	4.5	3.6
1.5	20	130	3	6.7	4.2	3.3
1.5	20	130	5	6.2	3.5	2.7
1.5	20	130	7	6.2	3.6	2.7
1.5	20	500	2	5.6	3.0	2.2
1.5	20	500	3	5.2	2.7	2.0
1.5	20	500	5	4.6	2.2	1.6
1.5	20	500	7	4.7	2.3	1.7
1.5	20	1000	2	4.3	2.0	1.4
1.5	20	1000	3	3.9	1.7	1.3
1.5	20	1000	5	3.1	1.3	0.9
1.5	20	1000	7	3.5	1.5	1.1
1.5	30	130	2	6.4	3.8	2.9
1.5	30	130	3	6.1	3.5	2.7
1.5	30	130	5	5.5	2.9	2.2
1.5	30	130	7	5.6	3.0	2.2
1.5	30	500	2	4.8	2.3	1.7
1.5	30	500	3	4.4	2.1	1.5
1.5	30	500	5	3.8	1.7	1.2
1.5	30	500	7	4.0	1.8	1.3
1.5	30	1000	2	3.3	1.4	1.0
1.5	30	1000	3	2.9	1.2	0.9
1.5	30	1000	5	2.4	1.0	0.7
1.5	30	1000	7	2.6	1.1	0.8
2	10	130	2	7.3	4.9	4.0
2	10	130	3	6.5	4.0	3.1
2	10	130	5	6.7	4.2	3.3
2	10	130	7	6.8	4.3	3.4
2	10	500	2	6.0	3.4	2.6
2	10	500	3	5.4	2.8	2.1
2	10	500	5	5.5	2.9	2.2
2	10	500	7	5.8	3.2	2.4

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
2	10	1000	2	4.5	2.1	1.5
2	10	1000	3	4.1	1.9	1.3
2	10	1000	5	4.4	2.1	1.5
2	10	1000	7	4.7	2.3	1.7
2	20	130	2	6.5	3.9	3.1
2	20	130	3	5.9	3.3	2.5
2	20	130	5	6.0	3.4	2.6
2	20	130	7	6.1	3.5	2.7
2	20	500	2	4.7	2.2	1.6
2	20	500	3	4.1	1.9	1.4
2	20	500	5	4.3	2.0	1.5
2	20	500	7	4.6	2.2	1.6
2	20	1000	2	2.7	1.1	0.8
2	20	1000	3	2.7	1.1	0.8
2	20	1000	5	2.9	1.2	0.9
2	20	1000	7	3.2	1.4	1.0
2	30	130	2	5.9	3.3	2.5
2	30	130	3	5.3	2.7	2.0
2	30	130	5	5.4	2.8	2.1
2	30	130	7	5.5	2.9	2.2
2	30	500	2	3.8	1.7	1.2
2	30	500	3	3.1	1.3	0.9
2	30	500	5	3.6	1.5	1.1
2	30	500	7	3.9	1.7	1.2
2	30	1000	2	2.1	0.8	0.6
2	30	1000	3	2.0	0.8	0.6
2	30	1000	5	2.3	0.9	0.7
2	30	1000	7	2.6	1.0	0.7
3.5	10	130	2	6.4	3.8	3.0
3.5	10	130	3	6.6	4.0	3.1
3.5	10	130	5	6.7	4.2	3.3
3.5	10	130	7	6.8	4.3	3.4
3.5	10	500	2	4.7	2.3	1.7
3.5	10	500	3	5.0	2.5	1.8
3.5	10	500	5	5.4	2.8	2.1
3.5	10	500	7	5.7	3.1	2.3
3.5	10	1000	2	3.2	1.3	1.0
3.5	10	1000	3	3.7	1.6	1.2
3.5	10	1000	5	4.2	1.9	1.4
3.5	10	1000	7	4.6	2.2	1.6
3.5	20	130	2	5.5	2.9	2.2

Output Current (mA)	Frequency (Hz)	Pulse Width (µsec)	DC-DC Converter Code	Worst Case Time from N EOS to EOS (Months)		
				10% Duty Cycle Life	33% Duty Cycle Life	50% Duty Cycle Life
3.5	20	130	3	5.7	3.0	2.3
3.5	20	130	5	5.9	3.3	2.5
3.5	20	130	7	6.1	3.4	2.6
3.5	20	500	2	3.2	1.4	1.0
3.5	20	500	3	3.7	1.6	1.2
3.5	20	500	5	4.2	1.9	1.4
3.5	20	500	7	4.5	2.1	1.5
3.5	20	1000	2	2.1	0.8	0.6
3.5	20	1000	3	2.3	0.9	0.7
3.5	20	1000	5	2.8	1.1	0.8
3.5	20	1000	7	3.1	1.3	0.9
3.5	30	130	2	4.8	2.3	1.7
3.5	30	130	3	5.0	2.5	1.8
3.5	30	130	5	5.2	2.7	2.0
3.5	30	130	7	5.4	2.8	2.1
3.5	30	500	2	2.5	1.0	0.7
3.5	30	500	3	2.8	1.1	0.8
3.5	30	500	5	3.2	1.3	1.0
3.5	30	500	7	3.7	1.6	1.2
3.5	30	1000	2	1.6	0.6	0.5
3.5	30	1000	3	1.8	0.7	0.5
3.5	30	1000	5	2.1	0.8	0.6
3.5	30	1000	7	2.4	1.0	0.7

9.2 Appendix B — Model 103/104/8103 Battery Longevity and Programmed Setting Choices

Parameters at 3kOhms (M103/104/8103)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
0.5	10	130	>10	>10	>10	2.8	2.5	2.4	2.2	2.0	1.9
0.5	15	130	>10	>10	>10	2.7	2.2	1.9	2.1	1.7	1.5
0.5	20	130	>10	>10	>10	2.5	1.9	1.7	2.0	1.5	1.3
0.5	25	130	>10	>10	>10	2.4	1.7	1.4	1.9	1.4	1.2
0.5	30	130	>10	>10	9.5	2.3	1.6	1.3	1.8	1.3	1.0
0.5	10	250	>10	>10	>10	2.7	2.3	2.0	2.1	1.8	1.6
0.5	15	250	>10	>10	>10	2.5	1.9	1.6	2.0	1.5	1.3
0.5	20	250	>10	>10	>10	2.4	1.7	1.4	1.9	1.3	1.1
0.5	25	250	>10	>10	8.7	2.3	1.5	1.2	1.8	1.2	0.9
0.5	30	250	>10	9.8	7.6	2.1	1.3	1.0	1.7	1.0	0.8
0.5	10	500	>10	>10	>10	2.5	1.9	1.6	1.9	1.5	1.2
0.5	15	500	>10	>10	8.9	2.3	1.5	1.2	1.8	1.2	0.9
0.5	20	500	>10	9.3	7.2	2.1	1.2	1.0	1.6	1.0	0.8
0.5	25	500	>10	8.1	6.1	1.9	1.1	0.8	1.5	0.9	0.6
0.5	30	500	>10	7.1	5.2	1.8	0.9	0.7	1.4	0.8	0.6
0.5	10	750	>10	>10	9.4	2.3	1.6	1.3	1.8	1.2	1.0
0.5	15	750	>10	9.1	7.0	2.1	1.2	0.9	1.6	1.0	0.7
0.5	20	750	>10	7.5	5.6	1.9	1.0	0.7	1.5	0.8	0.6
0.5	25	750	>10	6.4	4.7	1.7	0.9	0.6	1.3	0.7	0.5
0.5	30	750	>10	5.5	4.0	1.5	0.7	0.5	1.2	0.6	0.4
0.5	10	1000	>10	>10	7.9	2.2	1.4	1.1	1.7	1.1	0.8
0.5	15	1000	>10	7.7	5.8	1.9	1.0	0.8	1.5	0.8	0.6
0.5	20	1000	>10	6.3	4.6	1.7	0.8	0.6	1.3	0.7	0.5
0.5	25	1000	>10	5.3	3.8	1.5	0.7	0.5	1.2	0.6	0.4
0.5	30	1000	>10	4.6	3.2	1.4	0.6	0.4	1.1	0.5	0.3
1	10	130	>10	>10	>10	2.6	2.1	1.9	2.0	1.5	1.3
1	15	130	>10	>10	>10	2.5	1.9	1.6	1.9	1.4	1.1
1	20	130	>10	>10	>10	2.4	1.6	1.3	1.8	1.2	0.9
1	25	130	>10	>10	9.3	2.2	1.5	1.2	1.7	1.1	0.8
1	30	130	>10	>10	8.2	2.1	1.3	1.0	1.6	1.0	0.8
1	10	250	>10	>10	>10	2.4	1.7	1.4	1.8	1.3	1.0
1	15	250	>10	>10	8.9	2.2	1.4	1.1	1.7	1.1	0.9
1	20	250	>10	9.4	7.2	2.1	1.2	0.9	1.6	0.9	0.7
1	25	250	>10	8.1	6.1	1.9	1.1	0.8	1.5	0.8	0.6
1	30	250	>10	7.1	5.3	1.8	0.9	0.7	1.4	0.7	0.5
1	10	500	>10	>10	7.9	2.1	1.2	1.0	1.5	0.9	0.7

