

OPTIMIZER® Smart Mini Implantable Pulse Generator

INSTRUCTIONS FOR USE

Federal (US) law restricts this device to sale by or on the order of a physician

Part No.: 13-290-015-US Rev. 03

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The OPTIMIZER Smart Mini system and the CCM technology are protected by several U.S. Patents. For an up-to-date list of relevant patents and patent applications, visit our patents page: http://www.impulse-dynamics.com/us/patents

Please read the documentation provided completely before you use the device.

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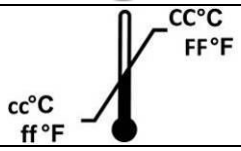
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EXPLANATION OF SYMBOLS ON LABELS

Symbol	Description
CE 0344	CE Conformity marking, 0344 - Notified Body Number
Rx Only	Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.
	Consult instructions for use
	Do not use if package is damaged
	Storage and transport temperature limits
	Date of manufacture
	Manufacturer
EC REP	Authorized representative in the European Community
REF	Catalogue number
SN	Serial number
LOT	Lot number
	Use-by date
STERILE EO	Sterilized with ethylene oxide
	Do not re-use
	Caution, consult instructions for use
MD	Medical Device
	MR Conditional

Symbol	Description
	Single sterile barrier system with protective packaging inside
	Open here
	Torque wrench
	Port plug

1.0 THE OPTIMIZER SMART MINI SYSTEM

The OPTIMIZER® Smart Mini system is comprised of the following components:

- OPTIMIZER Smart Mini Implantable Pulse Generator (IPG)
- Intelio Programmer
- Guardio/Vesta Charger

1.1 Description of the OPTIMIZER Smart Mini System

The OPTIMIZER Smart Mini Implantable Pulse Generator (IPG) is an FDA-approved Class III medical device intended for the treatment of moderate to severe heart failure; a condition wherein the heart muscle does not pump blood as well as it should, resulting in reduced cardiac output. The OPTIMIZER Smart Mini IPG monitors the heart's intrinsic activity and delivers Cardiac Contractility Modulation (CCM®) therapy to cardiac tissue during the ventricular absolute refractory period, when the cardiac tissue is not capable of activation, thus rendering the CCM therapy as non-excitatory. CCM therapy delivery is synchronized with the detected local electrical activity and is designed to treat heart failure by increasing the cardiac output or increasing cardiac muscle contractility.

Note: The OPTIMIZER Smart Mini IPG only delivers non-excitatory CCM pulses to the heart and has no pacemaker or ICD functions.

The Intelio Programmer uses telemetry to interrogate and program the OPTIMIZER Smart Mini IPG. With the Intelio Programmer, the physician can obtain diagnostic data from the OPTIMIZER Smart Mini IPG as well as tailor the operating parameters of the OPTIMIZER Smart Mini IPG to meet the specific requirements of each patient.

The Guardio/Vesta Charger is powered by a rechargeable battery and is used by the patient to charge their implanted OPTIMIZER Smart Mini IPG transcutaneously using inductive energy transfer. It incorporates a graphical display that shows a different screen for each operational state as well as alerts and other information it receives through daily communications with the OPTIMIZER Smart Mini IPG.

1.2 OPTIMIZER Smart Mini IPG Implantable Leads Requirements

The OPTIMIZER Smart Mini IPG is designed to be used with two (2) or three (3) commercially available transvenous intracardiac pacing leads; two (2) leads are implanted in the right ventricle and one (1) optional lead implanted in the right atrium. The OPTIMIZER Smart Mini IPG is compatible with a standard pacemaker lead equipped with an IS-1 connector.

The implanting physician may select any standard transvenous intracardiac pacing lead with the following characteristics:

- Bipolar lead approved for transvenous intracardiac pacing
- Standard IS-1 BI (bipolar) connector
- Maximum lead diameter 8 French
- Active fixation with an electrically-active corkscrew and distal electrode with an electrically-active surface area of ≥ 3.6 mm^2
- Distal (tip) electrode coated with a low-polarization coating (e.g., titanium nitride or iridium oxide)
- Proximal (Ring) electrode electrically-active surface of at least 15 mm^2, and Tip-Ring spacing between 8 and 30 mm
- Maximum total wire resistance of 200 Ω

Note: The leads qualified for delivering CCM therapy from OPTIMIZER IPGs must be commercial models that are FDA approved.

Pacing Leads Suitable for use with the OPTIMIZER IPG for CCM Signal Delivery

Current Offerings as of January 2, 2021

Requirement for CCM	**Medtronic CapSureFix Novus MRI™ SureScan™ 4076, 5076, 5086 Leads**	**Medtronic SelectSecure ™ MRI SureScan™ 3830 Lead**	**Abbott (St Jude) 2088TC Tendril STS lead**	**Abbott (St Jude) LPA1200M Tendril MRI Lead**	**Boston Scientific Ingevity + 7840, 7841, 7842 Leads**	**Biotronik Solia-S Leads**
Bipolar lead approved for transvenous intracardiac pacing	YES	YES	YES	YES	YES	YES
Standard IS-1 bipolar connector	YES	YES	YES	YES	YES	YES
Active fixation with an electrically-active corkscrew distal electrode with a minimal electrically-active surface area of 3.6 mm^2	YES, 4.2 mm^2	YES, 3.6 mm^2	YES, 6.9 mm^2	YES, 6.0 mm^2	YES, 4.5 mm^2	YES, 4.5 mm^2
Distal electrode coated with a low-polarization coating (e.g., titanium nitride or iridium oxide)	YES, titanium nitride coating	YES, titanium nitride coating	YES, titanium nitride coating	YES, titanium nitride coating	YES, IROX™ (iridium oxide) coating	YES, “Fractal Iridium” (iridium oxide) coating

1.3 OPTIMIZER Smart Mini IPG Lead Connectors

The connector block accepts three (3) bipolar IS-1-BI connectors. The terminals are marked as follows:

- “A”: Atrium
    - When operating in 2-lead mode, the “A” port is to be plugged with a silicone port plug provided with the IPG
    - When operating in 3-lead mode, for sensing
- “V1”: Ventricle 1 – for sensing and CCM therapy delivery
- “V2”: Ventricle 2 – for sensing and CCM therapy delivery

1.4 OPTIMIZER Smart Mini IPG Physical Characteristics

Model	CCM X11
Height (mm)	61.3 ± 1.5
Width (mm)	44.0 ± 0.5
Thickness (mm)	11.0 ± 0.5
Volume (cm^3)	23.0 ± 0.5
Mass (g)	31 ± 3.0
Exposed Metallic Surface[a] (cm^2)	32.5
X-ray ID The ID comprises the following 3 elements: • Manufacturer Code: "ID" for Impulse Dynamics • Model Number Code: "OSM" for OPTIMIZER Smart Mini • Year code: "A" for 2019, "B" for 2020, "C" for 2021, etc.	**ID.OSM.y** "y" is replaced by the letter code for the year of manufacture.
Materials in Contact with Human Tissue[b]	Titanium, Epoxy resin, Silicone rubber
Lead Connectors	3.2 mm; IS-1/VS-1

[a] When using unipolar ventricular or atrial sensing, the case of the OPTIMIZER Smart Mini device serves as indifferent electrode.

[b] Tests have revealed that these materials are biocompatible. The OPTIMIZER Smart Mini IPG does not cause any temperature elevation capable of damaging the surrounding tissue.

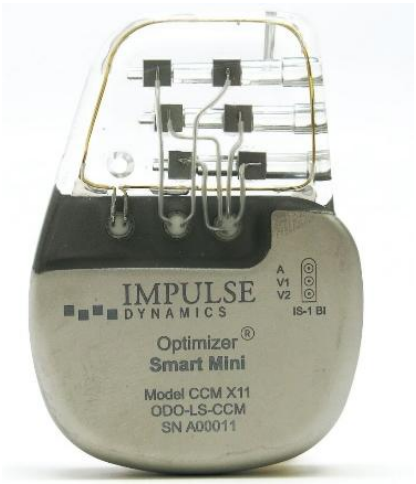


Figure 1: OPTIMIZER Smart Mini IPG

1.5 OPTIMIZER Smart Mini IPG Battery

1.5.1 Battery Specifications

The OPTIMIZER Smart Mini IPG is powered by a medical-grade, rechargeable, lithium-ion (Li-ion) battery, Model 2993, manufactured by Integer. It has a maximum voltage of 4.1 V and a usable charge capacity of 0.215 Ah.

1.5.2 Battery Behavior

When fully charged, the voltage of the battery in the OPTIMIZER Smart Mini IPG is approximately 4.1 V.

When battery voltage of the OPTIMIZER Smart Mini IPG drops to 3.5 V, the IPG places itself in OOO mode (Standby mode) and stops performing any functions except for telemetric communication with the Intelio Programmer and Guardio/Vesta Charger. The OPTIMIZER Smart Mini IPG will regain its full functionality whenever its battery voltage rises above 3.6 V during the battery recharging process.

If the battery voltage of the OPTIMIZER Smart Mini IPG drops below 3.2 V, the IPG disconnects its circuitry from the battery and stops performing any functions, including telemetric communication with the Intelio Programmer and Guardio/Vesta Charger (charging of the device can still be performed). The OPTIMIZER Smart Mini IPG will resume its normal operation whenever the battery is recharged.

It is therefore recommended that the patient be instructed to charge the OPTIMIZER Smart Mini IPG at least once a week. Immediate recharging is also recommended if the battery level of the OPTIMIZER Smart Mini IPG, after interrogation with the Intelio Programmer, is noted to be at or below 3.6 V.

1.5.3 Expected Service Life

The expected service life of the OPTIMIZER Smart Mini IPG is limited by the service life of its rechargeable battery. The rechargeable battery inside the OPTIMIZER Smart Mini IPG should provide at least 20 years of service under normal use.

Over time the rechargeable battery in the OPTIMIZER Smart Mini IPG, being subjected to repeated charge and discharge cycles, will lose its ability to maintain its charge capacity.

Once the OPTIMIZER Smart Mini IPG reaches its 20th year of service, it should be evaluated for elective replacement. The OPTIMIZER Smart Mini IPG will need to be replaced when its battery, after being fully recharged, can no longer maintain enough charge to deliver CCM therapy for a full week without becoming severely depleted.

In order to evaluate the OPTIMIZER Smart Mini IPG for elective replacement, it is important that the patient be instructed to fully charge their OPTIMIZER Smart Mini IPG 7 days prior to their scheduled routine checkup visit so that the physician may perform an evaluation of the battery charge capacity of their OPTIMIZER Smart Mini IPG.

1.6 OPTIMIZER Smart Mini IPG Packaging

The OPTIMIZER Smart Mini IPG is packaged in a sterile TYVEK/PETG blister package and placed inside a shelf box that also contains the following items:

- Peel-off labels for use with implantation documents
- Literature pack (includes a printed copy of this document, a patient ID Card, and other important information)

The TYVEK/PETG blister package has been sterilized with ethylene oxide gas and is comprised of an inner TYVEK/PETG blister pack within an outer TYVEK/PETG blister package.

The inner blister pack contains the following items:

- One (1) OPTIMIZER Smart Mini IPG
- One (1) Allen #2 torque wrench (77.68 mNm = 11 oz-in)
- One (1) IS-1 Port Plug

1.7 OPTIMIZER Smart Mini IPG Storage

The recommended storage conditions for the OPTIMIZER Smart Mini IPG are as follows:

- Ambient temperature: 0°C to 40°C (32°F to 104°F)
- Atmospheric pressure: 50 kPa to 304 kPa (14.81 inHg to 90.02 inHg)

Relative humidity has no impact on the OPTIMIZER Smart Mini IPG.

2.0 USER PROFILE AND TRAINING

The operators of the OPTIMIZER Smart Mini system include patients, physicians (and the trained medical personnel who assist them), and Impulse Dynamics representatives. Physicians, medical personnel, and Company representatives who operate the OPTIMIZER Smart Mini system should be familiar with the operation of electronic medical equipment, particularly the operation of implanted medical devices and programmers.

Physicians and medical personnel can participate in a Company-sponsored training program that will provide theoretical and hands-on training regarding the technology, device features, and detailed operating instructions for the OPTIMIZER Smart Mini IPG, the Intelio Programmer, and the Guardio/Vesta Charger. The need for future retraining regarding the OPTIMIZER Smart Mini System is determined by Company personnel based on the user's individual implant history and frequency.

Patient training will be limited to the use of the Guardio/Vesta Charger and will be offered by Impulse Dynamics Representatives post-implant.

3.0 INDICATIONS OF USE

The OPTIMIZER Smart Mini System, which delivers Cardiac Contractility Modulation (CCM™) therapy, is indicated to improve 6-minute hall walk, quality of life, and functional status of NYHA Class III heart failure patients who remain symptomatic despite guideline directed medical therapy, are not receiving Cardiac Resynchronization Therapy (CRT), and have a left ventricular ejection fraction ranging from 25% to 45%.

4.0 CONTRAINDICATIONS AND PRECAUTIONS

Use of the OPTIMIZER Smart Mini system is **contraindicated** in:

1. Patients with a mechanical tricuspid valve
2. Patients in whom vascular access for implantation of the leads cannot be obtained

5.0 WARNINGS

5.1 Potential Complications of Device Implantation

Just like any surgical procedure, implantation of an OPTIMIZER Smart Mini IPG is associated with certain risks. Complications of device implantation reported in the literature include, but are not limited to:

- Infection
- Skin necrosis
- Device migration
- Hematoma formation
- Seroma formation
- Histotoxic reactions (also see: Potential Adverse Effects, Section 7)

Programming high sensitivities (i.e., sensitivity settings less than 2 mV) may increase the system's susceptibility to electromagnetic interference, which could either inhibit or trigger CCM therapy delivery.

Acute and chronic complications reported in the literature include, but are not limited to:

- Lead fracture
- Lead displacement
- Atrial or ventricular perforation
- Rare cases of pericardial tamponade

Perforation of the ventricular wall can induce direct stimulation of the phrenic nerve or the diaphragm. A significant impedance change noted during a routine check-up can indicate a lead fracture, lead displacement, lead insulation damage, or perforation (also see: Potential Adverse Effects, Section 7).

In very rare cases (<1%), transvenous lead placement can lead to venous thrombosis and subsequent SVC syndrome.

Loss of sensing shortly after implant can be the result of lead displacement. In addition, loss of CCM therapy delivery could be due to a lead fracture.

5.2 Potential Arrhythmias

5.2.1 Atrial and Ventricular Arrhythmias Potentially Caused by Lead Implantation

The use of transvenous leads may lead to arrhythmias, some of which may be life-threatening, such as ventricular fibrillation and ventricular tachycardia. The use of screw-in leads, such as those used for CCM therapy delivery, has the potential of causing conduction disturbances such as bundle branch block. These can be minimized by performing the implant under fluoroscopic guidance, ensuring that the leads are placed in the appropriate position prior to fixation, as well as limiting the number of lead manipulations.

Please read and follow all directions in the Instruction for Use document provided with the leads that you intend to use in order to minimize adverse events associated with lead implantation.

5.2.2 Ventricular Arrhythmias Potentially Caused by CCM Therapy Pulses

CCM therapy pulses possess more energy than typical pacing pulses. Thus, they are capable of eliciting activation of cardiac tissue when delivered outside of the absolute refractory period. CCM therapy pulses delivered outside of the ventricular absolute refractory period have the potential of causing pulse-induced arrhythmias (some of which may be life-threatening, such as ventricular fibrillation and tachycardia). For this reason, CCM therapy delivery parameters must be chosen carefully. Most importantly, the various settings related to conditions that inhibit CCM therapy delivery (e.g., LS Alert Window, refractory periods, and IEGM sensitivities) must be selected to allow delivery of CCM therapy only on normally conducted (e.g., non-arrhythmic) beats, but inhibit them on beats of suspected ectopic or premature origin.

In addition, CCM therapy pulses may cause changes in the electrical conduction of tissue. For this reason, the delivery of CCM therapy pulses to the ventricular septum has the potential of causing bundle branch block that could lead to bradycardia. Through similar mechanisms, CCM-induced changes in the electrical conduction of the myocardium have the potential of inducing tissue refractoriness that may facilitate the induction of reentrant tachyarrhythmias. It is recommended that the patient be monitored carefully for changes in heart rhythm when CCM therapy is temporarily activated during lead implantation, as well as during the first permanent activation of CCM therapy after implant and subsequent follow-up visits. Changes in ventricular rhythm caused by the delivery of CCM therapy pulses may require repositioning the leads and/or changing the CCM train delay and CCM amplitude parameters to values that do not adversely affect the patient’s ventricular rhythm.

5.2.3 Atrial Arrhythmias Potentially Caused by CCM Therapy Pulses

Atrial and supraventricular arrhythmias could theoretically be initiated when CCM-induced ventricular activity is conducted retrograde to the atria, resulting in premature atrial depolarization. The OPTIMIZER Smart Mini IPG may sense the ventricular activation resulting from the retrograde-induced atrial event and deliver CCM therapy as programmed. In addition, strong CCM therapy pulses delivered through leads implanted in a basal position close to the atria can directly stimulate the atria. If CCM therapy causes atrial activation through either of these mechanisms, and the atrial signal is then conducted to the ventricles, it may look like couplet PACs (AVAV), but the second complex would be identified as a “PVC” or “VT” by the OPTIMIZER Smart Mini IPG.

The main variables that may cause CCM therapy pulses to lead to atrial activation are ventricular lead placement location on the right ventricular septum, CCM pulse amplitude, and CCM train delay. To prevent atrial arrhythmias due to CCM therapy pulses, it is recommended that basal lead implant locations be avoided.

The potential for direct atrial activation by CCM therapy pulses can be tested during implant by setting the CCM pulse amplitude to the highest possible value and extending the CCM train delay by 40 to 50 ms beyond its recommended setting while ensuring that the CCM therapy pulse train, including its balancing phase, remains entirely within the bounds of the ventricular absolute refractory period, then delivering CCM therapy while monitoring the patient’s heart rhythm for episodes of atrial activation. The testing should confirm the absence of atrial activation with the increased CCM amplitude and extended CCM train delay.

In addition to proper lead location and CCM parameter programming, another protective measure that must be implemented is the programming of the Atrial Tachycardia Rate (ODO-LS-CCM mode only) to a sufficiently low value to prevent CCM therapy delivery from inducing atrial arrhythmias while still allowing for the consistent delivery of CCM therapy.

5.3 Electrocautery

Warning: The use of surgical electrocautery devices, especially of the monopolar kind, can induce CCM therapy inhibition or cause the OPTIMIZER Smart Mini IPG to revert to its Safe Mode (OOO mode, with no CCM delivery). If the device is found to have reverted to its Safe Mode, it will need to be reset, which will clear the statistical data stored in the device. The device can be damaged if high energies are coupled into the system.

Use of electrocautery in close proximity to an implanted OPTIMIZER Smart Mini IPG can also couple radiofrequency (RF) energy directly through the leads and lead tips into the cardiac muscle tissue, producing burns or possibly cardiac arrhythmias. If electrocautery is used, brief signal bursts should be considered, with the neutral electrode positioned such that its effects on the OPTIMIZER Smart Mini IPG and its attached leads are minimized. The risk of adverse effects can be mitigated by placing the OPTIMIZER Smart Mini IPG into OOO mode. The patient’s peripheral pulse should be monitored throughout the procedure and the correct operation of the OPTIMIZER Smart Mini IPG should be verified immediately after the procedure.

5.4 RF Ablation

Warning: RF ablation can cause the OPTIMIZER Smart Mini IPG to inhibit CCM therapy delivery or to revert to its Safe Mode (equivalent to OOO mode, with no CCM delivery) with the possible loss of statistical data. Depending on the amount of energy coupled into the system, the device could also be damaged. If an RF ablation procedure is performed in close proximity to the leads, the leads can couple radiofrequency (RF) energy via the lead tips into the myocardium, producing burns or possibly cardiac arrhythmias.

If an RF ablation procedure has to be performed, the neutral electrode should be positioned such that the current flowing through the OPTIMIZER Smart Mini IPG and the leads is minimized. Avoid direct contact between the ablation catheter and the OPTIMIZER Smart Mini IPG or its leads. The risk of adverse effects can be mitigated by placing the OPTIMIZER Smart Mini IPG into OOO mode. The patient's peripheral pulse should be monitored throughout the procedure and the correct operation of the OPTIMIZER Smart Mini IPG should be verified immediately after the procedure. If the device has gone into Safe Mode, it will need to be reset by qualified personnel. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

5.5 Diathermy (Medical "Short Wave" Induction Heating)

Warning: Medical diathermy is generally contraindicated in patients with implanted devices. The effects of such intense energies on the OPTIMIZER Smart Mini IPG cannot be predicted. Although damage to the circuitry of the IPG and/or the myocardium appears unlikely, it nevertheless could occur.

If diathermy is to be used notwithstanding the contraindication, it should not be applied in close proximity to the OPTIMIZER Smart Mini IPG and its associated leads. The risk of adverse effects can be mitigated by placing the OPTIMIZER Smart Mini IPG into OOO mode. The patient's peripheral pulse should be monitored throughout the procedure and the correct operation of the OPTIMIZER Smart Mini IPG should be verified immediately after the procedure. If the device has gone into Safe Mode, it will need to be reset by qualified personnel. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

5.6 Defibrillation and Cardioversion

Warning: Any implanted device can be damaged by external cardioversion or defibrillation. In addition, the myocardium adjacent to the lead tips and/or the tissue in the area of the device may be damaged. Altered signal thresholds could also be one of the consequences. The defibrillation current can also make the OPTIMIZER Smart Mini IPG revert to its Safe Mode (equivalent to OOO mode, with no CCM delivery). In addition, the OPTIMIZER Smart Mini IPG and its leads may be damaged by exposure to the high energies discharged by external defibrillators.