Parameters at 3kOhms (M103/104/8103)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1	15	500	>10	7.8	5.8	1.8	1.0	0.7	1.4	0.7	0.5
1	20	500	>10	6.3	4.6	1.6	0.8	0.6	1.2	0.6	0.4
1	25	500	>10	5.3	3.8	1.5	0.7	0.5	1.1	0.5	0.4
1	30	500	>10	4.6	3.2	1.3	0.6	0.4	1.0	0.4	0.3
1	10	750	>10	8.0	6.0	1.8	1.0	0.7	1.3	0.7	0.5
1	15	750	>10	6.0	4.3	1.5	0.7	0.5	1.1	0.5	0.4
1	20	750	>10	4.7	3.4	1.3	0.6	0.4	1.0	0.4	0.3
1	25	750	9.3	3.9	2.8	1.2	0.5	0.3	0.9	0.4	0.3
1	30	750	8.3	3.4	2.3	1.1	0.4	0.3	0.8	0.3	0.2
1	10	1000	>10	6.6	4.9	1.6	0.8	0.6	1.2	0.5	0.4
1	15	1000	>10	4.8	3.4	1.3	0.6	0.4	1.0	0.4	0.3
1	20	1000	9.0	3.8	2.7	1.1	0.5	0.3	0.8	0.3	0.2
1	25	1000	7.8	3.1	2.2	1.0	0.4	0.3	0.7	0.3	0.2
1	30	1000	6.9	2.7	1.8	0.9	0.3	0.2	0.6	0.2	0.2
1.5	10	130	>10	>10	8.8	2.2	1.4	1.1	1.6	1.0	0.8
1.5	15	130	>10	>10	7.9	2.1	1.3	1.0	1.6	0.9	0.7
1.5	20	130	>10	9.3	7.1	2.0	1.1	0.9	1.5	0.8	0.6
1.5	25	130	>10	8.3	6.3	1.9	1.0	0.8	1.4	0.7	0.5
1.5	30	130	>10	7.6	5.7	1.8	0.9	0.7	1.3	0.6	0.5
1.5	10	250	>10	>10	8.8	2.1	1.3	1.0	1.5	0.8	0.6
1.5	15	250	>10	8.9	6.8	1.9	1.0	0.8	1.3	0.7	0.5
1.5	20	250	>10	7.5	5.6	1.7	0.9	0.6	1.2	0.6	0.4
1.5	25	250	>10	6.4	4.7	1.6	0.8	0.5	1.1	0.5	0.4
1.5	30	250	>10	5.6	4.0	1.4	0.7	0.5	1.0	0.5	0.3
1.5	10	500	>10	7.3	5.4	1.7	0.8	0.6	1.2	0.6	0.4
1.5	15	500	>10	5.7	4.1	1.4	0.7	0.5	1.0	0.4	0.3
1.5	20	500	>10	4.7	3.3	1.2	0.5	0.4	0.9	0.4	0.2
1.5	25	500	9.2	3.9	2.7	1.1	0.4	0.3	0.8	0.3	0.2
1.5	30	500	8.2	3.3	2.3	1.0	0.4	0.3	0.7	0.3	0.2
1.5	10	750	>10	5.3	3.8	1.4	0.6	0.4	0.9	0.4	0.3
1.5	15	750	9.5	4.1	2.9	1.1	0.5	0.3	0.8	0.3	0.2
1.5	20	750	8.1	3.3	2.3	1.0	0.4	0.3	0.6	0.2	0.2
1.5	25	750	7.0	2.7	1.9	0.8	0.3	0.2	0.6	0.2	0.1
1.5	30	750	6.2	2.3	1.6	0.7	0.3	0.2	0.5	0.2	0.1
1.5	10	1000	9.7	4.2	3.0	1.1	0.5	0.3	0.8	0.3	0.2
1.5	15	1000	7.8	3.1	2.2	0.9	0.4	0.2	0.6	0.2	0.2
1.5	20	1000	6.5	2.5	1.7	0.8	0.3	0.2	0.5	0.2	0.1
1.5	25	1000	5.6	2.1	1.4	0.7	0.2	0.2	0.4	0.2	0.1
1.5	30	1000	4.9	1.8	1.2	0.6	0.2	0.1	0.4	0.1	0.1

Parameters at 3kOhms (M103/104/8103)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
2	10	130	>10	8.7	6.6	1.9	1.1	0.8	1.4	0.7	0.5
2	15	130	>10	7.2	5.3	1.7	0.9	0.6	1.2	0.6	0.4
2	20	130	>10	6.2	4.5	1.6	0.8	0.5	1.1	0.5	0.4
2	25	130	>10	5.5	4.0	1.4	0.7	0.5	1.0	0.5	0.3
2	30	130	>10	5.0	3.5	1.3	0.6	0.4	1.0	0.4	0.3
2	10	250	>10	6.4	4.7	1.6	0.8	0.6	1.2	0.5	0.4
2	15	250	>10	5.2	3.8	1.4	0.6	0.4	1.0	0.4	0.3
2	20	250	>10	4.4	3.1	1.2	0.5	0.4	0.9	0.4	0.3
2	25	250	9.1	3.8	2.7	1.1	0.5	0.3	0.8	0.3	0.2
2	30	250	8.3	3.4	2.3	1.0	0.4	0.3	0.7	0.3	0.2
2	10	500	9.5	4.1	2.9	1.2	0.5	0.3	0.8	0.3	0.2
2	15	500	7.8	3.1	2.2	1.0	0.4	0.3	0.7	0.3	0.2
2	20	500	6.7	2.6	1.8	0.8	0.3	0.2	0.6	0.2	0.1
2	25	500	5.9	2.2	1.5	0.7	0.3	0.2	0.5	0.2	0.1
2	30	500	5.2	1.9	1.3	0.6	0.2	0.1	0.4	0.1	0.1
2	10	750	7.5	2.9	2.0	0.9	0.3	0.2	0.6	0.2	0.2
2	15	750	5.9	2.2	1.5	0.7	0.3	0.2	0.5	0.2	0.1
2	20	750	5.0	1.8	1.2	0.6	0.2	0.1	0.4	0.1	0.1
2	25	750	4.3	1.5	1.0	0.5	0.2	0.1	0.3	0.1	0.1
2	30	750	3.7	1.3	0.9	0.4	0.1	0.1	0.3	0.1	0.1
2	10	1000	6.1	2.3	1.6	0.7	0.3	0.2	0.5	0.2	0.1
2	15	1000	4.7	1.7	1.1	0.6	0.2	0.1	0.4	0.1	0.1
2	20	1000	3.9	1.3	0.9	0.5	0.2	0.1	0.3	0.1	0.1
2	25	1000	3.3	1.1	0.8	0.4	0.1	0.1	0.3	0.1	0.1
2	30	1000	2.9	1.0	0.6	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	130	>10	7.2	5.3	1.7	0.9	0.6	1.3	0.6	0.5
2.5	15	130	>10	6.0	4.4	1.5	0.7	0.5	1.1	0.5	0.4
2.5	20	130	>10	5.1	3.7	1.4	0.6	0.4	1.0	0.4	0.3
2.5	25	130	>10	4.5	3.2	1.2	0.5	0.4	0.9	0.4	0.3
2.5	30	130	9.3	4.0	2.8	1.1	0.5	0.3	0.8	0.3	0.2
2.5	10	250	>10	5.4	3.9	1.4	0.6	0.5	1.0	0.4	0.3
2.5	15	250	9.6	4.1	2.9	1.2	0.5	0.3	0.8	0.3	0.2
2.5	20	250	8.4	3.4	2.4	1.0	0.4	0.3	0.7	0.3	0.2
2.5	25	250	7.4	2.9	2.0	0.9	0.3	0.2	0.6	0.2	0.2
2.5	30	250	6.7	2.5	1.7	0.8	0.3	0.2	0.5	0.2	0.1
2.5	10	500	8.0	3.2	2.2	1.0	0.4	0.3	0.7	0.3	0.2
2.5	15	500	6.3	2.4	1.6	0.8	0.3	0.2	0.5	0.2	0.1
2.5	20	500	5.3	1.9	1.3	0.6	0.2	0.2	0.4	0.2	0.1
2.5	25	500	4.6	1.6	1.1	0.5	0.2	0.1	0.4	0.1	0.1