No particular paddle placement can avoid such damage. To decrease the risk, it is recommended to position the paddles anterior and posterior, as far away from the OPTIMIZER Smart Mini IPG as possible. In addition, paddle positions that would bring the OPTIMIZER Smart Mini IPG into the direct path of the defibrillation current should be avoided.

After defibrillation, the function of the OPTIMIZER Smart Mini IPG should be closely monitored. In the unlikely event of abnormal function, lead repositioning (or replacement), and IPG reprogramming (or replacement) may be required. If the device is found to have reverted to its Safe Mode, it will need to be reset by qualified personnel. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

Internal defibrillation will not damage the device.

5.7 Therapeutic Ultrasound

Warning: Direct exposure of the OPTIMIZER Smart Mini IPG to therapeutic ultrasound can damage the device. In addition, the OPTIMIZER Smart Mini IPG can inadvertently concentrate the ultrasound field and cause harm to the patient.

Therapeutic ultrasound can be used, provided the implant is located far away from the ultrasound field. The risk of adverse effects can be mitigated by placing the OPTIMIZER Smart Mini IPG into OOO mode. The patient's peripheral pulse should be monitored during the procedure. Immediately after the treatment, the OPTIMIZER Smart Mini IPG should be checked for proper function. If the device is found to have reverted to its Safe Mode, it needs to be reset. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

5.8 Nuclear Magnetic Resonance (NMR), Magnetic Resonance Imaging (MRI)

The OPTIMIZER Smart Mini IPG is Magnetic Resonance (MR) Conditional, and patients with this device may be scanned safely with magnetic resonance imaging (MRI) **if all the requirements for the implanted components and for scanning are met.**

The MR Conditional OPTIMIZER Smart Mini CCM system is composed of the OPTIMIZER Smart Mini IPG and MR Conditional leads suitable for CCM delivery and with established conditions for safe use in the 1.5T and 3T MRI environment.

Warning: Scanning under other conditions may result in severe patient injury, death, or device malfunction.

Please refer to the MRI Safety Information Leaflet contained in the IPG packaging and on the company website under Technical Documentation for detailed MRI Safety Information and required conditions for use.

5.9 Radiation Therapy

Warning: Therapeutic equipment generating ionizing radiation, such as linear accelerators and cobalt machines employed for treating malignant diseases, can damage the circuits used in most active implantable devices. Because the effect is cumulative, both dose rate and total dose determine if damage will occur and its possible extent. Be aware that certain types of damage might not be immediately detectable. In addition, the electromagnetic fields generated by some types of radiation equipment for beam “steering” purposes can affect the function of the OPTIMIZER Smart Mini IPG.

Radiation therapy can lead to a broad spectrum of effects, reaching from transient interference to permanent damage. Therefore, it is advisable to locally shield the OPTIMIZER Smart Mini IPG against radiation if radiation therapy is to be used. During a radiation treatment and thereafter, the function of the IPG needs to be monitored. If the tissue in the vicinity of the implant has to be irradiated, it may be advisable to relocate the OPTIMIZER Smart Mini IPG.

5.10 Lithotripsy

Warning: Direct exposure of the OPTIMIZER Smart Mini IPG to shock waves can damage the device. A device implanted outside the shock wave path presents no clear-cut contraindication to lithotripsy. The risk of adverse effects can be mitigated by placing the OPTIMIZER Smart Mini IPG into OOO mode. The patient’s peripheral pulse should be monitored during the procedure. Immediately after the treatment, the OPTIMIZER Smart Mini IPG should be checked for proper function. If the device is found to have reverted to its Safe Mode, it will need to be reset by qualified personnel. A consequence of a device reset is that all statistical data stored in the IPG is cleared.

5.11 Transcutaneous Electrical Nerve Stimulation (TENS)

Warning: TENS is generally contraindicated in patients with implanted electrical devices. The high-voltage impulse delivered into the body by the TENS unit can impair the operation of the OPTIMIZER Smart Mini IPG.

If a TENS unit is used, the TENS electrodes should be attached as far as possible from the OPTIMIZER Smart Mini IPG and its leads. In addition, aiming for a limited current path, consider placing the TENS electrodes as close to each other as possible. The patient’s peripheral pulse should be closely monitored while TENS is applied. The risk of adverse effects can be mitigated by placing the OPTIMIZER Smart Mini IPG into OOO mode.

5.12 Handling

Warning: Do not implant the OPTIMIZER Smart Mini IPG if the package is damaged or if the device has been dropped onto a hard surface from a height of 12 in or more while still in the shipping box. Do not implant the device if it has been dropped onto a hard surface after unpacking. Damaged packages or dropped devices should be returned to Impulse Dynamics for evaluation.

5.13 Resterilization and Reuse

Warning: An OPTIMIZER Smart Mini IPG or Port Plug that has been explanted for any reason must not be reused in another patient.

Do not resterilize and/or reuse the OPTIMIZER Smart Mini IPG, the Port Plug, or the torque wrench provided with the device.

5.14 Cremation

Warning: Never incinerate an OPTIMIZER Smart Mini IPG. The IPG must be explanted before the deceased patient is cremated.

The OPTIMIZER Smart Mini IPG contains a sealed chemical battery. Make absolutely certain that an implanted OPTIMIZER Smart Mini IPG is removed before a deceased patient is cremated.

6.0 CAUTIONS

6.1 Environmental Conditions

The following discussion on potential hazards from the environment focuses on maintaining the utmost patient safety. Although the OPTIMIZER Smart Mini IPG was designed to provide the highest possible protection against such hazards, complete immunity against these risks cannot be guaranteed.

The OPTIMIZER Smart Mini IPG should not be used in the vicinity of other electrical equipment capable of producing signals that could interfere with its operation. If proper separation is not feasible, the OPTIMIZER Smart Mini IPG must be monitored to ensure normal function.

Similar to other cardiac rhythm management IPGs, the OPTIMIZER Smart Mini IPG can be affected by interference from magnetic, electrical, and electromagnetic signals, provided these are sufficiently strong or have characteristics resembling cardiac activity. Most interference will lead to inhibition of CCM therapy delivery. In rare cases, an interfering signal could trigger inappropriate CCM therapy delivery. In addition, interfering signals exceeding a certain threshold may couple enough energy into the IPG to damage the IPG circuits and/or the myocardial tissue in the vicinity of the leads. The Patient's Manual addresses these risks, which should be discussed during consultations with the patient.

The susceptibility of a particular device is dependent on the location of the IPG pocket, the type of interfering signal, and the programmed operating parameters.

Because of the diversity of the potential causes of electromagnetic interference, Impulse Dynamics cannot characterize and describe all sources of interference and their effects in this manual.

Caution: Patients should be instructed to be cautious in the vicinity of equipment that generates strong electrical or electromagnetic fields and seek medical advice before entering an area with posted warnings advising pacemaker patients (or patients with other types of implantable devices) not to approach.

6.2 Home Appliances

Home and commercial microwave ovens do not affect the operation of the OPTIMIZER Smart Mini IPG, provided they are in good condition and used as intended. Even microwave energy from a severely defective microwave oven directly radiating onto the IPG does not damage the device. However, such exposure may impair the sensing function of the device, which could eventually impact CCM therapy delivery.

Patients with an implanted OPTIMIZER Smart Mini IPG should be advised not to use or come in close proximity to induction stoves as they could interfere with the normal operation of the OPTIMIZER Smart Mini IPG.

Patients with an implanted OPTIMIZER Smart Mini IPG should be advised that some electric razors, electric power tools, and electric ignition systems, including those of gasoline-powered engines, could cause interference. Generally, patients implanted with an OPTIMIZER Smart Mini IPG may use gasoline-powered engines, provided that protective hoods, shrouds, and other shielding devices have not been removed.

6.3 Store Anti-Theft Systems/Airport Security Screening Systems

Certain types of anti-theft systems, such as those installed at entrances/exits of stores, libraries, and other facilities, as well as airport security systems can interfere with the OPTIMIZER Smart Mini IPG. Such interference would most often inhibit CCM therapy delivery. Patients should be advised to walk through such systems at a normal pace, i.e. not to slow down while passing through. Prior to passing through airport security systems, patients should notify the attendant security personnel that they carry an implant and should present their implant ID card.

6.4 Industrial Machinery

High voltage power lines, electric and arc welders, electric smelters, and power-generating equipment can interfere with the operation of the OPTIMIZER Smart Mini IPG. For that reason, one needs to consider the field strengths and modulation characteristics of all electromagnetic fields that patients are exposed to in their workplaces or due to their lifestyle. Patients need to be specifically warned about these risks, or the OPTIMIZER Smart Mini IPG should be programmed to minimize its susceptibility.

6.5 Transmitting Devices

Communication equipment such as radio and TV transmitters (including amateur [“ham radio”] transmitters, microwave radio, and CB radio transmitters with power amplifiers) as well as radar transmitters can interfere with the operation of the OPTIMIZER Smart Mini IPG. For that reason, one needs to consider the field strengths and modulation characteristics of all electromagnetic fields patients are exposed to in their workplaces or due to their lifestyle. Patients need to be specifically warned about these risks, or the OPTIMIZER Smart Mini IPG should be programmed to minimize its susceptibility.

6.6 Cellular and Mobile Phones

Cell phones and other mobile phones can adversely affect the operation of the OPTIMIZER Smart Mini IPG. They can be caused by the radio frequencies emitted by the phones or by the phones’ speaker and charging magnets (e.g., iPhone 12). The potential consequences of exposure include inhibition of or inappropriate CCM therapy delivery if the phone is in very close proximity (within 10 in) of an OPTIMIZER Smart Mini IPG and the corresponding leads. Because of the incredible variety of mobile phones as well as the significant physiologic differences between patients, it is impossible to make generally applicable recommendations.

As a general guideline, patients implanted with an OPTIMIZER Smart Mini IPG who would like to use a mobile phone are advised to hold the phone to the ear that is contralateral to the implant site. Patients should not carry the phone in a breast pocket or on a belt closer than 10 inches from the implanted IPG because some phones emit signals even when they are turned on but not in use.

Compared to smaller cell phones, portable (handbag) and mobile (permanent car or boat installation) phones will generally transmit at higher power levels. For phones with higher transmission power levels, it is recommended to maintain a minimum separation of 20 inches between the antenna and the implanted IPG.

7.0 POTENTIAL ADVERSE EFFECTS

Examples of adverse effects that may occur as the result of the surgical procedure are listed below in the order of their clinical severity:

1. Death
2. Arrhythmias (brady or tachyarrhythmias including fibrillation)
3. Stroke or TIA (“transient ischemic attack”)
4. Formation of blood clots
5. Respiratory/ventilatory failure
6. RA/RV perforation
7. Hemorrhage
8. Infection

9. Pleura or pericardial effusion
10. Pneumothorax
11. Injury to the heart or blood vessels
12. Damage to the heart muscle
13. Damage to the tricuspid valve, potentially resulting in tricuspid valve regurgitation
14. Damage to specialized tissue in the heart responsible for initiating each heartbeat (i.e., the heart's conduction system)
15. Pain at the incision site

Examples of additional adverse effects potentially occurring secondary to CCM therapy delivery are listed below in the order of their clinical severity:

1. Abnormal cardiac function
2. Atrial and ventricular tachyarrhythmias
3. Atrial and ventricular bradyarrhythmias
4. Worsening heart failure
5. Myocardial tissue damage
6. Lead dislodgement
7. Chest pain
8. Chest wall sensations
9. Inappropriate ICD behavior as a result of interaction with an implanted OPTIMIZER Smart Mini IPG

8.0 DEVICE IMPLANTATION

8.1 General Considerations

Generally, the OPTIMIZER Smart Mini IPG is implanted in the right pectoral region of the chest. Two right ventricular leads are placed for CCM therapy delivery, one preferably in an anterior septal and the other in a posterior septal location, approximately halfway between base and apex. Placing both leads in an anterior or posterior septal location is an acceptable alternative, provided the leads are separated by at least 2 cm. In patients who have an implantable ICD, ensure that there is adequate separation between implanted CCM leads and ICD leads.

Warning: The use of general anesthesia for the implant procedure will result in the inability to assess patient comfort during CCM therapy delivery and may cause adverse events associated with CCM therapy.

An optional atrial lead may be positioned in the right atrial appendage (RAA).

Note: The implantation of an optional atrial sensing lead is recommended if the expansion of some CCM timing and delivery parameter ranges is required in order to ensure sufficient CCM therapy delivery. The atrial lead option gives the physician the opportunity to treat patients with weak ventricular IEGM signals or an intrinsically high sinus rate.

8.2 Opening the Lead Package(s)

Visually inspect the lead packages before opening them for implantation. Damaged packages should be returned to the lead manufacturer. To prepare the lead for vascular implantation, follow the instructions provided by the lead manufacturer. Unless otherwise indicated by the lead manufacturer, proceed as follows with each sterile package:

- Open the shelf box outside the sterile field and remove the TYVEK/PETG molded tray.
- Using the provided tab, peel back the TYVEK from the outer PETG molded tray, taking strict care not to touch the inner sterile package.
- Maintaining strict sterile technique, make the inner sterile package accessible to the scrub nurse. At the recess adjacent to the molded tab, the inner TYVEK/PETG container can be removed from the outer tray with a pair of forceps.

- Peel back the inner cover starting at the provided peel tab.
- Remove the lead from the inner package and place it on a sterile and lint-free surface.

8.3 Implanting the Leads

Implant the leads in accordance with the instructions in the lead manufacturer's literature provided with the leads.

Please follow all indications listed in the lead manufacturer's literature.

Warning: Pinching the lead can damage the lead conductor or insulation, which may cause unwanted high-voltage therapies or result in the loss of sensing or pacing therapy.

Warning: Avoid Subclavian crush by proper lead access and placement. Patients need to be monitored closely after the implantation procedure.

Warning: Exercise care while placing the leads to avoid swelling of the steroid plug or formation of a blood clot, which could prevent extension and/or retraction of the helix.

Warning: It is important to avoid prolonged manipulation of the leads and catheters in the venous system, which could lead to venous thrombosis.

Warning: During implantation, leads and catheters need to be manipulated with extra caution to avoid right ventricular wall perforation. Obtain X-rays, perform echocardiography, and device interrogation after implantation to detect perforations even in the absence of related symptoms. Throughout the procedure and post-operative care, cardiac hemodynamic and respiratory status should be continuously monitored by subjective assessment, pulse oximetry, and blood pressure monitoring via automatic cuff or intra-arterial cannula.

Warning: In order to prevent vascular injury and hemorrhage, be extremely cautious when introducing catheters and leads into veins

8.4 Opening the OPTIMIZER Smart Mini Sterile Package

Caution: Visually inspect the package before opening it for the implantation procedure. Check the package for any signs of damage suggesting that the sterility of the package or its contents has been compromised. Damaged packages should be returned to Impulse Dynamics for evaluation. Do not attempt to resterilize any of the contents of the sterile inner blister pack that has been damaged or compromised.

Open the shelf box outside the sterile field and remove the TYVEK/PETG molded insert. Establish a link between the IPG and the Programmer by performing the following steps:

1. Place the Intelio Programming Wand over the OPTIMIZER Smart Mini IPG
2. Open the Optimizer SM application on the Intelio Programmer
3. Click on the **Start OPTIlink** button shown on the **OPTIlink Session Pane**
4. If the link is successful, the **OPTIlink Session Pane** will display the device model and serial number along with the **Close OPTIlink** button. In addition, the **CCM Status Pane** will display the current CCM therapy status.

Once the programmer is linked to the IPG, proceed to the opening of the sterile OPTIMIZER Smart Mini IPG package.

To open the sterile package, proceed as follows:

1. Starting at the provided tab, peel back the TYVEK from the outer PETG molded insert, taking care not to touch the sterile inner package.
2. Maintaining strict sterile technique, make the inner sterile blister pack accessible to the scrub nurse. The inner TYVEK/PETG container can be removed from the outer tray with a pair of forceps inserted at the recess next to the molded tab.
3. Peel back the inner cover starting at the provided peel tab.
4. Remove the OPTIMIZER Smart Mini IPG and the accessories from the inner pack and place them on a sterile, lint-free surface.

8.5 Connecting the Implanted Leads to the OPTIMIZER Smart Mini IPG

Before connecting the implanted leads to the OPTIMIZER Smart Mini IPG, it is recommended that each ventricular lead be tested with a Pacing System Analyzer (PSA).

Using a PSA, measure the impedance and sensing amplitude for each implanted ventricular lead. When measuring the sensing and pacing thresholds, measure between the tip (cathode) and ring or coil (anode) of each bipolar pacing/sensing lead.

It is also recommended that the pacing capture threshold, which is a traditional indicator of proper electrode anchoring into the myocardium, be measured for each ventricular lead. Lastly, test each ventricular lead for stimulation and discomfort.

Acceptable values for ventricular lead assessment are as follows:

- Lead impedance: between 250 Ω and 1500 Ω with no more than 20% fluctuation in readings
- Sensing amplitude: ≥ 5 mV
- Pacing Capture Threshold: ≤ 1 V at 0.5 ms pulse width
- No palpable diaphragmatic stimulation or chest discomfort with the delivery of an 8 V pacing pulse at 1.0 ms pulse width

Important points to consider when connecting the implanted leads to the OPTIMIZER Smart Mini IPG include:

- When tightening or loosening the set screws, always insert the tip of the torque wrench fully and in line with the set screw. Do not insert the wrench into the set screw at an angle.
- Before inserting the IS-1 lead connectors, visually verify that none of the set screws protrude into any of the IPG header cavities (please refer to the diagram on the IPG). Back off any set screw found protruding beyond the wall into the header cavity by turning it back with the Allen wrench in a counterclockwise direction. Turn the set screw just enough so that its tip is no longer inside the header cavity.

  Caution: Do not back the set screw completely out of the terminal block.
- Under no circumstances should items other than the implantable lead connectors (or Port Plug) be introduced into the port of the IPG connector terminal.

Note: Provided the connectors are correctly installed, the connector retention force in the terminals is at least 10 N (2.24 lbf).

Clean each IS-1 lead connector pin with sterile distilled water (if using saline, wipe the connector dry with a surgical sponge afterwards) and then fully insert each lead connector into its respective connector terminal in the header of the OPTIMIZER Smart Mini IPG.

Warning: Fluid in the IS-1 connector terminal may lead to poor sensing, high impedance readings, and inability of IPG to deliver CCM therapy.

Note: Before tightening the set screws, visually inspect each connector terminal in the header of the IPG and verify that the tip of each lead connector is fully inserted into its respective lead tip terminal.

Tighten the tip set screw for each lead using the sterile #2 Allen torque wrench included in the IPG package. Turn the torque wrench clockwise until you hear and feel clicking. Carefully apply traction on the strain relief of each lead to make sure that each lead is securely anchored in its respective terminal.

Tighten the ring set screw for each lead using the torque wrench. Turn the torque wrench clockwise until you hear and feel clicking.

8.6 Using a Port Plug with the OPTIMIZER Smart Mini IPG

If an atrial lead is not going to be used with the OPTIMIZER Smart Mini IPG, insert the Port Plug provided with the OPTIMIZER Smart Mini IPG package into the top port, labeled “A”, of the IPG.

Note: Alternately, any commercially available bipolar IS-1 port plug may be used to plug the atrial port of the OPTIMIZER Smart Mini IPG.

Tighten the tip set screw. The protruding length of the Port Plug may be shortened, but it is recommended to leave at least 1 cm (3/8 in) length protruding from the IPG to enable future removal of the Port Plug if it becomes necessary to connect an atrial sensing lead.

8.7 Verifying Lead Placement

Note: If the OPTIMIZER Smart Mini Programmer application is still linked to the OPTIMIZER Smart Mini IPG, then the Intelio Programming Wand does not need to be introduced into the sterile field. However, if the OPTIlink between the OPTIMIZER Smart Mini Programmer application and the OPTIMIZER Smart Mini IPG has closed, the Intelio Programming Wand will need to be introduced into the sterile field and placed directly over the OPTIMIZER Smart Mini IPG before the OPTIlink can be reestablished.

Note: The Intelio Programming Wand is not sterile and cannot be sterilized. If the Intelio Programming Wand needs to be introduced into the sterile field, it must first be placed in a sterile probe cover or sleeve.

Ask the person operating the Intelio Programmer (outside the sterile field) to perform the following using the OPTIMIZER Smart Mini Programmer application:

1. Program the OPTIMIZER Smart Mini IPG to deliver CCM therapy by performing the following steps:
    a. On the **CCM Status Pane**, set **Mode** to **OVO-LS-CCM** mode (**ODO-LS-CCM** mode if implanted with 3 leads)
    b. Set **CCM Therapy Mode** to **ON**
    c. Select the **CCM Settings** tab
    d. Click the **OPTIset Wizard**
    e. Click the **OPTIset: Propose IEGM Sensitivities** button
    f. When **OPTIset** has completed its proposal of sensitivities, click the **Accept & Continue** button
    g. When the **OPTIset** window appears again, click the **OPTIset: Propose CCM Algorithm Timing** button
    h. When **OPTIset** has completed its proposal of CCM algorithm timing, click the **Accept & Continue** button
    i. When the **OPTIset** window appears again, click the **OPTIset: Propose CCM Amplitude** button
    j. When the **OPTIset: CCM AMPLITUDE** is shown, enable the **CCM Channels** (one at a time)
    k. When **OPTIset** has completed its proposal of CCM algorithm amplitude, set the **CCM Amplitude** to 7.5 V and then click the **Accept & Continue** button
    l. When the **OPTIset** window appears again, click the **Accept & Continue** button
    m. Click the blinking **Program** button on the **Programming Buttons Pane** to load modified parameters into the OPTIMIZER Smart Mini IPG

2. Measure lead impedances by performing the following steps:
    a. Click the **Diagnostics** button on the **Mode Bar**
    b. Select the **Leads** tab
    c. Click the **Measure Leads Impedance** button
    d. Verify that they are within expected values.

Under local anesthesia or conscious sedation, ask the patient if they feel any sensation while the OPTIMIZER Smart Mini IPG is delivering CCM therapy. If the patient reports having sensation at 7.5 V, step decrease the CCM amplitude in 0.5 V increments until the sensation is no longer felt by the patient.

If the patient expresses discomfort or any other kind of sensation at 6.0 V or lower, identify the lead causing it by disabling the CCM delivery to the RV channel. If the patient continues to experience sensations, re-enable the RV channel and disable the LS channel. Once the lead that is causing the sensation has been identified, its placement should be relocated to allow cardiac contractility modulation therapy to be delivered at the maximum amplitude through both CCM channels.

It is good practice to check fluoroscopy in a steep LAO (left anterior oblique) 45 degree or greater angle to visually identify any placement issues with the offending lead prior to repositioning.

Once the leads are in place, secure each lead to its respective lead anchor sleeve. Clean the lead body with sterile saline before securing the anchoring sleeve to the lead. Secure the anchoring sleeve with two non-absorbable ligatures and tighten gently -- Do Not Over-Tighten.

Note: Any significant lead impedance deviation at a subsequent check-up may be a sign of lead displacement or indicative of another problem requiring further investigation.

8.8 Dissection of the IPG Pocket

Surgical dissection directly on top of the fascia is the preferred method for creating the pocket, which should be large enough to accommodate the OPTIMIZER Smart Mini IPG and any loops of excess lead.

Note: When dissecting the pocket, please bear in mind that for charging to be possible, the distance between the charging wand and the OPTIMIZER Smart Mini IPG must not exceed 4 cm (1.5 in).

8.9 Inserting the OPTIMIZER Smart Mini IPG and Closing the Pocket

Insert the OPTIMIZER Smart Mini IPG into the subcutaneous pocket. Although the OPTIMIZER Smart Mini IPG can theoretically be interrogated and charged in any position, the preferred placement is such that the engraved side of the device is facing superior towards the skin, which provides the best link between the charging coil inside the header and the Guardio/Vesta Charger.

While the OPTIMIZER Smart Mini IPG may be implanted at a depth of up to 4 cm (1.5 in), the maximum recommended depth of implant for proper device interrogation and charging is 2.5 cm (1 in).

When placing the IPG into the subcutaneous pocket, take special care to allow a smooth curvature of redundant lead segments within the pocket and place them around the IPG or in the pocket inferior to the device. Secure the IPG to the fascia with a non-absorbable suture and close the pocket.

Radiographs should be obtained after device implantation to verify device and lead placement, as well as rule out pneumothorax and other surgical complications, even if there are no symptoms. Thereafter, patients should receive the facility’s standard post-operative care for similar procedures such as a pacemaker implantation.

Prior to discharge, check the lead sensitivity threshold for each implanted lead, measure the lead impedance, and then compare these results to the values obtained during implant. Any significant changes may indicate lead dislodgement.

Note: As the depth of the implant increases, the charger's efficiency in charging the implanted device decreases. This may impact the time it takes to charge the implanted device

Note: If the patient is also implanted with an ICD, concomitant device interaction testing should be performed (see Appendix III).

9.0 DEVICE EXPLANTATION / REPLACEMENT

9.1 Device Removal

Important points to consider when explanting the OPTIMIZER Smart Mini IPG include:

- Special care should be exercised when opening the IPG pocket so as not to damage the leads implanted with the OPTIMIZER Smart Mini IPG.
- When loosening a set screw, always insert the tip of the torque wrench fully into and in line with the set screw. Do not insert the torque wrench into the set screw at an angle.
- If the OPTIMIZER Smart Mini IPG is being explanted and not replaced, abandoned leads need to be capped after they are disconnected from the IPG.

Carefully open the IPG pocket and gently remove the IPG from the pocket. Once the IPG is out of the pocket, loosen the set screws with a sterile #2 Allen wrench. When all the set screws have been loosened, grasp the connector of a lead between the thumb and forefinger of one hand while holding the IPG in the other hand, and pull the lead connector from the terminal by cautious application of constant traction.

Note: Grasping the lead connector with a sterile pad can help improve traction.

Caution: Never apply traction to the actual lead body; it could damage the lead and result in lead failure.

9.2 Device Replacement

Important points to consider when replacing the OPTIMIZER Smart Mini IPG include:

- When tightening a set screw, always insert the tip of the torque wrench fully into and in line with the set screw. Do not insert the torque wrench into the set screw at an angle.
- Make sure to visually verify that the lead insulation is intact when replacing an OPTIMIZER Smart Mini IPG. Prior to connecting the leads to the replacement IPG, the impedances, sensing thresholds, and pacing thresholds should be assessed with a Pacer System Analyzer (PSA).
- Before inserting the IS-1 lead connectors, visually verify that none of the set screws protrude into any of the IPG header cavities (please refer to the diagram on the IPG). Back off any set screw found protruding beyond the wall into the header cavity by turning it back with the Allen wrench in a counterclockwise direction. Turn the set screw just enough so that its tip is no longer inside the header cavity.

  Caution: Do not back the set screw completely out of the terminal block.
- Under no circumstances should items other than the implantable lead connectors (or Port Plug) be introduced into the port of the IPG connector terminal.

Clean each IS-1 lead connector pin with sterile distilled water (if using saline, wipe the connector dry with a surgical sponge afterwards) and then fully insert each lead connector into its respective connector terminal in the header of the OPTIMIZER Smart Mini IPG.

Note: Before tightening the set screws, visually inspect each connector terminal in the header of the IPG and verify that the tip of each lead connector is fully inserted into its respective lead tip terminal.

Tighten the tip set screw for each lead using the sterile #2 Allen torque wrench included in the IPG package. Turn the torque wrench clockwise until you hear and feel clicking. Carefully apply traction on the strain relief of each lead to make sure that each lead is securely anchored in its respective terminal.

Tighten the ring set screw for each lead using the torque wrench. Turn the torque wrench clockwise until you hear and feel clicking.

9.3 Using a Port Plug with the OPTIMIZER Smart Mini IPG

If an atrial lead is not going to be used with the OPTIMIZER Smart Mini IPG, insert the Port Plug provided with the OPTIMIZER Smart Mini IPG package into the top port, labeled “A”, of the IPG.

Note: Alternately, any commercially available bipolar IS-1 port plug may be used to plug the atrial port of the OPTIMIZER Smart Mini IPG.

Tighten the tip set screw. The protruding length of the Port Plug may be shortened, but it is recommended to leave at least 1 cm (3/8 in) length protruding from the IPG to enable future removal of the Port Plug if it becomes necessary to connect an atrial sensing lead.

9.4 Disposition of Explanted OPTIMIZER Smart Mini IPGs

All explanted OPTIMIZER Smart Mini IPGs should be returned to Impulse Dynamics for testing and analysis, which can provide valuable information on how to further improve device quality and reliability.

Warning: An OPTIMIZER Smart Mini IPG or Port Plug that has been explanted for any reason must not be reused in another patient.

10.0 OPTIMIZER SMART MINI IPG: FUNCTIONS AND PROGRAMMING OPTIONS

10.1 CCM Therapy

10.1.1 Device Modes

The implantable OPTIMIZER Smart Mini IPG features three device modes:

- **OOO**: The device is in standby; no events are sensed, and no CCM therapy is delivered.
- **ODO-LS-CCM**: The device senses atrial, ventricular (RV), and local sense (LS) events and is capable of CCM therapy delivery.
- **OVO-LS-CCM**: The device senses RV and LS events while ignoring any atrial events and is capable of CCM therapy delivery without the need for the detection of atrial sense events.

10.1.2 CCM Therapy Mode

The OPTIMIZER Smart Mini IPG features two CCM therapy modes:

- **OFF**: Turns OFF the delivery of CCM therapy
- **ON**: Enables the OPTIMIZER Smart Mini IPG to deliver CCM therapy a set number of hours per day within the timeframe set by the Start Time and End Time parameters. The delivery of CCM therapy occurs in one-hour intervals with pauses in between each interval for a calculated amount of time based on the hours per day, Start Time, and End Time parameter settings.

10.1.3 CCM Therapy Hours/Day

The **CCM hs/days** parameter sets the total number of hours per day the OPTIMIZER Smart Mini IPG is scheduled to deliver CCM therapy. By default, the **CCM hs/days** parameter is set to 7 hs/day.

Note: The default setting in the U.S. is for 5 hours of programmed CCM therapy per 24 hours (repeated intervals of 1 hour ON Time followed by 3:48 hours OFF Time).

10.1.4 Start Time and End Time

The **Start Time** and **End Time** parameters set the general start and end time of CCM therapy delivery during each day. By default, the CCM therapy schedule is set to be distributed over a 24 hour period each day.

10.1.5 Extend on Low CCM%

If the percentage of CCM therapy a patient receives during scheduled CCM therapy delivery periods is lower than 90%, the OPTIMIZER Smart Mini IPG offers the option of extending this CCM therapy delivery time period. When the **Extend on Low CCM%** feature is enabled, the OPTIMIZER Smart Mini IPG extends the On Time period for CCM therapy delivery based on the percentage of CCM therapy delivered during the original 1 hour On Time period. The amount in which the On Time is extended is as follows:

- If the CCM% is 80% to 90%, the On Time is extended 11%
- If the CCM% is 70% to 79%, the On Time is extended 26%
- If the CCM% is 60% to 69%, the On Time is extended 46%
- If the CCM% is less than 60%, the On Time is extended 72%

In all cases, the Off Time is correspondingly reduced by the same amount.

10.1.6 Suspension of CCM Delivery

The OPTIMIZER Smart Mini IPG will suspend the delivery of CCM therapy if the following conditions are present:

- **CCM Magnet Mode**: In this state, the OPTIMIZER Smart Mini IPG still senses and classifies cardiac events. A health care provider (or patient) can force the OPTIMIZER Smart Mini IPG into the CCM Magnet Mode state by placing a cardiac device magnet [minimum field strength of 90 Gauss @ 4.0 cm (1.5 in)] over the implant site of the OPTIMIZER Smart Mini IPG and by maintaining it in close proximity to the device for at least two cardiac cycles (3 seconds). This CCM Magnet Mode state is maintained even after the magnet is removed from the implant site. The CCM Magnet Mode has two setting options:
    - **Off 1 day**: At this setting, the OPTIMIZER Smart Mini IPG shall remain in a CCM Off state for 24 hours. This 24-hour period starts the moment the magnet is moved away from the implanted device. When this 24 hour period has been completed, the device will resume delivering CCM therapy using the previously programmed parameters.

      Note: If at any time during this 24 hour period, a cardiac device magnet is reapplied over the implant site of the OPTIMIZER Smart Mini IPG for at least two cardiac cycles (3 seconds) and then removed again from the implant site, the 24-hour period is restarted.
    - **Off**: At this setting, the OPTIMIZER Smart Mini IPG shall remain in a CCM Permanent Off state until the Program command is sent to the device. This status can only be changed by using the OPTIMIZER Smart Mini Programmer application to reprogram the OPTIMIZER Smart Mini IPG under the direction or supervision of a physician.
- **Safe Mode**: In this state, the OPTIMIZER Smart Mini IPG may not sense cardiac events. The reversal of this state can only be accomplished by resetting the OPTIMIZER Smart Mini IPG with the OPTIMIZER Smart Mini Programmer application under the direction or supervision of a physician. In the unlikely event of inconsistent operation of the system's logic circuits, the OPTIMIZER Smart Mini IPG will automatically assume the Safe state until it is reset.

10.2 Sensing

Through leads implanted in the heart, the OPTIMIZER Smart Mini IPG can sense, detect, and analyze electrical signals from the heart. The signal input and controller circuitry of the OPTIMIZER Smart Mini IPG are designed to receive these electrical signals, analyze the characteristics of each signal (for example, magnitude and timing), and to determine whether or not to deliver CCM therapy, if CCM therapy is to be delivered, and when to deliver it.

Note: The atrial (A) parameter settings are active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode.

10.2.1 Sensing Leads

Right heart events are detected through two (or optionally three) sensing leads:

- Atrium (optional): lead placed in the right atrium (A)
- Ventricular 1: lead placed on the septum of the right ventricle (V)
- Ventricular 2: lead placed on the septum of the right ventricle (V)

10.2.2 Sensing Parameters

Sensitivity and polarity are the parameters determining how right heart events are sensed.

- **Sensitivity**: To configure lead sensitivity, the OPTIMIZER Smart Mini Programmer application provides the following settings:
    - **Atrium**: Atrium sensitivity can be set to any one of 11 values between 0.3 mV and 5 mV.
    - **Ventricle 1 and 2**: Ventricle sensitivity to set to any one of 16 values between 0.3 mV and 10 mV.

      Note: When the OPTIMIZER Smart Mini IPG is in OVO-LS-CCM mode, the minimum allowable setting for the Ventricle sensitivity is 1 mV.
- **Polarity**: To configure lead polarity, the OPTIMIZER Smart Mini Programmer application provides the following options:
    - **Bipolar**: The signal is sensed between the lead “tip” (distal electrode) and “ring” (proximal electrode) of a bipolar lead.
    - **Unipolar**: The signal is sensed between the lead tip (distal electrode) and the case of the OPTIMIZER Smart Mini IPG.

10.3 CCM Timing

10.3.1 Post Ventricular A/V Refractory Periods

The Post Ventricular A/V Refractory Periods are the time intervals when the OPTIMIZER Smart Mini IPG does not detect input events. The refractory periods are applicable to the right heart sensing:

- **Post-V Atrial Refractory Period**: The time interval after a ventricular (RV) event when signals sensed on the atrial lead are not acknowledged as atrial events. With the OPTIMIZER Smart Mini Programmer application, the Post-V Atrial Refractory Period can be set to values between 148.0 ms and 452.2 ms, in 7.8 ms increments.

  Note: This parameter is active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode.
- **Post-V Ventricular (RV) Refractory Period**: The time interval after a ventricular (RV) event when signals sensed on the RV channel are not acknowledged as ventricular (RV) events. With the OPTIMIZER Smart Mini Programmer application, the Post-V Ventricular (RV) Refractory Period can be set to values between 148.0 ms and 452.2 ms, in 7.8 ms increments.

10.3.2 CCM Inhibit Parameters

By analyzing the train of sensed cardiac events based on their succession and their temporal order, the OPTIMIZER Smart Mini IPG “decides” for each heartbeat whether to deliver CCM therapy or not.

10.3.2.1 CCM Inhibit Cycles

One can program the number of cycles for which CCM therapy delivery will continue to be inhibited after the initial inhibiting event. With the OPTIMIZER Smart Mini Programmer application, the number of CCM inhibit cycles can be set to values between 1 and 16. This means that CCM therapy delivery can be inhibited from zero to 15 additional cycles beyond the initial inhibiting event.

Note: The number of inhibited cycles applies to the most recent detected event that caused CCM therapy inhibition. If a new inhibiting event is detected during a period of CCM therapy inhibition, this will trigger a new inhibition period.

10.3.2.2 Conditions Causing Inhibition

When the OPTIMIZER Smart Mini IPG is in its **Active** state, certain conditions may cause CCM therapy delivery to be inhibited. A record of each condition that caused the inhibition of CCM therapy delivery is stored by the IPG and can be viewed as statistical data whenever the device is interrogated by the OPTIMIZER Smart Mini Programmer application. The conditions that cause inhibition of CCM therapy delivery are the following:

- **Short AV**: Intervals between an atrial and a ventricular event are considered “Short AV” if they fall below a programmed threshold. Using the OPTIMIZER Smart Mini Programmer application, the Short AV threshold can be set to one of 49 possible values between 23 ms and 397 ms. CCM therapy delivery is *always inhibited* if a Short AV condition is detected.

  Note: This parameter is active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode.

- **Long AV**: Intervals between an atrial and a ventricular event are considered “Long AV” if they exceed a programmed threshold. Using the OPTIMIZER Smart Mini Programmer application, the Long AV threshold can be set to one of 49 possible values between 23 ms and 397 ms. CCM therapy delivery is *always inhibited* if a Long AV condition is detected.

  Note: This parameter is active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode.

- **Atrial Tachycardia (AT)**: Whenever the atrial tachycardia rate limit is exceeded, CCM therapy delivery is automatically inhibited. Using the OPTIMIZER Smart Mini Programmer application, the atrial tachycardia rate limit can be set to one of 51 possible values between 62 bpm and 179 bpm. CCM therapy delivery is *always inhibited* when atrial tachycardia rate limit is exceeded.

  Note: This parameter is active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode.

- **Premature Ventricular Contractions (PVC)**: A sensed right ventricular event is considered a PVC if it was preceded by another right ventricular sensing event without an interposing atrial sense event. CCM therapy delivery is inhibited each time a PVC condition is detected.

  Note: This parameter is active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode.

- **LS Out of Alert**: A local sense event detected before or after the end of the Local Sense Alert Window triggers an LS Out of Alert condition. The Local Sense Alert Window is the time interval during which the leading edge of valid LS events triggers CCM therapy delivery. How this is programmed is detailed in Section 10.3.3.3.
- **Ventricular Tachycardia (VT)**: Whenever the ventricular tachycardia rate limit is exceeded, CCM therapy delivery is automatically inhibited. Using the OPTIMIZER Smart Mini Programmer application, the ventricular tachycardia rate limit can be set to one of 25 possible values between 62 bpm and 110 bpm. CCM therapy delivery is *always inhibited* when ventricular tachycardia rate limit is exceeded.

  Note: This parameter is active only when the OPTIMIZER Smart Mini IPG is in OVO-LS-CCM mode.
- **Atrial and Ventricular Noise**: Despite various methods for detecting and filtering noisy signals implemented in the OPTIMIZER Smart Mini IPG, noise from powerful electromagnetic sources (e.g., from portable telephones, radio transmitters, etc.) as well as noise from physiological events (e.g., myopotentials, etc.) can interfere with the detection of cardiac events.

  Any time higher rate signals (greater than 11.6 Hz) are detected on the atrial or ventricular channel, the control logic of the OPTIMIZER Smart Mini IPG assumes the presence of noise and declares an A/V noise condition. CCM therapy delivery is *always inhibited* if atrial or ventricular noise is detected.

10.3.3 Local Sense Parameters

The detected local electrical activity of the ventricular myocardium with respect to right ventricle (RV) electrical activity is known as Local Sense (LS) events.

10.3.3.1 Assignment of Local Sense Channel

The OPTIMIZER Smart Mini IPG features the option of allowing the Local Sense (LS) channel to be assigned to either ventricular port. Using the OPTIMIZER Smart Mini Programmer application, the physical port V1 or V2 can be electrically designated as the LS channel. Accordingly, when one physical port is designated as the LS channel, the other physical port is automatically designated as the RV channel.

10.3.3.2 CCM Triggering Based on Local Sense Events

Delivery of CCM therapy is dependent on the intrinsic myocardial electrical activity in the vicinity of the designated Local Sense (LS) channel. The LS channel is configured to sense the electrical activity of a small, localized area of the heart (near the fixation site of the designated ventricular electrode). In response to this sensed activity, the OPTIMIZER Smart Mini IPG evaluates the myocardial electrical signal to determine whether it meets the criteria defined by the set of LS parameter values programmed into the device. If the criteria are met, then the IPG delivers CCM therapy. Within a cardiac cycle, the timing of the signal detected by the ventricular lead designated as the LS channel, especially with regards to the R wave, is the main criterion for the OPTIMIZER Smart Mini IPG to classify the cycle as normal or abnormal. CCM therapy is *not delivered* during cycles classified as abnormal.

10.3.3.3 Local Sense Alert Window

When the internal logic of the device detects ventricular events corresponding to cardiac cycles not classified as abnormal because of noise, atrial tachycardia, or suspected PVCs, it will open a Local Sense Alert Window. The Alert Window can be inside the AV interval, inside the VA interval, or partially inside the AV and partially inside the VA interval.

The first event detected within the window serves as a trigger for CCM therapy delivery.

Valid Local Sense events detected outside the Alert Window are considered invalid and inhibit CCM therapy delivery for a programmable number of cycles. Inhibiting Local Sense events can be detected even between a triggering Local Sense event and the start of the corresponding CCM therapy, which in this case will not be delivered.

The Local Sense Alert Window is the time interval during which the leading-edge of a valid LS event is used to trigger CCM therapy delivery.

The temporal characteristics of this window are determined by two programmable parameters:

- **LS Alert Start**: The start of the time interval during which a valid LS event must be sensed in order to trigger the delivery of CCM therapy. Using the OPTIMIZER Smart Mini Programmer application, Alert Start can be set to values between -40 ms and 80 ms, in 2 ms increments.