Parameters at 3kOhms (M103/104/8103)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
2.5	30	500	4.0	1.4	0.9	0.5	0.2	0.1	0.3	0.1	0.1
2.5	10	750	6.1	2.3	1.6	0.7	0.3	0.2	0.5	0.2	0.1
2.5	15	750	4.7	1.7	1.1	0.6	0.2	0.1	0.4	0.1	0.1
2.5	20	750	3.9	1.3	0.9	0.5	0.2	0.1	0.3	0.1	0.1
2.5	25	750	3.3	1.1	0.7	0.4	0.1	0.1	0.3	0.1	0.1
2.5	30	750	2.8	0.9	0.6	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	1000	5.0	1.8	1.2	0.6	0.2	0.1	0.4	0.1	0.1
2.5	15	1000	3.7	1.3	0.9	0.4	0.1	0.1	0.3	0.1	0.1
2.5	20	1000	3.0	1.0	0.7	0.4	0.1	0.1	0.2	0.1	0.1
2.5	25	1000	2.5	0.8	0.6	0.3	0.1	0.1	0.2	0.1	0.0
2.5	30	1000	2.2	0.7	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3	10	130	>10	6.3	4.6	1.6	0.7	0.5	1.1	0.5	0.4
3	15	130	>10	5.0	3.6	1.3	0.6	0.4	1.0	0.4	0.3
3	20	130	9.6	4.2	2.9	1.2	0.5	0.3	0.8	0.3	0.2
3	25	130	8.6	3.6	2.5	1.0	0.4	0.3	0.7	0.3	0.2
3	30	130	7.8	3.1	2.2	0.9	0.4	0.3	0.7	0.2	0.2
3	10	250	>10	4.4	3.1	1.2	0.5	0.4	0.8	0.3	0.2
3	15	250	8.1	3.3	2.3	1.0	0.4	0.3	0.7	0.3	0.2
3	20	250	6.8	2.6	1.8	0.8	0.3	0.2	0.6	0.2	0.1
3	25	250	5.9	2.2	1.5	0.7	0.3	0.2	0.5	0.2	0.1
3	30	250	5.3	1.9	1.3	0.6	0.2	0.2	0.4	0.1	0.1
3	10	500	6.6	2.5	1.7	0.8	0.3	0.2	0.5	0.2	0.1
3	15	500	5.0	1.8	1.2	0.6	0.2	0.1	0.4	0.1	0.1
3	20	500	4.0	1.4	0.9	0.5	0.2	0.1	0.3	0.1	0.1
3	25	500	3.4	1.2	0.8	0.4	0.1	0.1	0.3	0.1	0.1
3	30	500	3.0	1.0	0.7	0.3	0.1	0.1	0.2	0.1	0.1
3	10	750	4.9	1.7	1.2	0.6	0.2	0.1	0.4	0.1	0.1
3	15	750	3.6	1.2	0.8	0.4	0.1	0.1	0.3	0.1	0.1
3	20	750	2.8	0.9	0.6	0.3	0.1	0.1	0.2	0.1	0.0
3	25	750	2.4	0.8	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3	30	750	2.0	0.7	0.4	0.2	0.1	0.1	0.2	0.1	0.0
3	10	1000	3.8	1.3	0.9	0.4	0.2	0.1	0.3	0.1	0.1
3	15	1000	2.8	0.9	0.6	0.3	0.1	0.1	0.2	0.1	0.0
3	20	1000	2.2	0.7	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3	25	1000	1.8	0.6	0.4	0.2	0.1	0.0	0.1	0.0	0.0
3	30	1000	1.5	0.5	0.3	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	130	>10	4.7	3.4	1.3	0.6	0.4	0.9	0.4	0.3
3.5	15	130	9.0	3.8	2.6	1.1	0.4	0.3	0.8	0.3	0.2
3.5	20	130	7.7	3.1	2.1	0.9	0.4	0.3	0.6	0.2	0.2

Parameters at 3kOhms (M103/104/8103)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
3.5	25	130	6.8	2.6	1.8	0.8	0.3	0.2	0.6	0.2	0.1
3.5	30	130	6.1	2.3	1.6	0.7	0.3	0.2	0.5	0.2	0.1
3.5	10	250	8.0	3.2	2.2	1.0	0.4	0.3	0.7	0.3	0.2
3.5	15	250	6.4	2.4	1.7	0.8	0.3	0.2	0.5	0.2	0.1
3.5	20	250	5.3	1.9	1.3	0.6	0.2	0.2	0.4	0.2	0.1
3.5	25	250	4.6	1.6	1.1	0.5	0.2	0.1	0.4	0.1	0.1
3.5	30	250	4.0	1.4	0.9	0.5	0.2	0.1	0.3	0.1	0.1
3.5	10	500	4.7	1.7	1.1	0.6	0.2	0.1	0.4	0.1	0.1
3.5	15	500	3.6	1.2	0.8	0.4	0.1	0.1	0.3	0.1	0.1
3.5	20	500	3.0	1.0	0.7	0.3	0.1	0.1	0.2	0.1	0.1
3.5	25	500	2.5	0.8	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3.5	30	500	2.1	0.7	0.5	0.2	0.1	0.1	0.2	0.1	0.0
3.5	10	750	3.2	1.1	0.7	0.4	0.1	0.1	0.3	0.1	0.1
3.5	15	750	2.4	0.8	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3.5	20	750	2.0	0.6	0.4	0.2	0.1	0.0	0.2	0.1	0.0
3.5	25	750	1.7	0.5	0.4	0.2	0.1	0.0	0.1	0.0	0.0
3.5	30	750	1.4	0.5	0.3	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	1000	2.4	0.8	0.5	0.3	0.1	0.1	0.2	0.1	0.0
3.5	15	1000	1.9	0.6	0.4	0.2	0.1	0.0	0.2	0.0	0.0
3.5	20	1000	1.5	0.5	0.3	0.2	0.1	0.0	0.1	0.0	0.0
3.5	25	1000	1.3	0.4	0.3	0.1	0.0	0.0	0.1	0.0	0.0
3.5	30	1000	1.1	0.3	0.2	0.1	0.0	0.0	0.1	0.0	0.0