  Note: The Alert Window starts inside the AV interval if this value is negative.

- **LS Alert Width**: The time interval duration in which a valid LS event must be sensed in order to trigger the delivery of CCM therapy. Equivalent to the duration of the Alert Window. Using the OPTIMIZER Smart Mini Programmer application, the Alert Width can be set to values between 1 ms and 40 ms, in 1 ms increments. If the sum of Alert Start and Alert Width is negative, the Alert Window ends inside the AV interval.

The leading edge of the first event detected within this window is used to trigger CCM therapy delivery. When an event is detected, the Local Sense Alert Window is immediately closed. Any Local Sense events detected after the window closes are considered to lie outside the Alert Window and lead to the **LS Out of Alert Status**.

If a Local Sense event is detected outside the Alert Window, CCM therapy delivery is *always inhibited.*

10.3.4 Local Sense Blanking Refractory Periods

Local Sense (LS) Blanking Refractory Periods allows for the masking of signals (e.g., noise) that may be detected before or after an atrial, RV, or LS event.

The LS Blanking Refractory parameters are the following:

- **Pre A Refractory Period**: The time interval before the atrial event where all atrial signals are masked from detection. With the OPTIMIZER Smart Mini Programmer application, the duration can be set to values between 0 ms and 55 ms, in 5 ms increments.

  Note: This parameter is active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode.

- **Post A Refractory Period**: The time interval after the atrial event where all atrial signals are masked from detection. With the OPTIMIZER Smart Mini Programmer application, the duration can be set to values between 0 ms and 55 ms, in 5 ms increments.

  Note: This parameter is active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode.

- **Pre RV Refractory Period**: The time interval before the RV event where all signals are masked from detection. With the OPTIMIZER Smart Mini Programmer application, the duration can be set to values between 0 ms and 55 ms, in 5 ms increments.

- **Post RV Refractory Period**: The time interval after the RV event where all signals are masked from detection. With the OPTIMIZER Smart Mini Programmer application, the duration can be set to values between 0 ms and 39 ms, in 1 ms increments.

- **Post LS Refractory Period**: The time interval after the LS event where all signals are masked from detection. With the OPTIMIZER Smart Mini Programmer application, the duration can be set to values between 15 ms and 250 ms in 5 ms increments.

10.4 CCM Therapy Delivery

CCM therapy is a pulse train comprising a programmable number of consecutive pulses, each with two phases of opposite polarity and programmable duration.

10.4.1 CCM Train Parameters

The following are the CCM Train Parameters that can be programmed using the OPTIMIZER Smart Mini Programmer application:

- **CCM Train Delay**: CCM therapy delivery is triggered by the Local Sense event. The CCM Train Delay is the time interval between the leading edge of the Local Sense triggering event and the start of CCM pulse train delivery. With the OPTIMIZER Smart Mini Programmer application, the delay parameter can be set to values between 3 ms and 140 ms, in 1 ms increments and 85 ms (value for interaction testing).

  Note: When the OPTIMIZER Smart Mini IPG is in OVO-LS-CCM mode, the maximum allowable setting for this parameter is 45 ms.

- **CCM Amplitude**: This parameter sets the voltage of the CCM therapy pulse. With the OPTIMIZER Smart Mini Programmer application, the amplitude can be set to values between 4.5 V and 7.5 V, in 0.5 V increments.

- **Number of Biphasic Pulses**: With the OPTIMIZER Smart Mini Programmer application, the number of biphasic CCM therapy pulses can be set to 1, 2, or 3.

- **Balancing**: Delivery of each CCM pulse train is completed by a Balancing phase, which discharges any residual polarization at the electrode/tissue interface. Balancing is accomplished by short-circuiting the channels used to deliver the CCM therapy. With the OPTIMIZER Smart Mini Programmer application, the Balancing phase can be set to values between 40 ms and 100 ms, in 10 ms increments.

- **First Phase Polarity**: The first phase polarity of the CCM therapy pulse can be set with the OPTIMIZER Smart Mini Programmer application to “Positive” or “Negative”. When the polarity of the first phase is set to one value, the polarity of the second phase is automatically set to the opposite value.

  Note: If a patient expresses discomfort when the OPTIMIZER Smart Mini IPG is delivering CCM therapy, setting the first phase polarity to “Negative” may help alleviate this discomfort.

- **Phase Duration**: The width of each CCM therapy pulse phase can be set with the OPTIMIZER Smart Mini Programmer application to one of 4 possible values between 5.13 ms and 6.60 ms. The duration of both phases is automatically set to identical values.

  Note: Do not change the Phase Duration from the default setting of 5.13 ms unless directed by a physician.

- **Interval**: The interval is the time delay between each CCM therapy pulse phase. With the OPTIMIZER Smart Mini Programmer application, the interval can be set to values between 0 ms and 7 ms, in 1 ms increments.

  Note: If a patient expresses discomfort when the OPTIMIZER Smart Mini IPG is delivering CCM therapy, setting the Interval to a value > 1 ms may help alleviate this discomfort.

- **CCM Channels**: CCM therapy can either be delivered through one or both of the following channels:
  - **RV**
  - **LS**

10.5 Parameter Restrictions and Warnings

Whenever a parameter value is modified, the OPTIMIZER Smart Mini Programmer application performs a check of the modified value against all the other parameter values currently programmed into the OPTIMIZER Smart Mini IPG. If the modified parameter value violates one of the following restrictions, an error message is generated and displayed in the error message window.

1. *AV Limit Long shall be greater than AV Limit Short*

   Rationale: By definition, the AV Long Delay should always be greater than the AV Short Delay

2. *Total CCM event period (Alert Start + Alert Width +CCM Train Delay + CCM Train Duration + Balancing Phase Duration) must be shorter than the A/V refractory period minus 86 ms (noise window)*

   Rationale: To avoid false event detections, the CCM therapy must be delivered entirely within the atrial and ventricular refractory period. Before the end of these refractory periods, an 86 ms long noise window is activated to detect external interference. Therefore, CCM therapy delivery has to be completed before the noise window is opened.

3. *Alert Start + CCM Train Delay must be equal to or greater than 3 ms*

   Rationale: The Alert Start time relates to the right ventricular event. Thus, if the Alert Start value is negative and a local sense event is detected during the AV interval, a right ventricular event will have to occur and be detected before the device can determine if the event fell inside the alert window. This implies that CCM therapy delivery will not occur before the detection of a right ventricular event. Thus, this constraint allows for the detection of a right ventricular event before CCM therapy delivery.

4. *Post LS Refractory Period cannot be greater than the CCM Train Delay*

   Rationale: Since the Post LS Refractory Period masks any event (e.g., CCM event) that may occur after the detection of the LS event, the delivery of CCM therapy cannot begin during the Post LS Refractory Period.

5. *The period (in milliseconds) corresponding to the Atrial Tachycardia Rate shall be greater than the Post-V atrial refractory plus Short AV delay plus 50 ms (RA/RV)*

   Rationale: After an atrial event has been detected, a new atrial event can not be sensed until the Post-V Atrial Refractory period ends. In addition, the minimum required alert period to detect tachycardia is 50 ms.

6. *The period (in milliseconds) corresponding to the Ventricular Tachycardia Rate shall be greater than the Post-V ventricular refractory plus 50 ms (RA/RV)*

   Rationale: After a ventricular (RV) event has been detected, a new ventricular (RV) event can not be sensed until the Post-V RV Refractory period ends. In addition, the minimum required alert period to detect tachycardia is 50 ms.

7. *LS Alert Window Start shall not be in the Pre or Post Ventricular Refractory period*

   Rationale: If the LS Alert Window starts inside the Pre or Post RV Refractory period, only LS events falling inside the Alert Window and outside the RV Refractory Periods will be detected and trigger CCM therapy delivery. This effectively shortens the LS Alert window and may prevent the detection of an LS event.

8. *LS Alert Window End shall not be in the Pre or Post Ventricular Refractory period*

   Rationale: If the LS Alert Window ends inside the Pre or Post RV Refractory period, only LS events falling inside the Alert Window and outside the RV Refractory Periods will be detected and trigger CCM therapy delivery. This effectively shortens the LS Alert window and may prevent the detection of an LS event.

9. *Post LS Refractory period should not be greater than the CCM Train Delay*

   Rationale: If the CCM Train Delay is shorter than the Post LS Refractory period, then the CCM therapy will be delivered within the Post LS Refractory period while the LS event is not sensed.

11.0 SERVICE AND WARRANTY

11.1 Limited Warranty Information

Impulse Dynamics warrants that all IPGs (including the respective firmware and software) will be free from defects in workmanship and materials for 24 months after the original implantation of the IPG unless a longer period is required pursuant to applicable law (the “Warranty Period”).

If it appears that any IPG or part thereof appears to be defective in workmanship or materials, or fails to conform to applicable specifications, Impulse Dynamics shall either replace defective or non-conforming implantable components or repair or replace defective or non-conforming non-implantable components. The warranty period for a replaced or repaired IPG shall be the time remaining on the original warranty period or nine months from delivery of the repaired or replaced IPG, whichever is longer.

Under this warranty, Impulse Dynamics shall not be liable if tests and analyses reveal that the alleged defect or non-conformity of the IPG is not present or was caused by improper use, neglect, improper implantation, or follow-up, unauthorized repair attempts by the user, or due to accident, fire, lightning, or other hazards.

11.2 Mandatory Battery Charging

The rechargeable battery in the OPTIMIZER Smart Mini IPG is designed to provide optimal performance if it is completely recharged on a weekly basis. Regular weekly recharging sessions are required to prevent battery deterioration, which may lead to decreased device longevity.

APPENDIX I

As a convenience to the user, the following overview provides a brief and succinct summary of the characteristics of the OPTIMIZER Smart Mini IPG. Some of the information is also presented in the IFU in text form.

Physical Characteristics

Model	CCM X11
Height (mm)	61.3 ± 1.5
Width (mm)	44.0 ± 0.5
Thickness (mm)	11.0 ± 0.5
Volume (cm^3)	23.0 ± 0.5
Mass (g)	31 ± 3.0
Area of Exposed Metal Can (cm^2)	32.5
Radiopaque ID	**ID.OSM.y**[a]
Materials in Contact with Human Tissue	Titanium Epoxy resin Silicone rubber
Lead Connectors	3.2 mm; IS-1 BI

[a] "ID" is the manufacturer code for Impulse Dynamics; "OSM" is the model code for OPTIMIZER Smart Mini; "y" is replaced by the year code: "A" for 2019, "B" for 2020, "C" for 2021, etc…

Battery Specifications

Model and IEC Type	2993, rechargeable
Manufacturer	Greatbatch
Chemistry	Lithium-ion
Max Battery Voltage	4.1 V
Battery Service Life[a]	>20 years
Approximate Capacity After Recharging to LBI	215 mAh

[a] Replacement indicated when the IPG can no longer maintain the delivery of CCM therapy for a full week with routine weekly charging.

Current Consumption

Mode	**Current Consumption**
OOO	Less than 23 µA
OVO-LS-CCM OFF or ODO-LS-CCM OFF	Less than 48 µA
OVO-LS-CCM ON or ODO-LS-CCM ON	Less than 1300 µA[1]

[a] The current consumption of the OPTIMIZER Smart Mini IPG is dependent on the energy delivered by the CCM pulse train.

Safe Mode

Mode	Description
Safe Mode	Occurs when the device encounters conditions considered to be the result of faulty device hardware or firmware. In this mode, the device is completely quiescent; CCM therapy is not delivered and cardiac events are not sensed.

Programmable Parameters

CCM THERAPY PARAMETERS

Parameters Name	Values	Characteristics
Mode	OOO	Standby mode: no events are sensed and no CCM pulse trains are delivered
	ODO-LS-CCM	Active mode where the device senses atrial, ventricular and Local Sense events and is capable of CCM therapy delivery
	OVO-LS-CCM	Active mode where the device senses ventricular and local sense events and is capable of CCM therapy delivery without the need for the detection of atrial sense events.
CCM Therapy Mode	OFF	No pulse train enabled
	ON	As defined by the parameter values below
CCM Therapy (hs/day)	1 hs/day to 24 hs/day in 1 hs/day increments	
Start Time (hour)	00 h to 23 h in 1 h increments	
Start Time (minute)	00 m to 59 m in 1 m increments	
End Time (hour)	00 h to 23 h in 1 h increments	
End Time (minute)	00 m to 59 m in 1 m increments	
CCM Magnet Mode	Off 1 day or Off	
Extend on Low CCM%	ON or OFF	

A /V SENSING PARAMETERS

Parameter Name	Values
Atrium Sensitivity[a]	11 possible between 0.3 mV to 5 mV
Atrium Polarity[a]	Bipolar or Unipolar
Ventricle 1 Sensitivity	ODO-LS-CCM mode: 16 possible between 0.3 mV and 10 mV OVO-LS-CCM mode: 14 possible between 1.0 mV and 10 mV
Ventricle 1 Polarity	Bipolar or Unipolar
Ventricle 2 Sensitivity	ODO-LS-CCM mode: 16 possible between 0.3 mV and 10 mV OVO-LS-CCM mode: 14 possible between 1.0 mV and 10 mV
Ventricle 2 Polarity	Bipolar or Unipolar

[a] Active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode

A/V REFRACTORY PARAMETERS

Parameter Name	Values
Post-V Atrial Refractory Period[a]	148.0 ms to 452.2 ms in 7.8 ms increments
Post-V RV Refractory Period	148.0 ms to 452.2 ms in 7.8 ms increments

[a] Active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode

CCM INHIBIT PARAMETERS

Parameter Name	Values
CCM Inhibit Cycles	1 to 16 in increments of 1
Short AV Limit[a]	49 possible between 23 ms and 397 ms
Long AV Limit[a]	49 possible between 23 ms and 397 ms
Atrial Tracking[a]	51 possible between 62 bpm and 179 bpm
Ventricular Tracking[b]	25 possible between 62 bpm and 110 bpm

[a] Active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode

[b] Active only when the OPTIMIZER Smart Mini IPG is in OVO-LS-CCM mode

CCM TIMING PARAMETERS

Parameter Name	Values
LS Assignment	V1 or V2
LS Alert Start	–40 ms to 80 ms in 2 ms increments
LS Alert Width	1 ms to 40 ms in 1 ms increments

LS BLANKING REFRACTORY PARAMETERS

Parameter Name	Values
Pre A LS Refractory Period [a]	0 ms to 55 ms in 5 ms increments
Post A LS Refractory Period [a]	0 ms to 55 ms in 5 ms increments
Pre RV LS Refractory Period	0 ms to 55 ms in 5 ms increments
Post RV LS Refractory Period	0 ms to 39 ms in 1 ms increments
Post LS Refractory Period	15 ms to 250 ms in 5 ms increments

[a] Active only when the OPTIMIZER Smart Mini IPG is in ODO-LS-CCM mode

CCM TRAIN PARAMETERS

Parameters Name	Values
CCM Train Delay	ODO-LS-CCM mode: 3 ms to 140 ms in 1 ms increments and 85 ms (for interaction testing)
	OVO-LS-CCM mode: 3 ms to 45 ms in 1 ms increments and 85 ms (for interaction testing)
CCM Amplitude	4.5 V to 7.5 V in 0.5 V increments
Number of Biphasic Pulses	1, 2, or 3
Balancing	40 ms to 100 ms in 10 ms increments
First Phase Polarity	“Positive” or “Negative”.
Phase Duration	4 possible between 5.13 ms and 6.60 ms.
Interval	0 ms to 7 ms in 1 ms increments
CCM Channels	RV and/or LS

Nominal Settings

CCM THERAPY

Parameter Name	Nominal Value
Mode	OFF
Timed	5 hs/day
CCM Magnet Mode	Off 1 day
Extend on low CCM%	ON

CCM SCHEDULE

Parameter Name	Nominal Value
Start Time	00:00
End Time	23:59

SENSING

Parameter Name	Nominal Value
Atrium Sensitivity	1 mV
Atrium Polarity	Bipolar
Ventricle 1 Sensitivity	2 mV
Ventricle 1 Polarity	Bipolar
Ventricle 2 Sensitivity	2 mV
Ventricle 2 Polarity	Bipolar

A/V REFRACTORIES

Parameter Name	Nominal Value
Post-V Atrial Refractory Period	249.4 ms
Post-V Ventricular Refractory Period	249.4 ms

CCM INHIBIT

Parameter Name	Nominal Value
CCM Inhibit Cycles	1 beat
Short AV Delay	70 ms
Long AV Delay	397 ms
Tracking[a]	110 bpm

[a] Tracking controls the Atrial rate in ODO-LS-CCM mode and the Ventricular rate in OVO-LS-CCM mode

TIMING ALGORITHM

Parameter Name	Nominal Value
LS Assignment	V2
LS Alert Start	0 ms
LS Alert Width	15 ms

LS BLANKING REFRACTORIES

Parameter Name	Nominal Value
Pre A LS Refractory Period	0 ms
Post A LS Refractory Period	0 ms
Pre RV LS Refractory Period	0 ms
Post RV LS Refractory Period	0 ms
Post LS Refractory Period	30 ms

CCM TRAIN

Parameters Name	Nominal Value
CCM Train Delay	30 ms
CCM Amplitude	7.5 V
Number of Biphasic Pulses	2
Balancing	40 ms
First Phase Polarity	Positive
Phase Duration	5.13 ms
Interval	0 ms
CCM Channels	RV: On LS: On

DATA STORAGE

Parameter Name	Nominal Value
Activity Tracking	OFF
Accelerometer[a]	ON
Posture[a]	ON
HRV[a]	ON

[a] Parameter settings not visible unless Activity Tracking is set to ON

OPTIHome

Parameter Name	Nominal Value
OPTIHome Remote Monitoring	OFF
Patient Alerts[a]	ON
Activity Data[a]	OFF
CCM Statistics[a]	OFF
Lead Impedance IEGM Amplitudes[a]	OFF
Battery Data[a]	OFF
CCM Settings[a]	OFF

[a] Parameter settings not visible unless OPTIHome Remote Monitoring is set to ON

PATIENT ALERTS (See Intelio Programmer IFU for more information)

Parameters Name	Nominal Value
Alert Delivery Mode	Scheduled
Alert Delivery Mode Start Time, End Time	09:00, 21:00
Charger Battery Low	ON
Charger Failure	ON
Battery Low	ON
Battery Recharge Reminder	ON
Battery Recharge Reminder days	10 days
Long Time Without Communicating With the IPG	ON
Long Time Without Communicating With the IPG Days	3 days
Long Time Without Transmitting Data to the Remote Monitor	OFF
Long Time Without Transmitting Data to the Remote Monitor Days[a]	7 days
Minimum CCM%	ON
Minimum CCM% Percentage	70%
Maximum Lead Impedance Change	ON
Lead Impedance Change Percentage	50%
CCM Not Sensing/Noise	ON
CCM Therapy Suspended	ON
CCM Safe Mode	ON

[a] Parameter setting not visible unless Long Time Without Transmitting Data to the Remote Monitor is set to ON

APPENDIX II

Battery Charge Longevity

The battery charge longevity for the OPTIMIZER Smart Mini IPG can be estimated from the following tables.

Note: The battery charge longevity data below are conservative estimates.

Table 1 shows the charge longevity as a function of parallel lead impedance when CCM therapy delivery is set to 7 hours per day under the following conditions:

- Number of pulses per CCM train: 2
- Phase duration: 5.13 ms
- Heart rate: 75 bpm
- 100% CCM therapy delivery

Table 1

Parallel Lead (V1+V2) Impedance (Ω)	CCM Amplitude (V)	Charge Longevity (days)
220	4.5	27
220	6	18
220	7.5	12
250	4.5	37
250	6	21
250	7.5	14
300	4.5	41
300	6	25
300	7.5	16
600	4.5	63
600	6	41
600	7.5	23
900	4.5	81
900	6	55
900	7.5	26
1200	4.5	93
1200	6	60
1200	7.5	28

Table 2 shows the charge longevity as a function of parallel lead impedance when CCM therapy delivery is set to 5 hours per day under the following conditions:

- Number of pulses per CCM train: 2
- Phase duration: 5.13 ms
- Heart rate: 75 bpm
- 100% CCM therapy delivery

Table 2

Parallel Lead (V1+V2) Impedance (Ω)	CCM Amplitude (V)	Charge Longevity (days)
220	4.5	38
220	6	25
220	7.5	16
250	4.5	52
250	6	29
250	7.5	19
300	4.5	57
300	6	36
300	7.5	22
600	4.5	88
600	6	57
600	7.5	32
900	4.5	113
900	6	77
900	7.5	36
1200	4.5	130
1200	6	83
1200	7	39

Battery Current Drain

The battery current drain of the OPTIMIZER Smart Mini IPG is highly dependent on the amount of energy used when CCM therapy is delivered to the patient.

Table 3 shows the average measured current drain from the OPTIMIZER Smart Mini IPG battery during CCM therapy delivery under the following conditions:

- Number of pulses per CCM train: 2
- Phase duration: 5.13 ms
- Heart rate: 75 bpm
- 100% CCM therapy delivery

Table 3

V_{BAT} (V)	Parallel Lead (V1+V2) Impedance (Ω)	CCM Amplitude (V)	Average Measured Current Drain (mA)
3.5	220	4.5	0.96
3.5	220	6	1.84
3.5	220	7.5	2.9
3.5	250	4.5	0.88
3.5	250	6	1.36
3.5	250	7.5	2.4
3.5	300	4.5	0.75
3.5	300	6	1.22
3.5	300	7.5	2.2
3.5	600	4.5	0.41
3.5	600	6	0.78
3.5	600	7.5	1.5
3.5	900	4.5	0.34
3.5	900	6	0.6
3.5	900	7.5	1.3
3.5	1200	4.5	0.31
3.5	1200	6	0.5
3.5	1200	7.5	1.2
4.1	220	4.5	1.21
4.1	220	6	1.46
4.1	220	7.5	2.13
4.1	250	4.5	0.7
4.1	250	6	1.42
4.1	250	7.5	1.8
4.1	300	4.5	0.68
4.1	300	6	1.08
4.1	300	7.5	1.47
4.1	600	4.5	0.52
4.1	600	6	0.65
4.1	600	7.5	1.06
4.1	900	4.5	0.38
4.1	900	6	0.46
4.1	900	7.5	0.97
4.1	1200	4.5	0.32
4.1	1200	6	0.48
4.1	1200	7.5	0.91

APPENDIX III

Statement of FCC Compliance

FCC Compliance of the OPTIMIZER Smart Mini IPG

The OPTIMIZER Smart Mini IPG has been tested to the following FCC rules:

- 47 CFR Part 95 Subpart I - Medical Device Radio Communications Service

This device may not interfere with stations operating in the 400.150-406.000 MHz band in the Meteorological Aids, Meteorological Satellite, and Earth Exploration Satellite Services and must accept any interference received, including interference that may cause undesired operation.

This transmitter is authorized by rule under the Medical Device Radiocommunication Service (in part 95 of the FCC Rules) and must not cause harmful interference to stations operating in the 400.150-406.000 MHz band in the Meteorological Aids (i.e., transmitters and receivers used to communicate weather data), the Meteorological Satellite, or the Earth Exploration "Satellite Services and must accept interference that may be caused by such stations, including interference that may cause undesired operation. This transmitter shall be used only in accordance with the FCC Rules governing the Medical Device Radiocommunication Service. Analog and digital voice communications are prohibited. Although this transmitter has been approved by the Federal Communications Commission, there is no guarantee that it will not receive interference or that any particular transmission from this transmitter will be free from interference.

Electromagnetic Immunity

Electromagnetic Immunity of the OPTIMIZER Smart Mini IPG

<table>
<tr><th colspan="4">GUIDELINES AND MANUFACTURER'S DECLARATION – ELECTROMAGNETIC IMMUNITY OF THE OPTIMIZER SMART MINI IMPLANTABLE PULSE GENERATOR</th></tr>
<tr><td colspan="4">The OPTIMIZER Smart Mini IPG, part of the OPTIMIZER Smart Mini System, is intended for use in an electromagnetic environment as specified below. The patient implanted with the OPTIMIZER Smart Mini IPG must ensure that it is used within the specified environment.</td></tr>
<tr><td colspan="4">Essential Performance of the OPTIMIZER Smart Mini IPG:

The IPG shall be able to operate with safe settings. It is allowable that these settings disable CCM stimulation.[a]

Note: In case of emergency, placing a pacemaker magnet over the implant site of the OPTIMIZER Smart Mini IPG and maintaining it in close proximity to the device for at least two cardiac cycles (2–3 seconds), sets the OPTIMIZER Smart Mini IPG into Magnet Mode, suspending CCM therapy.</td></tr>
<tr><th>Immunity test[b]</th><th>Test level</th><th>Compliance level</th><th>Electromagnetic environment – guidelines[c, d]</th></tr>
<tr><td>ISO 14117:2019 Clause 4.2 – Induced lead current – 16.6 Hz to 20 kHz</td><td>Test 1 and Test 2 per standard</td><td>Induced lead current does not exceed limits for Test 1 and Test 2 per standard</td><td rowspan="4">See section on Cautions → Environmental Conditions in this manual.
Exercise caution in the vicinity of equipment that generates strong electrical or electromagnetic fields.
Do not enter an area with posted warnings advising pacemaker patients (or patients with other types of implantable devices) not to approach.
Interference may occur in the vicinity of equipment marked with the following symbol:
</td></tr>
<tr><td>ISO 14117:2019 Clause 4.3 - Protection from persisting malfunction attributable to ambient electromagnetic fields</td><td>Per clauses 4.3.2.1, 4.3.2.2, and 4.3.2.3 of standard</td><td>Does not exhibit malfunction which persists after the removal of the electromagnetic test signal per clauses 4.3.2.1, 4.3.2.2, and 4.3.2.3 of standard</td></tr>
<tr><td>ISO 14117:2019 Clause 4.4 - Protection from malfunction caused by temporary exposure to CW sources</td><td>Per standard</td><td>Maintains essential performance[a] per standard</td></tr>
<tr><td>ISO 14117:2019 Clause 4.5 - Protection from sensing EMI as cardiac signals</td><td>Per clauses 4.5.2, 4.5.3, 4.5.4</td><td>Maintains essential performance[a] per clauses 4.5.2, 4.5.3, 4.5.4</td></tr>
<tr><td>ISO 14117:2019 Clause 4.6 - Protection from static magnetic fields of flux density up to 1 mT</td><td>Per standard</td><td>Device operation is unaffected per standard</td><td>Maintain 6 inches (15 cm) distance between household magnets or items containing magnets (e.g. headphones, mobile phones, exercise equipment containing magnets, etc.) and implant</td></tr>
<tr><td>ISO 14117:2019 Clause 4.7 - Protection from static magnetic fields of flux density up to 50 mT</td><td>Per standard</td><td>Does not exhibit malfunction which persists after the removal from the field per standard</td><td>See section on Warnings → Nuclear Magnetic Resonance (NMR), Magnetic Resonance Imaging (MRI) in this manual</td></tr>
</table>

ISO 14117:2019 Clause 4.8 - Protection from AC magnetic field exposure in the range of 1 kHz to 140 kHz	Per standard	Does not exhibit malfunction which persists after the removal from the field per standard	See section on **Cautions → Environmental Conditions**, **Cautions → Industrial Machinery**, and **Cautions → Home Appliances** in this manual. • Exercise caution in the vicinity of equipment that generates strong AC magnetic fields. • Do not enter an area with posted warnings advising pacemaker patients (or patients with other types of implantable devices) not to approach.
ISO 14117:2019 Clause 4.9 - Test requirements for the frequency range of 385 MHz ≤ f ≤ 3000 MHz	Per standard	Functions as it did before the test without further adjustment after application of the test signal per standard	See section on **Cautions → Transmitting Devices** and **Cautions → Cellular and Mobile Phones** in this manual • Exercise caution in the vicinity of equipment that generates strong radio-frequency fields. • Do not enter an area with posted warnings advising pacemaker patients (or patients with other types of implantable devices) not to approach. • Interference may occur in the vicinity of equipment marked with the following symbol: 

ISO 14117:2019 Clause 5 - Testing above frequency of 3000 MHz	Standard does not require testing of devices above 3 GHz. Electromagnetic fields > 3 GHz are not expected to interfere with device operation because of the increased device protection afforded by the attenuation of the enclosure and body tissue at microwave frequencies, the expected performance of EMI control features implemented to meet lower-frequency requirements, and the reduced sensitivity of circuits at microwave frequencies.	N/A	Avoid direct exposure to the main lobe of high-power radar and microwave communication beams.
ISO 14117:2019 Clause 6.1 - Protection of the device from damage caused by high-frequency surgical exposure	Per standard	Does not exhibit malfunction which persists after the removal of the electromagnetic test signal per standard	See section on **Warnings → Electrocautery** and **Warnings → RF Ablation** in this manual
ISO 14117:2019 Clause 6.2 Protection of the device from damage caused by external defibrillators	Per standard	Does not exhibit malfunction which persists after the removal of the electromagnetic test signal per standard	See section on **Warnings → Defibrillation and Cardioversion** in this manual

GTRI E3 Representative Security and Logistical Systems (Electronic article surveillance, metal detectors, RFID)	Per E3 protocol	Per E3 protocol	See section on **Cautions → Store Anti-Theft Systems/Airport Security Screening Systems** in this manual Electronic Article Surveillance (EAS) systems, such as those found at department stores: • Do not linger near an EAS system longer than is necessary. • Be aware that EAS systems are often hidden or camouflaged near the exits for businesses such as retailers. • Do not lean against the system's sensors. Metal detector archways: • Do not stop or linger in a walk-through archway; simply walk through the archway at a normal pace. Radiofrequency identification (RFID) readers: • Maintain separation from wall unit (reader) and the implanted device. • Do not lean against the reader. Radiofrequency identification (RFID) and checkout counter tag deactivators: • Maintain an arm's length separation from the deactivator's surface. • Do not lean against the deactivator.

Notes:

[a] No inappropriate stimulation shall be delivered by the OPTIMIZER Smart Mini IPG. Normal CCM delivery or inhibition of CCM delivery due to interference is permissible, but inappropriate triggering of CCM delivery by interference is not allowed.

[b] The OPTIMIZER Smart Mini IPG is not a pacemaker, CRT, or ICD device. As such, the criteria of ISO 14117:2019 were adapted to be applicable to CCM.

[c] See sections on **WARNINGS** and **CAUTIONS** in this manual

[d] This guidance shall not be considered the exclusive or only source for this information. It is best practice to consult the original manufacturer of the item with potential electromagnetic interference to verify any specific guidance concerning operation and compatibility with implantable devices. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding the OPTIMIZER Smart Mini IPG.

Electromagnetic Emissions

Electromagnetic Emissions from the OPTIMIZER Smart Mini IPG

The OPTIMIZER Smart Mini IPG must emit electromagnetic energy in order to perform its intended function when communicating with the Intelio Programmer or the Guardio/Vesta Charger. Nearby electronic equipment may be affected.

FCC 47 CFR 95 Subpart I - Medical Device Radio Communications Service

GUIDELINES AND MANUFACTURER'S DECLARATION – ELECTROMAGNETIC EMMISSIONS OF THE OPTIMIZER SMART MINI IPG PURSUANT TO: **FCC - 47 CFR 95 Subpart I - Medical Device Radio Communications Service**		
The OPTIMIZER Smart Mini Implantable Pulse Generator, part of the OPTIMIZER Smart Mini System, is intended for use in an electromagnetic environment as specified below. The patient implanted with the OPTIMIZER Smart Mini Implantable Pulse Generator must ensure that it is used within the specified environment.		
Emissions Test	**Compliance**	**Electromagnetic environment - guidelines**
Duration of Transmissions	Complies with clause 95.2557	The OPTIMIZER Smart Mini IPG must emit electromagnetic energy in order to perform its intended function when communicating with the Intelio Programmer or the Guardio/Vesta Charger. Nearby electronic equipment may be affected.
Frequency Monitoring	Complies with clause 95.2559	
Frequency Accuracy	Complies with clause 95.2565	
EIRP	Complies with clause 95.2567(a)	
Field Strength	Complies with clause 95.2569	
Bandwidth	Complies with clause 95.2573	
Unwanted Emissions	Complies with clause 95.2579	
Permissible Exposure Evaluation	Complies with clause 95.2585	

ETSI EN 301 839

GUIDELINES AND MANUFACTURER'S DECLARATION – ELECTROMAGNETIC EMMISSIONS OF THE OPTIMIZER SMART MINI IPG PURSUANT TO: **ETSI EN 301 839 V2.1.1 - Ultra Low Power Active Medical Implants (ULP-AMI) and associated Peripherals (ULP-AMI-P) operating in the frequency range 402 MHz to 405 MHz; Harmonised Standard covering the essential requirements of article 3.2 of the Directive 2014/53/EU**		
The OPTIMIZER Smart Mini Implantable Pulse Generator, part of the OPTIMIZER Smart Mini System, is intended for use in an electromagnetic environment as specified below. The patient implanted with the OPTIMIZER Smart Mini Implantable Pulse Generator must ensure that it is used within the specified environment.		
Emissions Test	**Compliance**	**Electromagnetic environment - guidelines**
Frequency Error	Complies with clause 5.3.1	The OPTIMIZER Smart Mini IPG must emit electromagnetic energy in order to perform its intended function when communicating with the Intelio Programmer or the Guardio/Vesta Charger. Nearby electronic equipment may be affected.
Occupied Bandwidth	Complies with clause 5.3.2	
Power Output	Complies with clause 5.3.3	
Transmitter Spurious Emissions (30 MHz to 6 GHz)	Complies with clause 5.3.4	
Frequency Stability Under Low Voltage Conditions	Complies with clause 5.3.5	
Spurious Radiation of Receivers	Complies with clause 5.3.6	

ETSI EN 301 489-1 and ETSI EN 301 489-27

GUIDELINES AND MANUFACTURER'S DECLARATION – ELECTROMAGNETIC EMMISSIONS OF THE OPTIMIZER SMART MINI IPG PURSUANT TO:

ETSI EN 301 489-1 V2.2.3 - ElectroMagnetic Compatibility (EMC) standard for radio equipment and services; Part 1: Common technical requirements; Harmonised Standard for ElectroMagnetic Compatibility

ETSI EN 301 489-27 - ElectroMagnetic Compatibility (EMC) standard for radio equipment and services; Part 27: Specific conditions for Ultra Low Power Active Medical Implants (ULP-AMI) and related peripheral devices (ULP-AMI-P) operating in the 402 MHz to 405 MHz bands; Harmonised Standard covering the essential requirements of article 3.1(b) of Directive 2014/53/EU

The OPTIMIZER Smart Mini Implantable Pulse Generator, part of the OPTIMIZER Smart Mini System, is intended for use in an electromagnetic environment as specified below. The patient implanted with the OPTIMIZER Smart Mini Implantable Pulse Generator must ensure that it is used within the specified environment.

Emissions Test	Compliance	Electromagnetic environment - guidelines
Radiated Emissions EN 55032:2012/AC:2013	Class B	The OPTIMIZER Smart Mini IPG must emit electromagnetic energy in order to perform its intended function when communicating with the Intelio Programmer or the Guardio/Vesta Charger. Nearby electronic equipment may be affected.

APPENDIX IV

Wireless Technology

RF wireless technology is used in the communication between an OPTIMIZER Smart Mini Implantable Pulse Generator (IPG) and an Intelio Programmer. It occurs through an encrypted channel over an RF link that complies with the requirements of the Medical Implant Communication System (MICS) (range specified to 2 m, 402–405 MHz) of the MedRadio Band. The "OPTI*link*" encrypted MICS channel is established after the IPG is positively identified and encryption keys are exchanged via a very-short-range (<4 cm) communication over the 13.56 MHz recharge channel.

RF wireless technology is also used to transcutaneously transmit energy from the Guardio/Vesta Charger to recharge the OPTIMIZER Smart Mini IPG at the 13.56 MHz ISM frequency. The transmission range is specified at a maximum of 4 cm between the Charger's coil and the IPG's receiving coil. Control over the recharge process, as well as the communications of alert messages from the IPG to the Charger take place over an encrypted MICS channel.

OPTIMIZER Smart Mini IPG Wireless Nominal Specifications

Characteristic	Nominal
OPTI*link* MICS MedRadio	
Frequency Band	402 – 405 MHz Medical Implant Communication Service (MICS) Medical Device Radio Communication Service (MedRadio)
Bandwidth	< 145 kHz
Modulation	FSK
Radiated Power	< 25 µW E.I.R.P.
Range	0 to at least 1.5 m

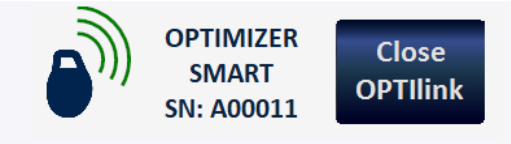
Quality of Service (QoS) for Wireless Technology

QoS for Communications between the Intelio Programmer and the OPTIMIZER Smart Mini IPG

MedRadio in the MICS sub-band (402 to 405 MHz) wireless technology enables communication between the OPTIMIZER Smart Mini IPG and the Intelio Programmer.

Before the Intelio Programmer can be used to program the OPTIMIZER Smart Mini IPG, an OPTI*link* communication session must first be established between the Intelio Programmer and the IPG. This is accomplished by means of the Intelio Programming Wand, which must be placed over the implant site and within 4 cm of the IPG. Once the Intelio Programming Wand is over the patient's implant site, the communication link is established by initiating the Start OPTI*link* command. Encryption keys are exchanged through a proprietary process using the 13.56 MHz Recharge Channel, after which the Intelio Programming Wand can be placed at a distance of up to 1.5 m away from the implant site, with communications taking place over MedRadio.

The OPTI*link* Signal Strength Indicator dynamically displays the Quality of Service (QoS) for the link between the Intelio Programming Wand and the OPTIMIZER Smart Mini IPG. Depending on the quality of the link, the curved "waves" of the Signal Strength Indicator are displayed in the following manner:

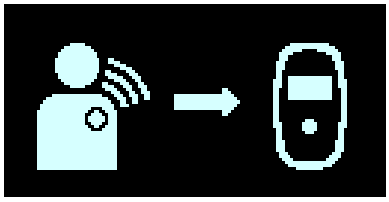


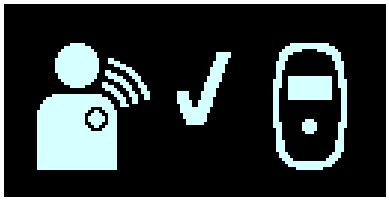
- Good quality link – 3 green signal waves
- Medium quality link – 2 yellow signal waves
- Low quality link – 1 red signal wave

QoS for Communications between the Guardio/Vesta Charger and the OPTIMIZER Smart Mini IPG

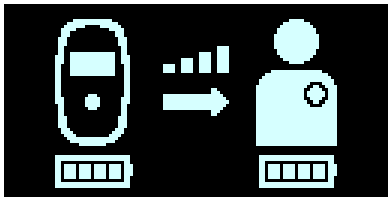
MedRadio in the MICS sub-band (402 to 405 MHz) wireless technology enables communication between the OPTIMIZER Smart Mini IPG and the Guardio/Vesta Charger. The requirements for the Quality of Service (QoS) vary depending on the use environment (operating room, recovery room, clinic, and home environment).

The Guardio/Vesta Charger will begin by displaying the IPG Data Download and IPG Data Download Success screens:





After the data download has been completed, the Charging IPG Status screen is displayed by the Guardio/Vesta Charger:

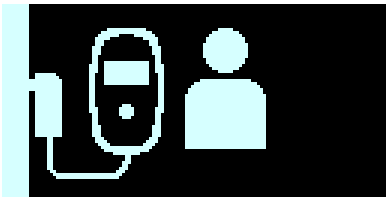


The Charging IPG Status screen's Coupling Level icon (), whose number of illuminated bars is proportional to the proximity of the charging wand to the implanted OPTIMIZER Smart Mini IPG, is indicative of the Quality of Service (QoS) for the transcutaneous energy transmission wireless link. The charging wand should be repositioned until at least 2 bars of the Charging IPG Status screen's Coupling Level icon are illuminated, indicating sufficient QoS for charging the OPTIMIZER Smart Mini IPG.

One illuminated bar indicates degraded QoS which may require a longer charging time. Zero illuminated bars on the Charging IPG Status screen's Coupling Level icon accompanied by an audible beeping tone indicates poor placement of the charging wand. If the charging wand is not repositioned onto the implant site within 20 seconds, the Guardio/Vesta Charger will emit 3 long beeping tones, display the Charging IPG Coupling Error screen, and then shut off.

Besides charging the OPTIMIZER Smart Mini, the Guardio/Vesta Charger also serves as a way of messaging the patient about alerts and other conditions. The Guardio/Vesta Charger is configured to communicate with the OPTIMIZER Smart Mini IPG at least once a day. This communication occurs whenever the IPG is within 1.5 m (5 ft) of the Guardio/Vesta Charger for a few minutes.

If the Guardio/Vesta Charger and the OPTIMIZER Smart Mini IPG do not communicate within a programmable time period, the patient may see the “Long Time Without Downloading Data From IPG” alert screen displayed by the Guardio/Vesta Charger:



In this case, instruct the patient to attempt to charge their OPTIMIZER Smart Mini IPG with their Guardio/Vesta Charger. If the patient is able to charge their implanted device successfully, then the alert screen should no longer be displayed by the Guardio/Vesta Charger. If the attempt to charge the OPTIMIZER Smart Mini IPG with the Guardio/Vesta Charger is unsuccessful, the Impulse Dynamics representative should be contacted.

Troubleshooting for Wireless Coexistence Issues

Troubleshooting OPTIlink Connection between the OPTIMIZER Smart Mini IPG and the Intelio Programmer

If you experience issues with establishing an OPTI*link* session between the OPTIMIZER Smart Mini IPG and the Intelio Programmer, try the following:

- Reposition the Intelio Programming Wand so that it lays parallel to the IPG’s plane and its center is coaxial with the center of the IPG’s header.
- Decrease the distance between the devices.
- Move the devices away from other devices that may be causing interference.
- Do not operate other wireless devices (i.e., programmers for other devices, laptop, tablet, mobile phone, or cordless phone) at the same time.

If you experience issues with maintaining an OPTI*link* session between the OPTIMIZER Smart Mini IPG and the Intelio Programmer, try the following:

- Decrease the distance between the devices.
- Move the devices so they share line of sight.
- Move the devices away from other devices that may be causing interference.
- Do not operate other wireless devices (i.e., programmers for other devices, laptop, tablet, mobile phone, or cordless phone) at the same time.
- Wait a few minutes and try connecting again

Note: Wireless communications equipment, such as wireless home network devices, mobile and cordless telephones, and tablets, could affect the quality of the OPTI*link* connection.