9.3 Appendix C — Model 105 Battery Longevity and Programmed Setting Choices

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
0.5	10	130	>10	>10	>10	2.5	1.6	1.3	1.9	1.2	0.9
0.5	15	130	>10	>10	>10	2.5	1.5	1.2	1.8	1.1	0.9
0.5	20	130	>10	>10	>10	2.4	1.4	1.1	1.7	1.0	0.8
0.5	25	130	>10	>10	>10	2.2	1.3	1.0	1.7	1.0	0.7
0.5	30	130	>10	>10	>10	2.2	1.2	0.9	1.6	0.9	0.7
0.5	10	250	>10	>10	>10	2.5	1.6	1.3	1.9	1.2	1.0
0.5	15	250	>10	>10	>10	2.4	1.4	1.1	1.8	1.1	0.8
0.5	20	250	>10	>10	>10	2.3	1.3	1.0	1.7	1.0	0.7
0.5	25	250	>10	>10	>10	2.2	1.2	0.9	1.6	0.9	0.7
0.5	30	250	>10	>10	>10	2.1	1.1	0.8	1.5	0.8	0.6
0.5	10	500	>10	>10	>10	2.4	1.4	1.1	1.7	1.0	0.8
0.5	15	500	>10	>10	>10	2.2	1.2	0.9	1.6	0.9	0.7
0.5	20	500	>10	>10	>10	2.0	1.1	0.8	1.5	0.8	0.6
0.5	25	500	>10	>10	9.0	1.9	0.9	0.7	1.4	0.7	0.5
0.5	30	500	>10	>10	8.6	1.8	0.9	0.6	1.3	0.7	0.5
0.5	10	750	>10	>10	>10	2.2	1.3	1.0	1.7	0.9	0.7
0.5	15	750	>10	>10	>10	2.0	1.1	0.8	1.5	0.8	0.6
0.5	20	750	>10	>10	8.9	1.9	0.9	0.7	1.4	0.7	0.5
0.5	25	750	>10	>10	7.7	1.7	0.8	0.6	1.3	0.6	0.4
0.5	30	750	>10	9.6	6.8	1.6	0.7	0.5	1.2	0.5	0.4
0.5	10	1000	>10	>10	>10	2.1	1.2	0.9	1.6	0.9	0.6
0.5	15	1000	>10	>10	8.9	1.9	0.9	0.7	1.4	0.7	0.5
0.5	20	1000	>10	>10	7.3	1.7	0.8	0.6	1.2	0.6	0.4
0.5	25	1000	>10	9.2	6.5	1.5	0.7	0.5	1.1	0.5	0.4
0.5	30	1000	>10	8.0	5.7	1.4	0.6	0.4	1.0	0.4	0.3
1	10	130	>10	>10	>10	2.4	1.4	1.1	1.7	0.9	0.7
1	15	130	>10	>10	>10	2.3	1.4	1.0	1.6	0.9	0.7
1	20	130	>10	>10	>10	2.3	1.3	1.0	1.6	0.9	0.7
1	25	130	>10	>10	>10	2.2	1.2	0.9	1.5	0.8	0.6
1	30	130	>10	>10	>10	2.1	1.1	0.8	1.5	0.8	0.6
1	10	250	>10	>10	>10	2.2	1.2	0.9	1.5	0.8	0.6
1	15	250	>10	>10	>10	2.1	1.1	0.8	1.5	0.8	0.6
1	20	250	>10	>10	>10	2.0	1.0	0.7	1.4	0.7	0.5
1	25	250	>10	>10	9.7	1.9	0.9	0.7	1.3	0.6	0.5
1	30	250	>10	>10	8.9	1.8	0.8	0.6	1.2	0.6	0.4

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1	10	500	>10	>10	>10	2.0	1.0	0.7	1.3	0.6	0.5
1	15	500	>10	>10	9.6	1.8	0.8	0.6	1.2	0.5	0.4
1	20	500	>10	>10	7.8	1.6	0.7	0.5	1.1	0.5	0.3
1	25	500	>10	9.3	6.6	1.4	0.6	0.4	1.0	0.4	0.3
1	30	500	>10	8.4	5.9	1.3	0.6	0.4	0.9	0.4	0.3
1	10	750	>10	>10	9.7	1.7	0.8	0.6	1.2	0.5	0.4
1	15	750	>10	>10	7.4	1.5	0.7	0.5	1.0	0.4	0.3
1	20	750	>10	8.6	6.0	1.3	0.6	0.4	0.9	0.4	0.3
1	25	750	>10	7.3	5.1	1.2	0.5	0.3	0.8	0.3	0.2
1	30	750	>10	6.4	4.4	1.1	0.4	0.3	0.7	0.3	0.2
1	10	1000	>10	>10	8.0	1.5	0.7	0.5	1.0	0.4	0.3
1	15	1000	>10	8.8	6.2	1.3	0.5	0.4	0.9	0.4	0.2
1	20	1000	>10	7.1	4.9	1.1	0.5	0.3	0.8	0.3	0.2
1	25	1000	>10	6.0	4.1	1.0	0.4	0.3	0.7	0.3	0.2
1	30	1000	>10	5.1	3.5	0.9	0.3	0.2	0.6	0.2	0.2
1.5	10	130	>10	>10	>10	2.0	1.1	0.8	1.5	0.7	0.6
1.5	15	130	>10	>10	>10	1.9	1.0	0.7	1.4	0.7	0.5
1.5	20	130	>10	>10	9.4	1.8	0.9	0.7	1.3	0.6	0.5
1.5	25	130	>10	>10	8.8	1.8	0.8	0.6	1.3	0.6	0.4
1.5	30	130	>10	>10	7.8	1.7	0.8	0.6	1.2	0.6	0.4
1.5	10	250	>10	>10	9.3	1.8	0.9	0.6	1.3	0.6	0.4
1.5	15	250	>10	>10	7.9	1.6	0.7	0.5	1.1	0.5	0.4
1.5	20	250	>10	>10	7.6	1.6	0.7	0.5	1.1	0.5	0.3
1.5	25	250	>10	9.1	6.5	1.4	0.6	0.4	1.0	0.4	0.3
1.5	30	250	>10	8.5	6.0	1.3	0.6	0.4	0.9	0.4	0.3
1.5	10	500	>10	9.4	6.6	1.4	0.6	0.4	1.0	0.4	0.3
1.5	15	500	>10	7.4	5.2	1.2	0.5	0.3	0.8	0.3	0.2
1.5	20	500	>10	6.5	4.5	1.1	0.4	0.3	0.7	0.3	0.2
1.5	25	500	>10	5.7	4.0	1.0	0.4	0.3	0.7	0.2	0.2
1.5	30	500	>10	5.1	3.5	0.9	0.3	0.2	0.6	0.2	0.1
1.5	10	750	>10	7.2	5.0	1.2	0.5	0.3	0.8	0.3	0.2
1.5	15	750	>10	5.5	3.8	1.0	0.4	0.2	0.7	0.2	0.2
1.5	20	750	>10	4.7	3.2	0.8	0.3	0.2	0.6	0.2	0.1
1.5	25	750	>10	4.0	2.7	0.7	0.3	0.2	0.5	0.2	0.1
1.5	30	750	10.0	3.6	2.4	0.7	0.2	0.2	0.4	0.2	0.1
1.5	10	1000	>10	5.7	4.0	1.0	0.4	0.3	0.7	0.2	0.2
1.5	15	1000	>10	4.3	2.9	0.8	0.3	0.2	0.5	0.2	0.1
1.5	20	1000	9.9	3.5	2.4	0.7	0.2	0.2	0.4	0.2	0.1

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1.5	25	1000	8.7	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
1.5	30	1000	7.8	2.7	1.8	0.5	0.2	0.1	0.3	0.1	0.1
2	10	130	>10	>10	9.4	1.8	0.9	0.6	1.3	0.6	0.4
2	15	130	>10	>10	8.0	1.7	0.8	0.5	1.2	0.5	0.4
2	20	130	>10	9.8	7.0	1.5	0.7	0.5	1.1	0.5	0.3
2	25	130	>10	8.8	6.2	1.4	0.6	0.4	1.0	0.4	0.3
2	30	130	>10	8.1	5.7	1.3	0.6	0.4	0.9	0.4	0.3
2	10	250	>10	9.7	6.9	1.5	0.7	0.5	1.0	0.4	0.3
2	15	250	>10	8.2	5.7	1.3	0.5	0.4	0.9	0.4	0.3
2	20	250	>10	6.8	4.7	1.1	0.5	0.3	0.8	0.3	0.2
2	25	250	>10	5.9	4.1	1.0	0.4	0.3	0.7	0.3	0.2
2	30	250	>10	5.2	3.6	0.9	0.4	0.2	0.6	0.2	0.2
2	10	500	>10	6.5	4.5	1.1	0.4	0.3	0.7	0.3	0.2
2	15	500	>10	5.0	3.4	0.9	0.3	0.2	0.6	0.2	0.1
2	20	500	>10	4.0	2.7	0.7	0.3	0.2	0.5	0.2	0.1
2	25	500	9.6	3.4	2.3	0.7	0.2	0.2	0.4	0.2	0.1
2	30	500	8.7	3.0	2.1	0.6	0.2	0.1	0.4	0.1	0.1
2	10	750	>10	4.8	3.3	0.9	0.3	0.2	0.6	0.2	0.1
2	15	750	>10	3.6	2.4	0.7	0.2	0.2	0.4	0.2	0.1
2	20	750	8.1	2.8	1.9	0.5	0.2	0.1	0.4	0.1	0.1
2	25	750	7.0	2.4	1.6	0.5	0.2	0.1	0.3	0.1	0.1
2	30	750	6.2	2.1	1.4	0.4	0.1	0.1	0.3	0.1	0.1
2	10	1000	>10	3.8	2.6	0.7	0.2	0.2	0.5	0.2	0.1
2	15	1000	8.0	2.8	1.9	0.5	0.2	0.1	0.4	0.1	0.1
2	20	1000	6.5	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2	25	1000	5.5	1.8	1.2	0.4	0.1	0.1	0.2	0.1	0.1
2	30	1000	4.8	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	130	>10	>10	8.3	1.7	0.8	0.6	1.2	0.5	0.4
2.5	15	130	>10	9.6	6.8	1.5	0.6	0.5	1.0	0.4	0.3
2.5	20	130	>10	8.5	6.0	1.4	0.6	0.4	0.9	0.4	0.3
2.5	25	130	>10	7.4	5.2	1.2	0.5	0.4	0.9	0.3	0.2
2.5	30	130	>10	6.7	4.7	1.1	0.5	0.3	0.8	0.3	0.2
2.5	10	250	>10	8.3	5.9	1.3	0.6	0.4	0.9	0.4	0.3
2.5	15	250	>10	6.5	4.5	1.1	0.4	0.3	0.8	0.3	0.2
2.5	20	250	>10	5.5	3.8	1.0	0.4	0.3	0.7	0.2	0.2
2.5	25	250	>10	4.6	3.2	0.8	0.3	0.2	0.6	0.2	0.1
2.5	30	250	>10	4.1	2.8	0.8	0.3	0.2	0.5	0.2	0.1
2.5	10	500	>10	5.4	3.7	0.9	0.4	0.2	0.6	0.2	0.2

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
2.5	15	500	>10	4.0	2.7	0.7	0.3	0.2	0.5	0.2	0.1
2.5	20	500	9.0	3.2	2.1	0.6	0.2	0.1	0.4	0.1	0.1
2.5	25	500	7.8	2.7	1.8	0.5	0.2	0.1	0.3	0.1	0.1
2.5	30	500	6.8	2.3	1.5	0.5	0.2	0.1	0.3	0.1	0.1
2.5	10	750	>10	3.9	2.7	0.7	0.3	0.2	0.5	0.2	0.1
2.5	15	750	8.2	2.9	1.9	0.5	0.2	0.1	0.4	0.1	0.1
2.5	20	750	6.6	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2.5	25	750	5.5	1.8	1.2	0.4	0.1	0.1	0.2	0.1	0.1
2.5	30	750	4.9	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	1000	8.8	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
2.5	15	1000	6.5	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2.5	20	1000	5.2	1.7	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	25	1000	4.3	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
2.5	30	1000	3.7	1.2	0.8	0.2	0.1	0.1	0.2	0.1	0.0
3	10	130	>10	>10	7.3	1.5	0.7	0.5	1.1	0.5	0.3
3	15	130	>10	8.5	6.0	1.3	0.6	0.4	0.9	0.4	0.3
3	20	130	>10	7.4	5.1	1.2	0.5	0.3	0.8	0.3	0.2
3	25	130	>10	6.2	4.3	1.1	0.4	0.3	0.7	0.3	0.2
3	30	130	>10	5.5	3.8	1.0	0.4	0.3	0.7	0.2	0.2
3	10	250	>10	6.9	4.8	1.2	0.5	0.3	0.8	0.3	0.2
3	15	250	>10	5.3	3.7	0.9	0.4	0.2	0.6	0.2	0.2
3	20	250	>10	4.4	3.0	0.8	0.3	0.2	0.5	0.2	0.1
3	25	250	>10	3.7	2.5	0.7	0.2	0.2	0.5	0.2	0.1
3	30	250	9.2	3.2	2.2	0.6	0.2	0.1	0.4	0.1	0.1
3	10	500	>10	4.1	2.8	0.8	0.3	0.2	0.5	0.2	0.1
3	15	500	8.7	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
3	20	500	7.1	2.4	1.6	0.5	0.2	0.1	0.3	0.1	0.1
3	25	500	6.1	2.0	1.4	0.4	0.1	0.1	0.3	0.1	0.1
3	30	500	5.3	1.7	1.2	0.3	0.1	0.1	0.2	0.1	0.0
3	10	750	8.4	2.9	2.0	0.6	0.2	0.1	0.4	0.1	0.1
3	15	750	6.3	2.1	1.4	0.4	0.1	0.1	0.3	0.1	0.1
3	20	750	5.1	1.7	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3	25	750	4.2	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3	30	750	3.6	1.2	0.8	0.2	0.1	0.1	0.2	0.0	0.0
3	10	1000	6.6	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
3	15	1000	4.9	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3	20	1000	3.9	1.3	0.8	0.3	0.1	0.1	0.2	0.1	0.0
3	25	1000	3.2	1.0	0.7	0.2	0.1	0.0	0.1	0.0	0.0