Troubleshooting Wireless Connection between OPTIMIZER Smart Mini IPG and Guardio/Vesta Charger

If you experience issues with establishing a wireless connection between the OPTIMIZER Smart Mini IPG and the Guardio/Vesta Charger, try the following:

- Whenever the Guardio/Vesta Charger is not being used to charge the OPTIMIZER Smart Mini IPG, place it in an area that is frequented by the patient (e.g., bedside table in the bedroom), connected to its AC Adapter, and the AC Adapter plugged into the wall outlet. This will ensure regular communications between the OPTIMIZER Smart Mini IPG and the Guardio/Vesta Charger.
- Remain stationary during the charging or data transfer process.
- Decrease the distance between the devices.
- Move the devices so they share line of sight.
- Move the devices away from other devices that may be causing interference.
- Do not operate other wireless devices (i.e., programmers for other devices, laptop, tablet, mobile phone, or cordless phone) at the same time.
- Wait a few minutes and try connecting again.

Note: Wireless communications equipment, such as wireless home network devices, mobile and cordless telephones, and tablets, could affect the quality of the wireless connection.

APPENDIX V

Procedure for IPG-ICD Interaction Testing:

Patients with a concomitantly-implanted defibrillator (ICD) require additional testing at the end of the implant procedure to ensure the appropriate function of both the OPTIMIZER Smart Mini IPG and the concomitant device. The steps of the required testing procedure are as follows:

1. Program the ICD so that it does not deliver antitachycardic therapy during this test.
2. Enable CCM therapy and program the sensing windows of the OPTIMIZER Mini IPG to consistently deliver CCM therapy in the presence of the concomitant device.
3. Extend the CCM Train Delay by a minimum of 40 ms up to 50 ms beyond the chronic CCM Train Delay setting repeatedly and observe the real-time intracardiac electrograms (ICD-EGM) to determine the maximum amount of CCM Train Delay allowed before the ICD begins to inappropriately sense the CCM therapy pulses as R waves.
4. Document the maximum CCM Train Delay and enter the information as part of the Implant data.
5. Reprogram the CCM Train Delay to the pre-test value.
6. Document reprogramming of the CCM Train Delay with a parameter printout of the IPG setting.
7. Reprogram the ICD so that it is able to deliver antitachycardic therapy.
8. Obtain the minimum R-R interval ICD VT zone from the ICD programmer or printout and enter the information as part of the Implant data.
9. Document reactivation of the antitachycardic therapy with a parameter printout of the ICD setting.

APPENDIX VI

Scientific Background About Heart Failure and Cardiac Contractility Modulation

Heart failure is a condition wherein the heart muscle does not pump blood as well as it should, generally resulting in reduced cardiac output, possibly due to reduced contraction force or impaired relaxation or other deficiencies. Chronic heart failure is associated with cardiac muscle remodeling, which is the result of abnormal genomic, molecular, cellular, and structural changes that typically manifest clinically as changes in size, shape, and function of the heart's ventricles. The reduced cardiac function is associated with multiple symptoms, such as fatigue, shortness of breath (dyspnea), co-morbidities, and limited ability to walk, exercise, or tolerate effort. The severity of symptoms is often classified by the physician in accordance with New York Heart Association (NYHA) classification (for example, NYHA class II represents moderate symptoms and class IV represents severe symptoms). Over time, chronic heart failure is a leading cause for hospitalizations and mortality. There are several medications that are used for treating heart failure according to the guidelines. In patients that are symptomatic despite appropriate medication, further evaluation of left ventricular ejection fraction (usually valuated by echocardiography) and QRS duration (evaluated by ECG) are useful in determining the possible need for an ICD, in cases having low ejection fraction, or a CRT, in cases with wide QRS, respectively.

Cardiac Contractility Modulation therapy is based on the delivery of non-excitatory electrical signals to the ventricles during the ventricular absolute refractory period. Published scientific research on cardiac contractility modulation therapy in animals and in humans explored various properties and effects. Some data suggests that cardiac contractility modulation has immediate effects on heart failure tissue, including potentially increasing the contraction force (contractility) of the muscle, possibly by immediate (i.e. less than a minute) improvement in the activity of the intracellular proteins that are associated with calcium cycling, for example by increased phosphorylation of the phospholamban protein, which is believed to modify the activity level of SERCA-2a, a protein responsible for intracellular calcium handling. Other data in heart failure animals and in humans suggest that after treating with cardiac contractility modulation for several hours, there may be normalization of mRNA expression levels of plurality of cardiac genes that are associated with heart failure (e.g. SERCA-2a, ANP, BNP, a-MHC, and others). Some data suggest that these changes and improvements in contraction are not associated with increase in myocardial oxygen consumption. Other data in animals over a period of a few months of cardiac contractility modulation delivery suggest the potential for improvements in the expression levels of several proteins that are associated with heart failure. In addition, some data suggest that with a few months of cardiac contractility modulation delivery, cardiac dimensions, structure, function (e.g. LVEDD, LVESD, and LVEF), cellular function, and/or tissue behavior may improve, providing the potential for reverse remodeling. Other studies explored clinical benefits with cardiac contractility modulation therapy in chronic heart failure patients, typically with a narrow QRS and New York Heart Association (NYHA) class of at least II, and suggest that several months (e.g. at least 3 months) of treatment potentially result in improvements in exercise tolerance (e.g. by six minute walk tests or by peak oxygen consumption in cardio pulmonary tests) and in quality of life (e.g. by NYHA classification or by questionnaire), which could be indicative of clinically significant improvements in cardiac function. Various studies explored effects of cardiac contractility modulation in patients with NYHA classes II, III, and IV, some with EF up to 35%, some with higher EF (e.g. 40%, 45%). The studies usually included population with a range of age, gender, etiology (e.g. ischemic, idiopathic) and other characteristics.

With regard to use of cardiac contractility modulation outside the United States, the 2016 European Society of Cardiology practice guidelines has reviewed clinical studies of cardiac contractility modulation in heart failure patients and mentioned cardiac contractility modulation as a treatment option that may be considered in selected patient population. Summaries of some of these studies are available on Impulse Dynamics' website (http://www.impulse-dynamics.com/int/for-physicians/clinical-data/).

Over the years of evaluation of cardiac contractility modulation therapy and use of the therapy outside the USA in countries that accept the CE Mark, CCM was delivered using various models of the OPTIMIZER System, which includes an implantable pulse generator (IPG) that is programmable and has a rechargeable battery. In principle, the OPTIMIZER System is implanted in a procedure which is similar to a pacemaker implantation. Unlike pacemakers or defibrillators, the OPTIMIZER System does not have integrated pacing or defibrillation capabilities, and is only used for delivering cardiac contractility modulation therapy. Often a patient may have concomitant implantable devices, as may be indicated per patient. The OPTIMIZER is connected to the heart's ventricles using leads, typically with the electrodes fixated to the right ventricular septum. For example, the ventricular leads may be spaced apart by a few centimeters and positioned on the septum, at or adjacent to an intersection of the septum and right ventricular free wall. The electrodes are used for sensing electrical activity of the heart and for delivery of CCM signals to the ventricular muscle at the proper timing and signal configuration. The OPTIMIZER can be programmed to deliver cardiac contractility modulation therapy for several hours every day: typically 5 hours per day in the US studies, and 7 or more hours per day in other countries. As part of the OPTIMIZER algorithm, the circuitry records one or more local electrical activity (i.e. activity in the vicinity of the electrode measured using the bipolar electrode configuration) or non-local electrical activity (i.e. wide-field electrogram using unipolar sensing between the electrode and the distant IPG can). The timing of the CCM delivery is determined to be at a certain delay and duration from the sensing, designed to deliver the CCM during the absolute refractory period of the muscle within the current beat cycle; this may maintain the CCM signal non-excitatory. If the patient has a concomitant pacing or defibrillation device, the OPTIMIZER can be configured to apply the CCM signals during a paced cardiac cycle, within the refractory period which follows the pacing. The OPTIMIZER can also be configured to apply the CCM signal during a non-paced cardiac cycle. The algorithm also applies criteria for delivery of the CCM signal or inhibiting the delivery of the CCM signal according to the relative timing of events, for example using criteria for minimum and maximum acceptable heart rate (R-R intervals), minimum and maximum acceptable time between sensed events in two locations on the RV septum, inhibition if signals are detected at an unexpected timing, and/or the use of an alert window in order to detect unexpected events and potentially block CCM delivery. Thus, the OPTIMIZER may deliver the non-excitatory CCM signal during the absolute refractory period of hundreds or thousands of beats out of 50,000 consecutive beats, taking into account the detection of any conditions that inhibit the CCM signal delivery (such as, for example, a detected arrhythmia). The parameters of the algorithm are configured per patient, with the purpose of enabling the normal delivery of the contractility modulating signal when the trace of events is indicative of an expected activation sequence of the heart.

APPENDIX VII

Current Clinical Summary: FIX-HF-5C

Study Design

FIX-HF-5C was a prospective, randomized, third-party blinded, multicenter study involving 160 patients. Key inclusion criteria included EF ≥ 25% and ≤ 45%, normal sinus rhythm, QRS duration <130 ms and NYHA Class III or ambulatory IV heart failure despite GDMT (including ICD when indicated). Main exclusion criteria included baseline peak VO_2 < 9 or > 20 mL/min/kg, hospitalization for heart failure 30 days before enrollment, clinically significant ambient ectopy (> 8,900 premature ventricular contractions [PVCs] / 24 hours), PR interval > 375 ms, and chronic atrial fibrillation or atrial flutter within 30 days of enrollment.

A device implant date was scheduled for all eligible patients, which served as the study start date (SSD) for all patients. Patients were then randomized 1:1 to either continued OMT alone (control group) or OMT plus CCM (CCM group). Patients randomized to the CCM group were implanted with the device and the implant date was canceled for patients randomized to the control group. Patients returned to the clinic for evaluation at 2 weeks, 12 weeks, and 24 weeks. Follow-up visits included 2 CPX tests, a blinded NYHA assessment, MLWHFQ quality of life assessment, and an assessment of adverse events (AEs).

Blinding of NYHA and CPX

NYHA was assessed by a blinded on-site clinician according to their standard clinical practice.

CPX tests were assessed by an independent core laboratory blinded to the randomization assignment of individual patients.

Primary Effectiveness Endpoint

The primary effectiveness endpoint was defined as the change in peak VO_2 from baseline at 24-weeks between the control and CCM groups as evaluated by the blinded core laboratory. The primary effectiveness analysis employed a Bayesian repeated measures linear model to estimate group differences in mean peak VO_2 at 24 weeks from baseline, with fixed 30% borrowing of information (70% down-weighting) from the corresponding treatment group difference observed in the FIX-HF-5 study subgroup defined as EF ≥ 25%.

Secondary Effectiveness Endpoints

Because there were multiple secondary hypotheses being tested, the method of alpha control was the closed form hierarchical method. For these analyses, if the one-sided p-value for the secondary endpoint was ≤ 0.025, the null hypothesis was rejected, and the next secondary endpoint was tested. The hierarchy for testing the secondary endpoints is the following:

- Minnesota Living with Heart Failure Questionnaire
- NYHA classification
- Peak VO_2 with a peak respiratory equivalent ratio (RER) ≥ 1.05

Safety Endpoints

The primary safety endpoint was the proportion of patients experiencing an OPTIMIZER device- or procedure-related complication through the 24-week follow up period as determined by the events adjudication committee (EAC). The primary safety endpoint was evaluated against a prespecified performance goal of 70% which was derived from several prior studies involving CRT (PMAs P010012: Contak CD CRT D, P030005: Contak Renewal TR, P030035: St. Jude Frontier, and P010012/S37: Contak Renewal 3AVT; Van Rees, 2011).

Other safety endpoints included all-cause death, cardiovascular death, composite rate of all-cause death or all-cause hospitalizations, composite rate of cardiovascular death or worsening heart failure-related hospitalizations, and overall rate of AEs and SAEs.

Demographics and Baseline Characteristics

Of the 160 eligible patients, 74 were randomized to the CCM group and 86 were randomized to the control group. In the CCM group, 6 patients did not receive the device and 2 patients died prior to the 24-week visit (including 1 patient who died prior to randomization). In the control group, 4 patients died, and 3 patients withdrew prior to the 24-week visit.

The groups were well-balanced with regards to demographic and baseline characteristics (**Table 4**). Overall, the mean age was approximately 63 years. The majority of patients were white and male, and the etiology was predominantly ischemic cardiomyopathy, characteristics which are typical of recent heart failure studies. Average peak VO_2 at baseline was approximately 15 mL/kg/min, which is moderately reduced compared to the normal population. Characteristics of the prospectively enrolled FIX-HF-5C patients were similar to those of the FIX-HF-5 subgroup used for Bayesian analysis (**Table 4**).

Table 4: Demographic and Baseline Characteristics

	FIX-HF-5C		FIX-HF-5 Subgroup (25% ≤ EF ≤ 35%)	
	CCM (N=74)	Control (N=86)	CCM (N=117)	Control (N=112)
Mean Age (years)	63	63	59	60
Male	73%	79%	71%	74%
White	74%	71%	75%	72%
Ischemic Heart Failure	62%	59%	72%	69%
Prior MI	49%	59%	67%	59%
Prior PM/ICD System	88%	85%	80%	79%
Diabetes	51%	49%	49%	52%
NYHA Class III Class IV	 87% 14%	 91% 9%	 93% 7%	 87% 13%
QRS Duration (ms)	103	104	99	101
LVEF (%)	33	33	31	32
LVEDD (mm)	58	60	57	56
Peak VO_2 (mL/kg/min)	15.5	15.4	14.6	14.8
Exercise Time (minutes)	11.4	10.6	11.3	11.7
6MHW (meters)	317	324	326	324
MLWHFQ (total score)	56	57	60	56

Mean or % (n/N)

Effectiveness Results

Primary Effectiveness Endpoint

The primary effectiveness endpoint was met. The model-based estimated mean difference in peak VO_2 at 24 weeks between CCM and control groups was 0.84 mL/kg/min with a 95% Bayesian credible interval of (0.12, 1.55) mL/kg/min. The probability that CCM is superior to control was 0.989, which exceeds the 0.975 criterion required for statistical significance of the primary endpoint.

Figure 2 shows that the Bayesian model's point estimate is very similar to the estimate from just the FIX-HF-5C study. However, the model further incorporates the high quality data from the previous randomized, blinded trial which increases the precision of the estimate. If FIX-HF-5C were a standalone trial, the middle CI would be appropriate. However, the Bayesian model allows us to incorporate the totality of the clinical experience which is an increased precision in the effect size estimate and is shown by the narrower 95% CI with the Bayesian estimate.

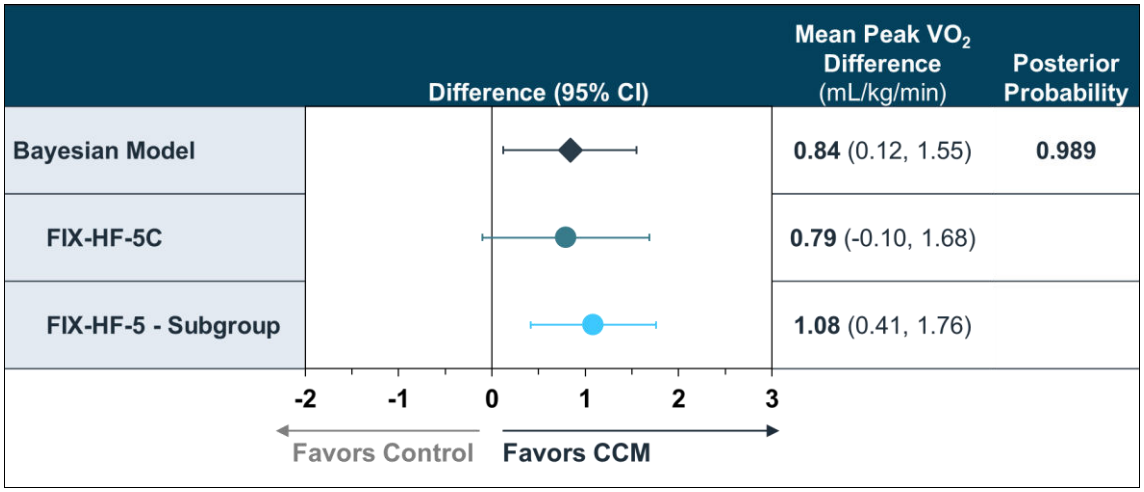


Figure 2: Peak VO_2 by Study

The improvement in peak VO_2 built up over time, from 3 to 6 months (**Figure 3**). The treatment effect can be seen in this graph to be a result of a significant decrease in VO_2 for the control group with relatively little increase in VO_2 for the treatment group.

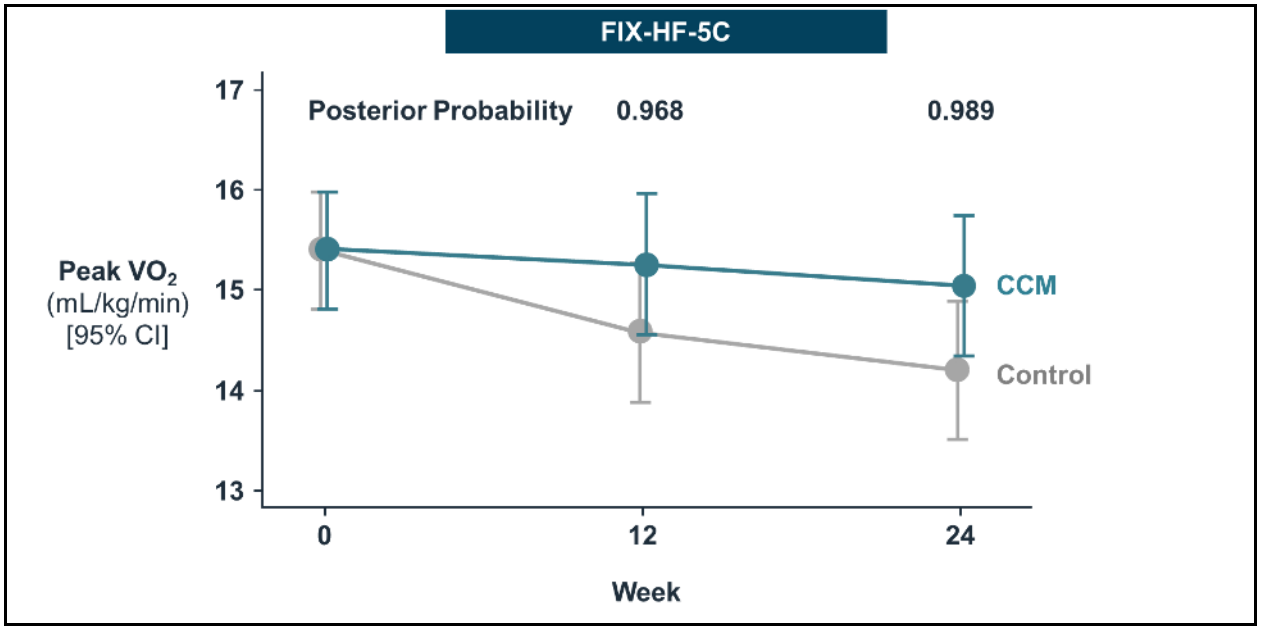


Figure 3: Time Course of Treatment Effect on Peak VO_2 (FIX-HF-5C)

Sensitivity analyses involving the primary effectiveness endpoint were conducted in which missing data were handled with different mechanisms or modifications (**Table 5**). Method of imputation affected the results and the VO_2 estimate varied from 0.48 to 0.84 depending on method. The conclusion of CCM superiority with respect to mean peak VO_2 was consistent across all sensitivity analyses. In addition, the primary analysis would achieve statistical significance with any borrowing weight of 0.11 or larger (as noted above, 0.30 was pre-specified in the analysis plan).

Table 5: Peak VO_2 Treatment Effect Across Studies

Study	Population	Bayesian VO_2 Estimate	Bayesian Posterior Probability
Primary Analysis with Borrowing FIX-HF-5C & FIX-HF-5	Imputation (Death = 0)	0.836	0.989
	Imputation (Death = lowest peak VO_2)	0.693	0.988
	Completed Cases (No Imputation)	0.603	0.978
Pooled FIX-HF-5C & FIX-HF-5	Completed Cases (No Imputation)	0.749	0.999
FIX-HF-5C Alone	Imputation (Death = 0)	0.799	0.960
	Imputation (Death = lowest peak VO_2)	0.611	0.957
	Completed Cases (No Imputation)	0.480	0.916
FIX-HF-5 Alone	Imputation (Death = 0)	1.074	1.00
	Completed Case (No Imputation)	1.080	1.00

Secondary Effectiveness Endpoints

MLWHFQ results at 24 weeks are presented in **Table 6** and show that the CCM group was statistically significantly superior over the control group ($p < 0.001$) in each study.

Table 6: Change in MLWHFQ at 24 Weeks by Study

	Difference (95% CI) in MLWHFQ Total Score Between Groups	p-value (1-sided)
Pooled data	-10.9 (-14.6, -7.2)	< 0.001
FIX-HF-5C	-11.7 (-17.6, -5.9)	< 0.001
FIX-HF-5 Subgroup	-10.8 (-15.6, -6.1)	< 0.001

The percentage of patients improving by 1 or more NYHA class by study was statistically significantly superior in the CCM group compared to the control group ($p < 0.001$ in each study; **Table 7**).