Parameters at 3kOhms (M105)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
3	30	1000	2.7	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	130	>10	6.7	4.7	1.2	0.5	0.3	0.9	0.4	0.2
3.5	15	130	>10	6.0	4.1	1.1	0.4	0.3	0.8	0.3	0.2
3.5	20	130	>10	5.0	3.4	0.9	0.4	0.2	0.7	0.2	0.2
3.5	25	130	>10	4.6	3.1	0.8	0.3	0.2	0.6	0.2	0.1
3.5	30	130	>10	4.1	2.8	0.8	0.3	0.2	0.5	0.2	0.1
3.5	10	250	>10	4.6	3.1	0.9	0.3	0.2	0.6	0.2	0.1
3.5	15	250	>10	3.6	2.5	0.7	0.2	0.2	0.5	0.2	0.1
3.5	20	250	8.7	3.0	2.1	0.6	0.2	0.1	0.4	0.1	0.1
3.5	25	250	7.5	2.6	1.7	0.5	0.2	0.1	0.3	0.1	0.1
3.5	30	250	6.7	2.3	1.5	0.5	0.2	0.1	0.3	0.1	0.1
3.5	10	500	7.2	2.4	1.6	0.5	0.2	0.1	0.4	0.1	0.1
3.5	15	500	5.9	2.0	1.3	0.4	0.1	0.1	0.3	0.1	0.1
3.5	20	500	5.0	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3.5	25	500	4.3	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3.5	30	500	3.7	1.2	0.8	0.2	0.1	0.1	0.2	0.1	0.0
3.5	10	750	5.2	1.7	1.1	0.4	0.1	0.1	0.3	0.1	0.1
3.5	15	750	4.1	1.3	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3.5	20	750	3.4	1.1	0.7	0.2	0.1	0.0	0.2	0.0	0.0
3.5	25	750	3.0	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	30	750	2.6	0.8	0.5	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	1000	4.4	1.4	1.0	0.3	0.1	0.1	0.2	0.1	0.0
3.5	15	1000	3.4	1.1	0.7	0.2	0.1	0.0	0.2	0.0	0.0
3.5	20	1000	2.8	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	25	1000	2.3	0.7	0.5	0.2	0.0	0.0	0.1	0.0	0.0
3.5	30	1000	2.0	0.6	0.4	0.1	0.0	0.0	0.1	0.0	0.0

9.4 Appendix D — Model 106 Battery Longevity and Programmed Setting Choices

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
0.5	10	130	>10	>10	>10	3.0	2.5	2.2	2.2	1.8	1.6
0.5	10	250	>10	>10	>10	2.9	2.3	2.0	2.2	1.7	1.5
0.5	10	500	>10	>10	>10	2.7	1.9	1.6	2.0	1.4	1.2
0.5	10	750	>10	>10	>10	2.6	1.7	1.3	1.9	1.2	1.0
0.5	10	1000	>10	>10	>10	2.4	1.5	1.1	1.8	1.1	0.8
0.5	15	130	>10	>10	>10	2.9	2.2	1.9	2.1	1.6	1.4
0.5	15	250	>10	>10	>10	2.8	2.0	1.7	2.1	1.5	1.2
0.5	15	500	>10	>10	>10	2.5	1.6	1.3	1.9	1.2	0.9
0.5	15	750	>10	>10	>10	2.3	1.4	1.0	1.7	1.0	0.8
0.5	15	1000	>10	>10	>10	2.1	1.2	0.9	1.6	0.9	0.6
0.5	20	130	>10	>10	>10	2.8	2.0	1.7	2.1	1.5	1.2
0.5	20	250	>10	>10	>10	2.7	1.8	1.5	2.0	1.3	1.1
0.5	20	500	>10	>10	>10	2.4	1.4	1.1	1.7	1.0	0.8
0.5	20	750	>10	>10	>10	2.1	1.1	0.9	1.6	0.8	0.6
0.5	20	1000	>10	>10	9.3	1.9	1.0	0.7	1.4	0.7	0.5
0.5	25	130	>10	>10	>10	2.7	1.8	1.5	2.0	1.4	1.1
0.5	25	250	>10	>10	>10	2.5	1.6	1.3	1.9	1.2	1.0
0.5	25	500	>10	>10	>10	2.2	1.2	0.9	1.6	0.9	0.7
0.5	25	750	>10	>10	9.6	1.9	1.0	0.7	1.4	0.7	0.5
0.5	25	1000	>10	>10	7.8	1.7	0.8	0.6	1.3	0.6	0.4
0.5	30	130	>10	>10	>10	2.6	1.7	1.3	1.9	1.3	1.0
0.5	30	250	>10	>10	>10	2.4	1.5	1.2	1.8	1.1	0.9
0.5	30	500	>10	>10	>10	2.1	1.1	0.8	1.5	0.8	0.6
0.5	30	750	>10	>10	8.3	1.8	0.9	0.6	1.3	0.6	0.5
0.5	30	1000	>10	9.5	6.7	1.6	0.7	0.5	1.2	0.5	0.4
1	10	130	>10	>10	>10	2.7	1.8	1.5	1.9	1.2	1.0
1	10	250	>10	>10	>10	2.5	1.6	1.2	1.7	1.0	0.8
1	10	500	>10	>10	>10	2.2	1.2	0.9	1.5	0.8	0.6
1	10	750	>10	>10	>10	2.0	1.0	0.7	1.3	0.6	0.4
1	10	1000	>10	>10	9.7	1.8	0.8	0.6	1.1	0.5	0.4
1	15	130	>10	>10	>10	2.6	1.7	1.4	1.8	1.2	0.9
1	15	250	>10	>10	>10	2.4	1.4	1.1	1.6	0.9	0.7
1	15	500	>10	>10	>10	2.0	1.1	0.8	1.3	0.7	0.5
1	15	750	>10	>10	8.7	1.7	0.8	0.6	1.1	0.5	0.4
1	15	1000	>10	9.8	7.0	1.5	0.7	0.5	1.0	0.4	0.3

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1	20	130	>10	>10	>10	2.5	1.6	1.3	1.8	1.1	0.9
1	20	250	>10	>10	>10	2.3	1.3	1.0	1.6	0.8	0.6
1	20	500	>10	>10	9.3	1.8	0.9	0.7	1.2	0.6	0.4
1	20	750	>10	9.7	6.9	1.5	0.7	0.5	1.0	0.4	0.3
1	20	1000	>10	7.8	5.5	1.3	0.5	0.4	0.8	0.3	0.2
1	25	130	>10	>10	>10	2.4	1.5	1.2	1.7	1.0	0.8
1	25	250	>10	>10	>10	2.1	1.2	0.9	1.5	0.8	0.6
1	25	500	>10	>10	7.8	1.7	0.8	0.6	1.1	0.5	0.3
1	25	750	>10	8.2	5.7	1.4	0.6	0.4	0.9	0.4	0.2
1	25	1000	>10	6.5	4.5	1.2	0.5	0.3	0.7	0.3	0.2
1	30	130	>10	>10	>10	2.4	1.4	1.1	1.7	1.0	0.7
1	30	250	>10	>10	>10	2.0	1.0	0.8	1.4	0.7	0.5
1	30	500	>10	9.5	6.7	1.5	0.7	0.5	1.0	0.4	0.3
1	30	750	>10	7.0	4.9	1.2	0.5	0.3	0.8	0.3	0.2
1	30	1000	>10	5.6	3.8	1.0	0.4	0.3	0.7	0.2	0.2
1.5	10	130	>10	>10	>10	2.3	1.3	1.0	1.6	0.9	0.7
1.5	10	250	>10	>10	>10	2.0	1.0	0.8	1.4	0.7	0.5
1.5	10	500	>10	>10	7.9	1.6	0.7	0.5	1.1	0.5	0.3
1.5	10	750	>10	8.1	5.7	1.2	0.5	0.4	0.8	0.3	0.2
1.5	10	1000	>10	6.4	4.4	1.0	0.4	0.3	0.7	0.3	0.2
1.5	15	130	>10	>10	>10	2.2	1.2	0.9	1.5	0.8	0.6
1.5	15	250	>10	>10	9.7	1.8	0.9	0.6	1.3	0.6	0.4
1.5	15	500	>10	8.5	6.0	1.3	0.5	0.4	0.9	0.4	0.3
1.5	15	750	>10	6.1	4.2	1.0	0.4	0.3	0.7	0.3	0.2
1.5	15	1000	>10	4.7	3.2	0.8	0.3	0.2	0.6	0.2	0.1
1.5	20	130	>10	>10	>10	2.0	1.1	0.8	1.5	0.7	0.6
1.5	20	250	>10	>10	8.5	1.7	0.8	0.5	1.1	0.5	0.4
1.5	20	500	>10	7.2	5.0	1.2	0.5	0.3	0.8	0.3	0.2
1.5	20	750	>10	5.0	3.4	0.9	0.3	0.2	0.6	0.2	0.1
1.5	20	1000	>10	3.8	2.6	0.7	0.2	0.2	0.5	0.2	0.1
1.5	25	130	>10	>10	>10	1.9	1.0	0.7	1.4	0.7	0.5
1.5	25	250	>10	>10	7.5	1.5	0.7	0.5	1.1	0.5	0.3
1.5	25	500	>10	6.3	4.4	1.0	0.4	0.3	0.7	0.3	0.2
1.5	25	750	>10	4.3	2.9	0.8	0.3	0.2	0.5	0.2	0.1
1.5	25	1000	9.2	3.3	2.2	0.6	0.2	0.1	0.4	0.1	0.1
1.5	30	130	>10	>10	9.8	1.8	0.9	0.7	1.3	0.6	0.4
1.5	30	250	>10	9.5	6.8	1.4	0.6	0.4	1.0	0.4	0.3
1.5	30	500	>10	5.5	3.8	0.9	0.4	0.2	0.6	0.2	0.2

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
1.5	30	750	>10	3.8	2.6	0.7	0.2	0.2	0.5	0.2	0.1
1.5	30	1000	8.2	2.8	1.9	0.5	0.2	0.1	0.4	0.1	0.1
2	10	130	>10	>10	>10	2.0	1.0	0.8	1.4	0.7	0.5
2	10	250	>10	>10	8.2	1.6	0.7	0.5	1.1	0.5	0.3
2	10	500	>10	7.2	5.0	1.2	0.5	0.3	0.8	0.3	0.2
2	10	750	>10	5.2	3.6	0.9	0.3	0.2	0.6	0.2	0.1
2	10	1000	>10	4.0	2.8	0.7	0.3	0.2	0.5	0.2	0.1
2	15	130	>10	>10	9.5	1.8	0.9	0.6	1.3	0.6	0.4
2	15	250	>10	8.9	6.3	1.4	0.6	0.4	0.9	0.4	0.3
2	15	500	>10	5.3	3.7	0.9	0.3	0.2	0.6	0.2	0.2
2	15	750	>10	3.8	2.6	0.7	0.2	0.2	0.5	0.2	0.1
2	15	1000	8.3	2.9	2.0	0.5	0.2	0.1	0.4	0.1	0.1
2	20	130	>10	>10	8.1	1.6	0.8	0.5	1.1	0.5	0.4
2	20	250	>10	7.3	5.1	1.2	0.5	0.3	0.8	0.3	0.2
2	20	500	>10	4.2	2.9	0.8	0.3	0.2	0.5	0.2	0.1
2	20	750	8.4	2.9	2.0	0.6	0.2	0.1	0.4	0.1	0.1
2	20	1000	6.6	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2	25	130	>10	>10	7.2	1.5	0.7	0.5	1.1	0.5	0.3
2	25	250	>10	6.4	4.4	1.1	0.4	0.3	0.7	0.3	0.2
2	25	500	>10	3.6	2.4	0.7	0.2	0.2	0.5	0.2	0.1
2	25	750	7.2	2.5	1.7	0.5	0.2	0.1	0.3	0.1	0.1
2	25	1000	5.6	1.9	1.2	0.4	0.1	0.1	0.2	0.1	0.1
2	30	130	>10	9.0	6.4	1.4	0.6	0.4	1.0	0.4	0.3
2	30	250	>10	5.6	3.9	1.0	0.4	0.3	0.7	0.2	0.2
2	30	500	8.9	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
2	30	750	6.4	2.1	1.4	0.4	0.1	0.1	0.3	0.1	0.1
2	30	1000	4.9	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	10	130	>10	>10	9.9	1.8	0.9	0.7	1.3	0.6	0.4
2.5	10	250	>10	9.3	6.6	1.4	0.6	0.4	1.0	0.4	0.3
2.5	10	500	>10	5.8	4.0	1.0	0.4	0.3	0.6	0.2	0.2
2.5	10	750	>10	4.1	2.8	0.7	0.3	0.2	0.5	0.2	0.1
2.5	10	1000	9.1	3.2	2.2	0.6	0.2	0.1	0.4	0.1	0.1
2.5	15	130	>10	>10	8.0	1.6	0.7	0.5	1.1	0.5	0.3
2.5	15	250	>10	7.2	5.0	1.2	0.5	0.3	0.8	0.3	0.2
2.5	15	500	>10	4.2	2.9	0.8	0.3	0.2	0.5	0.2	0.1
2.5	15	750	8.5	2.9	2.0	0.5	0.2	0.1	0.4	0.1	0.1
2.5	15	1000	6.7	2.3	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2.5	20	130	>10	9.3	6.6	1.4	0.6	0.4	1.0	0.4	0.3

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
2.5	20	250	>10	5.8	4.0	1.0	0.4	0.3	0.7	0.3	0.2
2.5	20	500	9.3	3.3	2.2	0.6	0.2	0.1	0.4	0.1	0.1
2.5	20	750	6.8	2.3	1.5	0.4	0.1	0.1	0.3	0.1	0.1
2.5	20	1000	5.3	1.7	1.2	0.3	0.1	0.1	0.2	0.1	0.0
2.5	25	130	>10	8.1	5.7	1.3	0.5	0.4	0.9	0.4	0.3
2.5	25	250	>10	4.9	3.4	0.9	0.3	0.2	0.6	0.2	0.1
2.5	25	500	7.9	2.7	1.8	0.5	0.2	0.1	0.4	0.1	0.1
2.5	25	750	5.7	1.9	1.3	0.4	0.1	0.1	0.3	0.1	0.1
2.5	25	1000	4.4	1.4	1.0	0.3	0.1	0.1	0.2	0.1	0.0
2.5	30	130	>10	7.2	5.1	1.2	0.5	0.3	0.8	0.3	0.2
2.5	30	250	>10	4.3	2.9	0.8	0.3	0.2	0.5	0.2	0.1
2.5	30	500	7.0	2.4	1.6	0.5	0.2	0.1	0.3	0.1	0.1
2.5	30	750	4.9	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
2.5	30	1000	3.8	1.2	0.8	0.2	0.1	0.1	0.2	0.1	0.0
3	10	130	>10	>10	8.4	1.7	0.8	0.6	1.1	0.5	0.4
3	10	250	>10	7.5	5.3	1.2	0.5	0.3	0.8	0.3	0.2
3	10	500	>10	4.4	3.0	0.8	0.3	0.2	0.5	0.2	0.1
3	10	750	8.6	3.0	2.0	0.6	0.2	0.1	0.4	0.1	0.1
3	10	1000	6.8	2.3	1.5	0.4	0.1	0.1	0.3	0.1	0.1
3	15	130	>10	9.3	6.6	1.4	0.6	0.4	1.0	0.4	0.3
3	15	250	>10	5.7	3.9	1.0	0.4	0.3	0.7	0.2	0.2
3	15	500	9.0	3.2	2.1	0.6	0.2	0.1	0.4	0.1	0.1
3	15	750	6.4	2.2	1.5	0.4	0.1	0.1	0.3	0.1	0.1
3	15	1000	5.0	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3	20	130	>10	7.7	5.4	1.2	0.5	0.4	0.8	0.3	0.2
3	20	250	>10	4.6	3.1	0.8	0.3	0.2	0.5	0.2	0.1
3	20	500	7.3	2.5	1.7	0.5	0.2	0.1	0.3	0.1	0.1
3	20	750	5.1	1.7	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3	20	1000	3.9	1.3	0.8	0.3	0.1	0.1	0.2	0.1	0.0
3	25	130	>10	6.6	4.6	1.1	0.4	0.3	0.8	0.3	0.2
3	25	250	>10	3.9	2.6	0.7	0.2	0.2	0.5	0.2	0.1
3	25	500	6.1	2.1	1.4	0.4	0.1	0.1	0.3	0.1	0.1
3	25	750	4.3	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3	25	1000	3.3	1.0	0.7	0.2	0.1	0.0	0.1	0.0	0.0
3	30	130	>10	5.8	4.0	1.0	0.4	0.3	0.7	0.3	0.2
3	30	250	9.3	3.3	2.2	0.6	0.2	0.1	0.4	0.1	0.1
3	30	500	5.3	1.7	1.2	0.3	0.1	0.1	0.2	0.1	0.0
3	30	750	3.7	1.2	0.8	0.2	0.1	0.0	0.2	0.0	0.0