Table 7: Patients Achieving ≥ 1 Class Improvement in NYHA at 24 Weeks by Study

Change in ≥ 1 Class in NYHA Class	CCM	Control	p-value (1-sided)
Pooled data	104/173 (60.1%)	59/169 (34.9%)	< 0.001
FIX-HF-5C	57/70 (81.4%)	32/75 (42.7%)	< 0.001
FIX-HF-5 Subgroup	47/103 (45.6%)	27/94 (28.7%)	< 0.001

In the FIX-HF-5C study, the p-value for the comparison of mean peak VO_2 at 24 weeks for CCM compared to control among observations with RER > 1.05 was 0.1100. Therefore, this secondary effectiveness endpoint was not met with FIX-HF-5C data alone. When data were pooled from the FIX-HF-5 and FIX-HF-5C studies, the treatment effect was estimated as 0.62 mL/kg/min with a p-value of 0.009. In addition, the endpoint was met in the FIX-HF-5 subgroup (**Table 8**).

Table 8: Change in Peak VO_2 in Tests with RER ≥ 1.05 at 24 Weeks by Study

	Difference (95% CI) in Peak VO_2 (mL/kg/min) Between Groups	p-value (1-sided)
Pooled data	0.62 (0.11. 1.14)	0.009
FIX-HF-5C	0.43 (-0.25, 1.11)	0.1100
FIX-HF-5 - Subgroup	0.83 (0.06, 1.61)	0.017

Safety Results

The incidence of AEs in this study was relatively low. Comparisons between the groups did not show any statistical differences between CCM and control groups with respect to any AE tabulated for the analysis.

Primary Safety Endpoint

The primary safety endpoint was met as shown in **Table 9**. The complication-free proportion in the CCM group cohort was 89.7% (61/68) with lower confidence limit of 79.9% (one-sided alpha=0.025), which was greater than the pre-defined threshold of 70%. The majority of complications (5/7, 71.4%) were lead dislodgements.

Table 9: Primary Safety Endpoint (FIX-HF-5C, As Treated CCM Group Only)

Complication Free Rate n/N (%)	95% LCL	95% UCL
61/68 (89.7%)	79.9%	95.8%

Secondary Safety Endpoints (FIX-HF-5C)

As shown in **Table 10**, the freedom from death, freedom from cardiovascular death, and freedom from all-cause death or all-cause hospitalization at 24 weeks were similar in both groups.

Table 10: Secondary Safety Endpoints at 24 Weeks (FIX-HF-5C)

Freedom from	CCM	Control	p-value
All-cause death	98.3%	95.3%	0.2549
Cardiovascular death	100%	96.5%	0.1198
All-cause death or all-cause hospitalization	78.1%	77.7%	0.9437

Current Clinical Summary: FIX-HF-5C2

Introduction

Prior versions of the OPTIMIZER device used under the current US IDE have required sensing of atrial depolarization via an atrial lead to properly time the delivery of CCM pulses. Accordingly, the presence of atrial fibrillation or flutter imposed a technical limitation to the delivery of CCM signals. The current version of the OPTIMIZER, the 2-Lead OPTIMIZER Smart, has overcome the need for atrial sensing while maintaining safe and effective delivery of CCM to the ventricle. The 2-Lead OPTIMIZER Smart reduces the total lead requirement from 3-leads to 2-leads enabling CCM therapy to be delivered to a broader range of symptomatic HF patients while reducing the total hardware burden and corresponding lead-related adverse events on all patients receiving CCM.

The most frequent complications observed in the FIX-HF-5 and FIX-HF-5C trials were lead dislodgment, lead insulation breech, and lead fracture requiring an additional surgery to revise or replace the lead. Similarly, such lead-related complications are the most frequently cited complications for CRT, ICD, and pacemaker devices. Therefore, the ability to reduce the total number of leads needed for any given device, such as the OPTIMIZER Smart, has the potential to reduce the overall complication rate of that device. Improving the inherent safety of the OPTIMIZER Smart will allow physicians to expand its use thereby helping more patients with chronic heart failure.

Overview of Study Design

The FIX-HF-5C2 study was a multicenter, prospective, single-arm treatment only study of the 2-Lead configuration of the OPTIMIZER Smart System. Sixty patients were enrolled and implanted with the OPTIMIZER Smart System. The primary effectiveness endpoint was an improvement in exercise tolerance as measured by peak VO_2 obtained on cardiopulmonary exercise testing (CPX). CPX data were evaluated by an independent core laboratory. Results for subjects implanted with the OPTIMIZER Smart were compared to the peak VO_2 results for the subjects in the control group of the FIX-HF-5C study with respect to mean change in peak VO_2 at 24-weeks from baseline.

The secondary effectiveness endpoint for the FIX-HF-5C2 study was an assessment of the average daily amount of CCM therapy provided over the 24-week study. A comparison between the OPTIMIZER 2-lead device subjects in the FIX-HF-5C2 study was made to the OPTIMIZER 3-lead device subjects of the FIX-HF-5C study to determine whether or not there was a difference between the therapy provided by the two device configurations.

The primary safety endpoint in the FIX-HF-5C2 study was the percentage of subjects experiencing an OPTIMIZER device or procedure related complication through the 24-week follow up period. Complications were adjudicated by an independent events committee.

Overview of Methodology

Sites identified potential patients from their clinic's chronic heart failure population. The target patient population consisted of subjects with ejection fractions from 25 to 45% (inclusive) whose symptoms were consistent with NYHA functional class III or ambulatory NYHA Class IV. Informed consent was obtained from potential subjects who were then enrolled in the study to undergo baseline screening testing to determine eligibility for the study. Baseline screening exams included: a medical history, physical examination, medication history, blood testing, cardiopulmonary exercise testing (CPX) to determine peak VO_2, echocardiography to determine left ventricular ejection fraction (LVEF), 12-Lead ECG, and an NYHA Class assessment. The CPX and echocardiography tests were evaluated by an independent core laboratory.

Subjects that passed baseline testing and eligibility criteria were scheduled to have the OPTIMIZER Smart with 2-leads implanted as soon as possible. Subjects then returned to the clinic for evaluation at 2 weeks, 12 weeks, and 24 weeks following the initial implantation. At the 12-week and 24-week visits, subjects completed a physical examination, medication evaluation, blood testing, CPX test, NYHA assessment, and an

assessment of adverse events. Data collection for assessment of the study endpoints was concluded with the 24-week visit.

Results

Number of Investigators and Number of Sites

There were 8 sites participating in the FIX-HF-5C2 study and 8 principal investigators are shown in **Table 11** below.

Table 11: List of Sites

Investigator/Investigational Site	Screened	Enrolled
Site A	7	4 (6.7%)
Site B	33	18 (30.0%)
Site C	3	1 (1.7%)
Site D	43	12 (20.0%)
Site E	8	3 (5.0%)
Site F	14	3 (5.0%)
Site G	6	1 (1.7%)
Site H	39	18 (30.0%)
TOTAL	**153**	**60**

Accountability of Subjects with Study Visits

Table 12 contains patient disposition. There were 153 subjects screened. Of these 60 subjects were enrolled and all 60 subjects were implanted with the study device. One subject withdrew prior to 24 weeks. There were no deaths. Follow-up by study visit is presented in the table along with the number and percent of subjects who successfully completed exercise testing for the primary endpoint. A total of 53 subjects returned for exercise testing at 12 weeks while 55 subjects completed the exercise testing visit at 24 weeks. One (1) subject had his testing deemed inadequate at 12 weeks while 3 subjects had inadequate tests at 24 weeks, leaving 52 evaluable tests at 12 weeks and 52 evaluable tests at 24 weeks. One subject withdrew from the study prior to 24 weeks.

Table 12: Patient Disposition

Variable	FIX-HF-5C2 OPTIMIZER
Screened	153
Enrolled / Implanted	60 (39.2%)
Per Protocol (PP)	59 (98.3%)
Died[1]	0 (0.0%)
Withdrawn[1]	1 (1.7%)
12 Week Visit Completed	59 (98.3%)
12 Week Exercise Tolerance Test Completed	53 (88.3%)
12 Week Exercise Tolerance Test Evaluable[2]	52 (86.7%)
24 Week Visit Completed	59 (98.3%)
24 Week Exercise Tolerance Test Completed	55 (91.7%)
24 Week Exercise Tolerance Test Evaluable[2]	52 (86.7%)

[1]Prior to 24 Week Visit
[2]Includes only subjects with valid Peak VO_2, as determined by the core lab, at the indicated visit.

Baseline Characteristics

Baseline characteristics of subjects in the FIX-HF-5C2 study are presented in **Table 13** along with baseline characteristics of the FIX-HF-5C study groups. Of primary note are the comparisons between the OPTIMIZER group in the FIX-HF-5C2 study and the Control group from the FIX-HF-5C study, as these groups form the primary comparison groups for the efficacy analyses. At a nominal 0.05 level of significance, FIX-HF-5C2 subjects were older (66.3 ± 8.9 vs. 62.8 ± 11.4), had a lower prevalence of diabetes (30% vs. 48.8%), and a lower LVEDD value (57.7 ± 6.8 vs. 60.2 ± 7.0) than subjects in the FIX-HF-5C Control group. Although FIX-HF-5C2 subjects had a smaller LVEDD, LVEF between the two groups (34.1 + 6.1 vs. 32.5 + 5.2%) was not statistically significantly different. Peak VO_2 on CPX testing at baseline was similar between the two groups, but the FIX-HF-5C2 subjects exercised for a full minute longer on average than the FIX-HF-5C control group subjects (11.6 + 2.9 vs. 10.6 + 3.1 minutes). This difference was statistically significant ($p<0.04$).

Consistent with the study purpose and design, significantly more subjects in the FIX-HF-5C2 study had permanent atrial fibrillation at baseline as evidenced by the presence of atrial fibrillation on the baseline ECG tracing. Although it did not reach statistical significance, there was only 1 NYHA Class IV subject in FIX-HF-5C2 while 8 subjects were NYHA Class IV in FIX-HF-5C. This difference reflects clinical practice. It is not a regulatory limitation as the protocol was established before the Indications for Use were narrowed to NYHA III subjects and NYHA IV subjects were allowed in the FIX-HF-5C2 study. The clear clinical practice selection of NYHA Class III subjects in the FIX-HF-5C2 study confirms that the NYHA III functional class group is the appropriate target for CCM therapy. All other characteristics were similar between the two groups.

Baseline medication usage is presented in **Table 14**.

Table 13: Baseline Characteristics: ITT Population

	FIX-HF-5C2	FIX-HF-5C			
Variable	**OPTIMIZER**	**OPTIMIZER**	**P-value[1]**	**Control**	**P-value[1]**
Age (yrs)	66.3 ± 8.9 (60)	63.1 ± 10.9 (74)	0.071	62.8 ± 11.4 (86)	0.049
Male	53 (88.3%)	54 (73.0%)	0.032	68 (79.1%)	0.182
Ethnicity (White)	40 (66.7%)	55 (74.3%)	0.346	61 (70.9%)	0.590
CHF Etiology (Ischemic)	41 (68.3%)	46 (62.2%)	0.473	51 (59.3%)	0.299
Prior MI	36 (60.0%)	36 (48.6%)	0.224	51 (59.3%)	1.000
Prior CABG	13 (21.7%)	18 (24.3%)	0.837	23 (26.7%)	0.560
Prior ICD or PM System	55 (91.7%)	67 (94.4%)	0.731	73 (85.9%)	0.432
Prior ICD (ICD,CRT-D,S-ICD)	53 (88.3%)	66 (93.0%)	0.382	73 (85.9%)	0.804
Prior PM	2 (3.3%)	1 (1.4%)	0.593	0 (0.0%)	0.170
Angina	2 (3.3%)	5 (6.8%)	0.459	6 (7.0%)	0.471
Diabetes	18 (30.0%)	38 (51.4%)	0.014	42 (48.8%)	0.027
Baseline Permanent Atrial Fibrillation	9 (15.0%)	0 (0%)	0.0005	0 (0%)	0.0002
History of Atrial Arrhythmias	34 (56.7%)	25 (33.8%)	0.009	35 (40.7%)	0.065
Atrial Flutter	5 (8.3%)	8 (10.8%)	0.772	6 (7.0%)	0.761
Atrial Fibrillation	28 (46.7%)	20 (27.0%)	0.029	27 (31.4%)	0.082
Frequent PACs	3 (5.0%)	3 (4.1%)	1.000	1 (1.2%)	0.306
Other Atrial Abnormalities	2 (3.3%)	2 (2.7%)	1.000	3 (3.5%)	1.000
History of Ventricular Arrhythmias	17 (28.3%)	26 (35.1%)	0.459	28 (32.6%)	0.716
Ventricle Fibrillation	5 (8.3%)	5 (6.8%)	0.752	8 (9.3%)	1.000
Ventricular Tachycardia	13 (21.7%)	19 (25.7%)	0.685	19 (22.1%)	1.000
Frequent PVCs	5 (8.3%)	8 (10.8%)	0.772	7 (8.1%)	1.000
NYHA					
Class III	59 (98.3%)	64 (86.5%)	0.023	78 (90.7%)	0.082
Class IV	1 (1.7%)	10 (13.5%)	0.023	8 (9.3%)	0.082

[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test for binary variables and two-sample t-test for continuous variables.

Table 14: Baseline Medications: ITT Population

	FIX-HF-5C2	FIX-HF-5C			
Variable	**OPTIMIZER**	**OPTIMIZER**	**P-value[1]**	**Control**	**P-value[1]**
ACEi/ARB/ARNi	45 (75.0%)	61 (82.4%)	0.393	72 (83.7%)	0.212
ACE inhibitor	29 (48.3%)	40 (54.1%)	0.603	49 (57.0%)	0.317
ARB	8 (13.3%)	18 (24.3%)	0.128	22 (25.6%)	0.096
ARNi	9 (15.0%)	3 (4.1%)	0.035	3 (3.5%)	0.028
Beta Blocker	57 (95.0%)	72 (97.3%)	0.656	82 (95.3%)	1.000
Diuretic	44 (73.3%)	57 (77.0%)	0.689	67 (77.9%)	0.558
Secondary Diuretic	5 (8.3%)	6 (8.1%)	1.000	8 (9.3%)	1.000
Ivabradine	3 (5.0%)	2 (2.7%)	0.656	4 (4.7%)	1.000
Digoxin	4 (6.7%)	10 (13.5%)	0.260	8 (9.3%)	0.762
Aldosterone Inhibitor	25 (41.7%)	26 (35.1%)	0.477	33 (38.4%)	0.733
Hydralazine	3 (5.0%)	5 (6.8%)	0.731	10 (11.6%)	0.240
Nitrates	11 (18.3%)	18 (24.3%)	0.527	26 (30.2%)	0.124
Calcium Channel Blocker	6 (10.0%)	9 (12.2%)	0.787	8 (9.3%)	1.000
Anti-arrhythmic	19 (31.7%)	14 (18.9%)	0.108	12 (14.0%)	0.013
Anti-platelet	41 (68.3%)	54 (73.0%)	0.572	59 (68.6%)	1.000
Anticoagulant	27 (45.0%)	19 (25.7%)	0.028	18 (20.9%)	0.003

[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test.

Baseline heart failure medications are summarized in **Table 14**. The only significant differences were a greater use of ARNi's, anti-arrhythmics, and anticoagulants in FIX-HF-5C2 subjects. The greater ARNi use reflects the fact that they were introduced toward the end of the FIX-HF-5C study. The greater use of anti-arrhythmics and anticoagulants likely represents the inclusion of patients with atrial fibrillation; those patients were excluded in the FIX-HF-5C study. **Table 15** breaks down the anti-arrhythmic medication usage in FIX-HF-5C2 and FIX-HF-5C studies for comparison.

Table 15: Baseline Anti-arrhythmic Medications

	FIX-HF-5C2	FIX-HF-5C	
Variable	**OPTIMIZER**	**OPTIMIZER**	**Control**
Anti-arrhythmic	19 (31.7%)	14 (18.9%)	12 (14.0%)
Amiodarone	12 (20.0%)	11 (14.9%)	6 (7.0%)
Sotalol	5 (8.3%)	3 (4.1%)	2 (2.3%)
Mexiletine	1 (1.7%)	0	3 (3.5%)
Dofetilide	1 (1.7%)	0	1 (1.2%)

Primary Effectiveness Endpoint

Bayesian Analysis

A Bayesian repeated measures model was used to estimate group differences in the mean peak VO_2 at 24 weeks from baseline in FIX-HF-5C2 device patients compared to FIX-HF-5C control patients, with 30% borrowing of information (70% down-weighting) from the corresponding group difference observed in the FIX-HF-5 subgroup data.

In the FIX-HF-5C2 device group, 55 of the 60 patients provided at least one post-baseline peak VO_2 measurement, and 52 patients provided 24-week peak VO_2 measurements. There were no deaths in FIX-HF-5C2 subjects at the 24-week assessment period, and there were no missing observations due to heart failure hospitalizations. However, patients in the FIX-HF-5C control group who are missing peak VO_2 observations due to death are imputed as zeros per the FIX-HF-5C protocol. There are a total of 146 patients and 397 non-missing peak VO_2 observations in the combined FIX-HF-5C2 device and FIX-HF-5C control groups for this analysis.

Tables 16 and 17 provide results of the Bayesian analyses while **Figures 4 and 5** show the peak VO_2 results graphically.

Table 16: Number of Observations, Mean, SD of Peak VO_2 by Group and Time

	Nobs (observed)		Nobs (missing)		Mean		Standard Deviation	
	Control	**Device**	**Control**	**Device**	**Control**	**Device**	**Control**	**Device**
Baseline	86	60	0	0	15.36	15.01	2.81	2.94
12 Weeks	73	52	13	8	14.59	16.01	4.29	3.34
24 Weeks	74	52	12	8	14.34	16.22	4.69	3.09

Table 17: Bayesian Primary Analysis Results (with Borrowing)

		Borrowing (Bayes)			
Time	**TmtDiff**	**LL**	**UL**	**SE**	**P(Superior)**
12 Weeks	1.079	0.381	1.776	0.356	0.999
24 Weeks	1.722	1.021	2.417	0.356	1.000

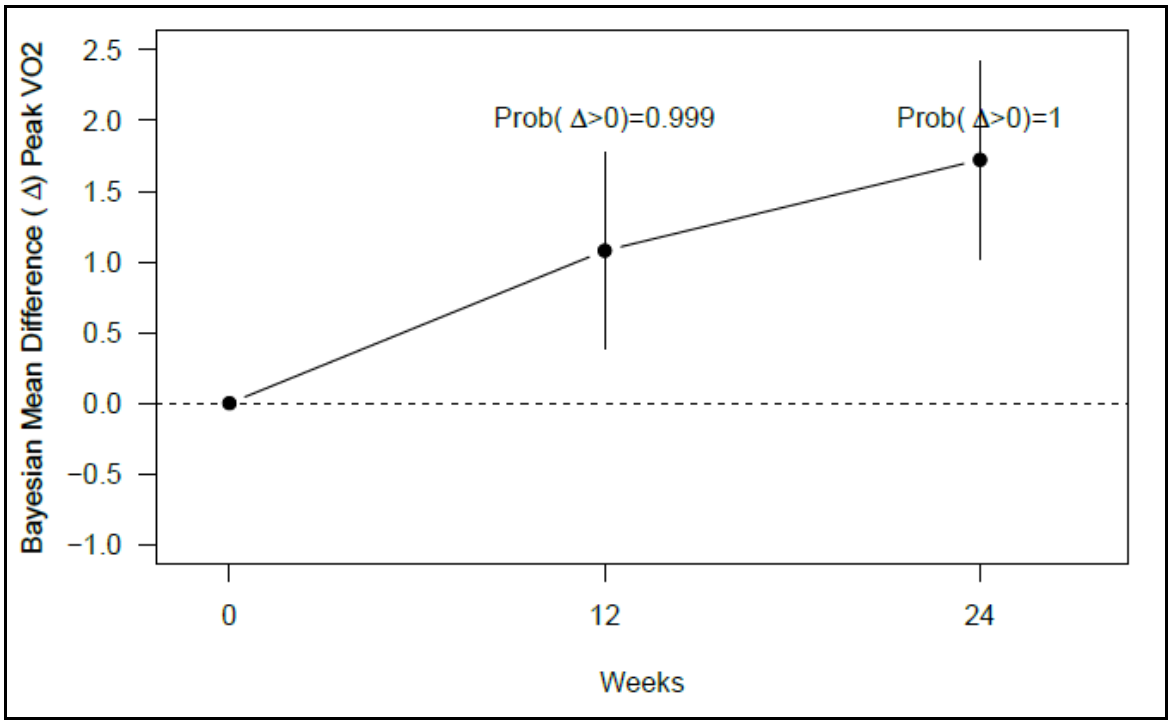


Figure 4: Bayesian Modeled Treatment Mean Difference (Δ) Peak VO_2 by Time

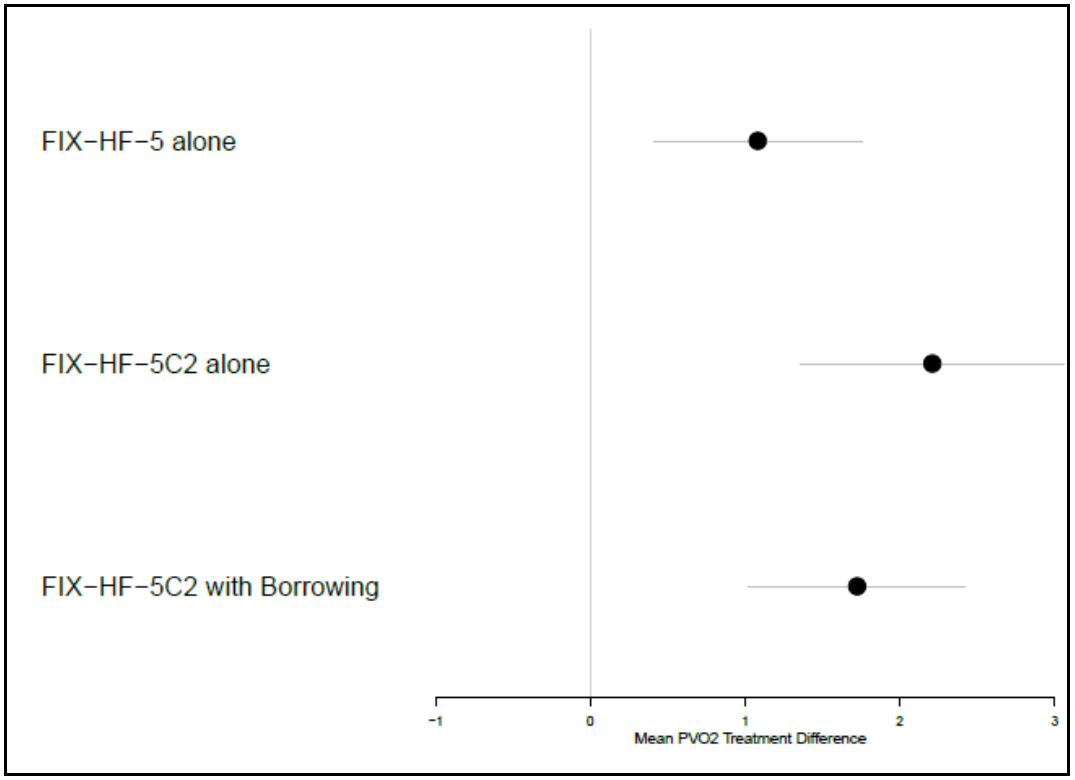


Figure 5: 24-Week Modeled Mean PVO_2 Treatment Difference by Study

The Bayesian Posterior Probability that Δ_3 is greater than 0 (indicating superiority of FIX-HF-5C2 device to FIX-HF-5C control) is 1. Because this exceeds 0.975, the null hypothesis is rejected and superiority is claimed with respect to the primary endpoint.