Parameters at 3kOhms (M106)			Time from BOL to IFI			Time from IFI to N EOS			Time from N EOS to EOS		
			10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle	10% Duty Cycle	33% Duty Cycle	50% Duty Cycle
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
3	30	1000	2.8	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	10	130	>10	7.2	5.1	1.3	0.5	0.4	0.9	0.4	0.3
3.5	10	250	>10	4.7	3.2	0.9	0.3	0.2	0.6	0.2	0.2
3.5	10	500	7.3	2.5	1.7	0.5	0.2	0.1	0.4	0.1	0.1
3.5	10	750	5.3	1.7	1.2	0.4	0.1	0.1	0.2	0.1	0.1
3.5	10	1000	4.5	1.4	1.0	0.3	0.1	0.1	0.2	0.1	0.0
3.5	15	130	>10	6.1	4.2	1.1	0.4	0.3	0.8	0.3	0.2
3.5	15	250	>10	3.7	2.5	0.7	0.3	0.2	0.5	0.2	0.1
3.5	15	500	5.9	2.0	1.3	0.4	0.1	0.1	0.3	0.1	0.1
3.5	15	750	4.2	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3.5	15	1000	3.4	1.1	0.7	0.2	0.1	0.0	0.2	0.0	0.0
3.5	20	130	>10	5.2	3.6	1.0	0.4	0.2	0.7	0.3	0.2
3.5	20	250	8.9	3.1	2.1	0.6	0.2	0.1	0.4	0.1	0.1
3.5	20	500	5.0	1.6	1.1	0.3	0.1	0.1	0.2	0.1	0.0
3.5	20	750	3.5	1.1	0.7	0.2	0.1	0.0	0.2	0.0	0.0
3.5	20	1000	2.8	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	25	130	>10	4.6	3.1	0.9	0.3	0.2	0.6	0.2	0.1
3.5	25	250	7.7	2.7	1.8	0.5	0.2	0.1	0.3	0.1	0.1
3.5	25	500	4.3	1.4	0.9	0.3	0.1	0.1	0.2	0.1	0.0
3.5	25	750	2.9	0.9	0.6	0.2	0.1	0.0	0.1	0.0	0.0
3.5	25	1000	2.4	0.7	0.5	0.2	0.0	0.0	0.1	0.0	0.0
3.5	30	130	>10	4.1	2.8	0.8	0.3	0.2	0.5	0.2	0.1
3.5	30	250	6.8	2.3	1.6	0.5	0.2	0.1	0.3	0.1	0.1
3.5	30	500	3.7	1.2	0.8	0.2	0.1	0.1	0.2	0.1	0.0
3.5	30	750	2.6	0.8	0.5	0.2	0.1	0.0	0.1	0.0	0.0
3.5	30	1000	2.0	0.6	0.4	0.1	0.0	0.0	0.1	0.0	0.0

9.5 Appendix E — Model 1000/1000-D Battery Longevity and Programmed Setting Choices

Parameters at 3kOhms			Normal Mode Duty Cycle								
			10% (30s ON/5 min OFF)			35% (30s ON/1.1 min OFF)			51% (60s ON/1.1 min off)		
			BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS	BOL to IFI	IFI to N EOS	N EOS to EOS
mA	Hz	µS	Years	Years	Years	Years	Years	Years	Years	Years	Years
0.5	20	250	11.9	1.2	1.2	6.1	0.6	0.6	4.6	0.5	0.5
0.5	20	500	11.8	1.2	1.2	6.0	0.6	0.6	4.5	0.5	0.5
0.5	30	250	10.2	1.0	1.0	4.7	0.5	0.5	3.5	0.4	0.4
0.5	30	500	10.1	1.0	1.0	4.6	0.5	0.5	3.4	0.3	0.3
1	20	250	11.7	1.2	1.2	5.9	0.6	0.6	4.5	0.5	0.4
1	20	500	11.6	1.2	1.1	5.8	0.6	0.5	4.4	0.4	0.4
1	30	250	10.0	1.0	1.0	4.5	0.5	0.5	3.3	0.3	0.3
1	30	500	9.9	1.0	1.0	4.4	0.4	0.4	3.2	0.3	0.3
1.5	20	250	11.4	1.1	1.1	5.7	0.6	0.5	4.2	0.4	0.4
1.5	20	500	9.4	0.9	0.8	4.1	0.4	0.3	3.0	0.3	0.2
1.5	30	250	9.8	1.0	0.9	4.4	0.4	0.4	3.2	0.3	0.3
1.5	30	500	7.7	0.7	0.7	3.1	0.3	0.2	2.2	0.2	0.2
2	20	250	9.7	0.9	0.8	4.3	0.4	0.3	3.2	0.3	0.2
2	20	500	7.2	0.7	0.6	2.8	0.3	0.2	2.0	0.2	0.2
2	30	250	8.2	0.8	0.7	3.3	0.3	0.3	2.4	0.2	0.2
2	30	500	5.6	0.5	0.5	2.0	0.2	0.2	1.4	0.1	0.1
2.5	20	250	7.9	0.7	0.7	3.2	0.3	0.2	2.3	0.2	0.2
2.5	20	500	5.5	0.5	0.4	1.9	0.2	0.1	1.4	0.1	0.1
2.5	30	250	6.5	0.6	0.5	2.4	0.2	0.2	1.7	0.2	0.1
2.5	30	500	4.2	0.4	0.3	1.4	0.1	0.1	1.0	0.1	0.1
3	20	250	6.4	0.6	0.5	2.4	0.2	0.2	1.7	0.2	0.1
3	20	500	4.2	0.4	0.3	1.4	0.1	0.1	1.0	0.1	0.1
3	30	250	5.1	0.5	0.4	1.8	0.2	0.1	1.2	0.1	0.1
3	30	500	3.1	0.3	0.2	1.0	0.1	0.1	0.7	0.1	0.1
3.5	20	250	5.2	0.5	0.4	1.8	0.2	0.1	1.3	0.1	0.1
3.5	20	500	3.2	0.3	0.2	1.0	0.1	0.1	0.7	0.1	0.1
3.5	30	250	4.0	0.4	0.3	1.3	0.1	0.1	0.9	0.1	0.1
3.5	30	500	2.3	0.2	0.2	0.7	0.1	0.1	0.5	0.0	0.0

10 Information and Support

If there are questions regarding use of the VNS Therapy System or any of its accessories, contact LivaNova:

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Report all adverse events related to the device to LivaNova and to your local regulatory authority.

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Canada - https://www.canada.ca/en/health-canada.html

UK - https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

EU - https://ec.europa.eu/growth/sectors/medical-devices/contacts_en