Frequentist Analysis

The Bayesian analysis indicates that the FIX-HF-5C2 OPTIMIZER group had a superior increase in Peak VO_2 over the FIX-HF-5C Control group with a posterior probability which exceeds the 0.975 required for statistical significance.

A supporting, non-Bayesian analysis of Peak VO_2 appears in **Table 18** overall summaries).

Eleven (11) subjects were missing evaluable Peak VO_2 results at weeks 12 or 24. Five (5) subjects were missing at both visits.

There were no deaths or missingness due to heart failure hospitalizations so there were no imputations of zeros or lowest value in the FIX-HF-5C2 data. Previous study results are presented for comparative purposes including differences between the current OPTIMIZER results and results from the FIX-HF-5C study. Peak VO_2 was significantly increased at both 12 and 24 weeks in the FIX-HF-5C2 OPTIMIZER group and the change from baseline was significantly different from the control group in the FIX-HF-5C study. This was confirmed in the frequentist mixed model results compared to the FIX-HF-5C study control.

In total, we observed an improvement in peak VO_2 for the device subjects in the FIX-HF-5C2 study which was not dependent on a decrease in VO_2 for the control group.

Table 18: Efficacy Summary: ITT Population

		FIX-HF-5C2	FIX-HF-5C			
Variable		**OPTIMIZER**	**OPTIMIZER**	**Difference[1]**	**Control**	**Difference[1]**
Peak VO_2 (ml/kg/min)						
Baseline	Mean ± SD (n)	15.0 ± 2.9 (60)	15.5 ± 2.6 (73)	-0.48 ± 2.76	15.4 ± 2.8 (86)	-0.36 ± 2.87
	(min, max)	(9.8, 19.9)	(9.8, 19.7)		(9.1, 19.9)	
	[95% CI]	[14.2,15.8]	[14.9,16.1]	[-1.44, 0.47]	[14.8,16.0]	[-1.31, 0.60]
	P-value[2]			0.317		0.462
12 Weeks	Mean ± SD (n)	16.0 ± 3.3 (52)	15.6 ± 3.2 (67)	0.43 ± 3.25	15.2 ± 3.1 (70)	0.80 ± 3.20
	(min, max)	(10.2, 22.2)	(9.0, 23.3)		(8.5, 21.9)	
	[95% CI]	[15.1,16.9]	[14.8,16.4]	[-0.76, 1.62]	[14.5,15.9]	[-0.36, 1.96]
	P-value[2]			0.478		0.174
Change Baseline to 12 Weeks	Mean ± SD (n)	0.77 ± 1.64 (52)	0.10 ± 2.34 (67)	0.67 ± 2.06	-0.35 ± 2.11 (70)	1.13 ± 1.92
	(min, max)	(-5.30, 4.60)	(-7.35, 5.95)		(-6.10, 4.80)	
	[95% CI]	[0.32,1.23]	[-0.47,0.67]	[-0.09, 1.42]	[-0.86,0.15]	[0.43, 1.82]
	P-value[2]	0.001	0.716	0.082	0.164	0.002
24 Weeks	Mean ± SD (n)	16.2 ± 3.1 (52)	15.5 ± 3.5 (66)	0.73 ± 3.33	15.2 ± 3.3 (70)	1.06 ± 3.20
	(min, max)	(10.2, 23.9)	(8.9, 23.2)		(8.8, 22.7)	
	[95% CI]	[15.4,17.1]	[14.6,16.3]	[-0.49, 1.95]	[14.4,15.9]	[-0.10, 2.21]
	P-value[2]			0.239		0.074
Change Baseline to 24 Weeks	Mean ± SD (n)	1.13 ± 1.50 (52)	-0.027 ± 2.745 (66)	1.15 ± 2.28	-0.50 ± 2.36 (70)	1.63 ± 2.04
	(min, max)	(-2.60, 4.20)	(-7.30, 5.90)		(-6.85, 4.90)	
	[95% CI]	[0.71,1.54]	[-0.701,0.648]	[0.32, 1.99]	[-1.07,0.06]	[0.89, 2.37]
	P-value[2]	<.001	0.938	0.007	0.078	<.001

[1]Compared to FIX-HF-5C2 OPTIMIZER Group.
[2]Values are compared to baseline using the paired t-test, and differences are compared using the two-sample t-test without taking into account other time points.

Secondary Effectiveness Analyses

Since the primary endpoint was met, the secondary endpoint of total CCM delivery could be formally tested. Total CCM delivery is presented in **Table 19** for the IP populations. Results are presented for all available data and for the multiple imputation approach as described previously. Although all subjects in FIX-HF-5C2 were implanted, 1 subject in the FIX-HF-5C OPTIMIZER group died prior to study start and an additional 5 subjects were not implanted, so the IP population differs for the FIX-HF-5C study used in comparison. As can be seen in **Table 19,** for all available data and imputed data, the total CCM delivery at 24 weeks is equivalent between the OPTIMIZER groups of the FIX-HF-5C2 and FIX-HF-5C studies since the 95% confidence interval of the difference between the 2 groups lies wholly within the interval defined by (Θ_L,Θ_U).

Table 19: Secondary Efficacy - OPTIMIZER Interrogation: IP Population

		FIX-HF-5C2	FIX-HF-5C		FIX-HF-5C2 Bsl Permanent AFIB
Variable		**OPTIMIZER (N=60)**	**OPTIMIZER (N=60)**	**Difference[1]**	**OPTIMIZER (N=9)**
Total CCM Delivery					
24 Weeks	Mean ± SD (n)	19892 ± 3472 (59)	19583 ± 4998 (67)	310 ± 4352	19734 ± 4187 (9)
	(min, max)	(11618, 28284)	(3645, 31009)		(12787, 24578)
	[95% CI]	[18988,20797]	[18364,20802]	[-1228, 1847]	[16515,22952]
	P-value[2]			0.691	
	(Θ_L,Θ_U)			(-2448,2448)	
Total CCM Delivery (IMPUTED)					
24 Weeks	Mean ± SE	19897 ± 463	19618 ± 610	279 ± 783	
	(min, max)	(19811, 20037)	(19553, 19722)		
	[95% CI]	[18988,20805]	[18421,20814]	[-1256,1813]	
	P-value[2]			0.722	
	(Θ_L,Θ_U)			(-2452,2452)	

[1]Bioequivalence is conceded if the two-sided 95% confidence interval, for the difference, is completely contained within the interval (Θ_L,Θ_U).
[2]P-value for mean from the two-sample t-test for the difference between groups.

Primary Safety Endpoint

The primary safety endpoint was the composite endpoint of the percentage of subjects in the OPTIMIZER group who experienced either an OPTIMIZER device or OPTIMIZER procedure related complication through the 24-week follow-up period, as determined by an independent events adjudication committee (EAC). The EAC reviewed all serious adverse event reports (SAEs), confirmed the classification of “serious”, and adjudicated the relationship of the event to the OPTIMIZER System device or procedure. SAEs that the EAC determined to be definitely related to either the OPTIMIZER System or the OPTIMIZER Procedure were considered a Complication.

There was only 1 complication observed in the FIX-HF-5C2 subjects. This was in a subject who had a minor hematoma at the OPTIMIZER IPG implant site and was kept in the hospital overnight for observation following the device implantation. The hematoma resolved without treatment, and there were no further complications in this case. The EAC adjudicated the event as a procedure related complication to account for the index hospital stay being prolonged an additional day for observation. There was no OPTIMIZER device-related SAE reported in the 2-lead device subjects.

Thus, the complication rate in FIX-HF-5C2 study ITT group was 1.7% (1/60) with exact 95% CI (0.0%, 8.9%). As can be seen in **Table 20**, the rate of complications in the FIX-HF-5C2 study was nominally lower than seen in the previous study although not statistically significant. The small sample size for the FIX-HF-5C2 study renders it difficult to show a statistical difference in percentage points. However, the absolute difference between the complication rate for the FIX-HF-5C2 study (1.7%) and the FIX-HF-5C study (10.3%) is clinically relevant.

We can therefore conclude that the primary safety endpoint of the FIX-HF-5C2 study was met and that delivery of CCM through a 2-Lead device is just as safe as delivery of CCM therapy through a 3-Lead device. These results may, in part, be due to a reduction in the number of leads implanted with the 2-Lead device as well as the reduction in the total volume of leads introduced in the venous vasculature.

Table 20: Safety: ITT Population

		FIX-HF-5C2	FIX-HF-5C	
Variable		**OPTIMIZER 2-lead**	**OPTIMIZER 3-lead**	**P-value[1]**
Primary Safety				
OPTIMIZER device- or procedure-related complication through 24 Weeks	N (%)	1 (1.7%)	7 (10.3%)	0.0660
	[95% CI]	(0.0%, 8.9%)	(4.2%, 20.1%)	
Secondary Safety				
PVC or VT SAEs	N (%)	0 (0.0%)	0 (0.0%)	
PVC	N (%)	0 (0.0%)	0 (0.0%)	
VT	N (%)	0 (0.0%)	0 (0.0%)	

[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test.
*Values are number and percent of subjects. Subjects are counted only once within each category.

Adverse Events

All site reported non-serious adverse events and adjudicated serious adverse events from study start date to 24 weeks; are tabulated in **Table 21** and **Table 22** in the ITT population. The total number of events and the number and percent of subjects having at least one event of the type listed is given. Event rates were similar to those seen in both the FIX-HF-5C OPTIMIZER and control groups. At a nominal 0.05 level of significance, there were fewer percentage of subjects that had a serious OPTIMIZER System malfunction in the FIX-HF-5C2 study than in the previous study (p=0.03).

Table 21: Adjudicated Serious Adverse Events, Day 0-168: ITT Population

	FIX-HF-5C2 OPTIMIZER		FIX-HF-5C OPTIMIZER			FIX-HF-5C Control		
Variable	**# Events**	**Subjects[2]**	**# Events**	**Subjects**	**P-value[1]**	**# Events**	**Subjects**	**P-value[1]**
All	26	19 (31.7%)	29	20 (27.0%)	0.572	27	19 (22.1%)	0.250
		(20.3%, 45.0%)		(17.4%, 38.6%)			(13.9%, 32.3%)	
General Medical	8	7 (11.7%)	7	7 (9.5%)	0.779	8	7 (8.1%)	0.571
		(4.8%, 22.6%)		(3.9%, 18.5%)			(3.3%, 16.1%)	
Arrhythmia	3	2 (3.3%)	3	3 (4.1%)	1.000	2	2 (2.3%)	1.000
		(0.4%, 11.5%)		(0.8%, 11.4%)			(0.3%, 8.1%)	
Worsening Heart Failure	7	5 (8.3%)	4	3 (4.1%)	0.466	8	7 (8.1%)	1.000
		(2.8%, 18.4%)		(0.8%, 11.4%)			(3.3%, 16.1%)	
General Cardiopulmonary	2	2 (3.3%)	4	3 (4.1%)	1.000	2	2 (2.3%)	1.000
		(0.4%, 11.5%)		(0.8%, 11.4%)			(0.3%, 8.1%)	
Bleeding	1	1 (1.7%)	0	0 (0.0%)	0.448	1	1 (1.2%)	1.000
		(0.0%, 8.9%)		(0.0%, 4.9%)			(0.0%, 6.3%)	
Neurologic	1	1 (1.7%)	0	0 (0.0%)	0.448	0	0 (0.0%)	0.411
		(0.0%, 8.9%)		(0.0%, 4.9%)			(0.0%, 4.2%)	
Thromboembolism	1	1 (1.7%)	1	1 (1.4%)	1.000	1	1 (1.2%)	1.000
		(0.0%, 8.9%)		(0.0%, 7.3%)			(0.0%, 6.3%)	
Local Infection	1	1 (1.7%)	1	1 (1.4%)	1.000	4	4 (4.7%)	0.649
		(0.0%, 8.9%)		(0.0%, 7.3%)			(1.3%, 11.5%)	
Sepsis	1	1 (1.7%)	1	1 (1.4%)	1.000	1	1 (1.2%)	1.000
		(0.0%, 8.9%)		(0.0%, 7.3%)			(0.0%, 6.3%)	
ICD or Pacemaker System Malfunction	1	1 (1.7%)	2	2 (2.7%)	1.000	0	0 (0.0%)	0.411
		(0.0%, 8.9%)		(0.3%, 9.4%)			(0.0%, 4.2%)	
OPTIMIZER System Malfunction	0	0 (0.0%)	6	6 (8.1%)	0.033		-	
		(0.0%, 6.0%)		(3.0%, 16.8%)				

Program Name: AE.sas
[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test.
[2]Number and percent of subjects. Subjects are counted only once within each category.

Table 22: Non-Serious Adverse Events, Day 0-168: ITT Population

	FIX-HF-5C2 OPTIMIZER		FIX-HF-5C OPTIMIZER			FIX-HF-5C Control		
Variable	**# Events**	**Subjects[2]**	**# Events**	**Subjects**	**P-value[1]**	**# Events**	**Subjects**	**P-value[1]**
All	39	26 (43.3%)	41	21 (28.4%)	0.101	35	23 (26.7%)	0.050
		(30.6%, 56.8%)		(18.5%, 40.1%)			(17.8%, 37.4%)	
General Medical	23	19 (31.7%)	22	14 (18.9%)	0.108	23	13 (15.1%)	0.025
		(20.3%, 45.0%)		(10.7%, 29.7%)			(8.3%, 24.5%)	
Arrhythmia	1	1 (1.7%)	1	1 (1.4%)	1.000	4	4 (4.7%)	0.649
		(0.0%, 8.9%)		(0.0%, 7.3%)			(1.3%, 11.5%)	
Worsening Heart Failure	3	3 (5.0%)	6	5 (6.8%)	0.731	4	4 (4.7%)	1.000
		(1.0%, 13.9%)		(2.2%, 15.1%)			(1.3%, 11.5%)	
General Cardiopulmonary	4	4 (6.7%)	3	3 (4.1%)	0.700	3	3 (3.5%)	0.446
		(1.8%, 16.2%)		(0.8%, 11.4%)			(0.7%, 9.9%)	
Bleeding	2	2 (3.3%)	2	2 (2.7%)	1.000	0	0 (0.0%)	0.167
		(0.4%, 11.5%)		(0.3%, 9.4%)			(0.0%, 4.2%)	
Neurologic	0	0 (0.0%)	1	1 (1.4%)	1.000	0	0 (0.0%)	
		(0.0%, 6.0%)		(0.0%, 7.3%)			(0.0%, 4.2%)	
Thromboembolism	1	1 (1.7%)	0	0 (0.0%)	0.448	0	0 (0.0%)	0.411
		(0.0%, 8.9%)		(0.0%, 4.9%)			(0.0%, 4.2%)	
Local Infection	5	5 (8.3%)	3	3 (4.1%)	0.466	1	1 (1.2%)	0.043
		(2.8%, 18.4%)		(0.8%, 11.4%)			(0.0%, 6.3%)	
Sepsis	0	0 (0.0%)	0	0 (0.0%)		0	0 (0.0%)	
		(0.0%, 6.0%)		(0.0%, 4.9%)			(0.0%, 4.2%)	
ICD or Pacemaker System Malfunction	0	0 (0.0%)	0	0 (0.0%)		0	0 (0.0%)	
		(0.0%, 6.0%)		(0.0%, 4.9%)			(0.0%, 4.2%)	
OPTIMIZER System Malfunction	0	0 (0.0%)	3	2 (2.7%)	0.502		-	
		(0.0%, 6.0%)		(0.3%, 9.4%)				

Program Name: AE.sas
[1]Compared to FIX-HF-5C2 OPTIMIZER Group via Fishers exact test.
[2]Number and percent of subjects. Subjects are counted only once within each category.

The incidence of overall non-serious adverse events was significantly higher in the OPTIMIZER subject cohort of the FIX-HF-5C2 study than for the control group of the FIX-HF-5C study. It was not significantly greater than the incidence on non-serious adverse events in the OPTIMIZER group for the FIX-HF-5C study. The higher rate between the FIX-HF-5C2 OPTIMIZER subjects and subjects in the control group for FIX-HF-5C can be attributed to differences in general medical events and localized infection. General medical events include a wide range of adverse events such as sore throats to more serious events like cholelithiasis. Clinically, it is difficult to interpret the meaning of any differences in general medical events. Only 1 of the 5 non-serious localized infections was device related (IPG pocket). The important point is that the localized infection rate was not high to begin with and was not significantly different between the OPTIMIZER subjects for the FIX-HF-5C2 study and the OPTIMIZER subjects for the FIX-HF-5C study.

Discussion

The study met its primary effectiveness endpoint based on the Bayesian analysis presented which was supported by frequentist analyses. With respect to safety, there were no device-related complications and only 1 procedure-related complication (<2%). This was significantly lower than the rate observed in the FIX-HF-5C 3-lead device study. There was no evidence of a difference between study groups with respect to adverse events or adjudicated serious adverse events, although the FIX-HF-5C2 OPTIMIZER group appeared to have a lower rate of serious OPTIMIZER System related events than was seen previously.

Thus, it can be concluded that the FIX-HF-5C2 study met its pre-specified endpoints and that the 2-Lead configuration of the OPTIMIZER Smart is at least as safe and effective as the 3-Lead configuration of the OPTIMIZER Smart approved by FDA in P180036.

Peak VO_2 improved more in the OPTIMIZER patients of the present FIX-HF-5C2 study than in the prior FIX-HF-5C study control group for both Bayesian and frequentist statistical analyses.

Risk-Benefit

The benefits of the 2-Lead configuration of the OPTIMIZER Smart are an improvement in peak VO_2, improved functional status as evidenced by improvements in NYHA functional class and a reduced incidence of procedural complications as compared to the 3-Lead configuration of the OPTIMIZER Smart (FIX-HF-5C study). Risks associated with the OPTIMIZER Smart system are similar to those associated with ICDs and pacemakers; which are well documented in the literature. In the FIX-HF-5C2 study, lead dislodgments were the primary complication reported. There were no lead dislodgments reported in the FIX-HF-5C2 study. Thus, it is clear that the potential benefits of the 2-Lead configuration of the OPTIMIZER Smart outweigh the potential risks.

Conclusions

Based on the results of the FIX-HF-5C2 study described herein, we conclude the following:

1. The 2-Lead configuration of the OPTIMIZER Smart System is safe and effective for the delivery of CCM therapy in patients with NYHA class III heart failure symptoms.
2. Exercise tolerance as evidenced by improved peak VO_2, is improved by CCM therapy delivered by the 2-Lead configuration of the OPTIMIZER Smart system.
3. CCM therapy delivery with the 2-Lead system is clinically effective and the same as delivery with the 3-Lead device.
4. Complication rates are lower with the 2-Lead device possibly due to the reduction in the number of implanted leads.
5. The serious adverse event profile for the 2-Lead device is not significantly different from that with the 3-Lead device.