OPTIMIZER® Smart System

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For the Treatment of

Moderate to Severe Heart Failure

Patient's Manual

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

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1. INTRODUCTION

Your doctor has determined that you have a form of heart failure. To help reduce your symptoms associated with this condition, your doctor has recommended implantation of the OPTIMIZER Smart Implantable Pulse Generator (IPG). The purpose of this manual is to help you understand the elements and operation of the OPTIMIZER Smart System.

Heart failure is a clinical condition that annually affects an estimated 10 million people worldwide. A recent study in the United States found the incidence of heart failure in men was 378 per 100,000, while in women it was 289 per 100,000[1].

Heart failure is the term doctors use to describe the signs and symptoms associated with the inability of the heart muscle to pump enough blood to meet the needs of the body without a dangerous rise in blood (diastolic) pressure. Symptoms of heart failure may first be manifested by fatigue, poor exercise tolerance, or mental confusion or by a combination of these symptoms with difficulty breathing, a build up of fluid in the lungs, the liver and elsewhere in the vascular bed of the body, the first sign of which is commonly swelling (edema) of the legs and/or arms.

A number of medications of differing actions are currently available for the treatment of heart failure. In spite of this growing list, some patients fail to adequately benefit from this approach alone.

The OPTIMIZER Smart IPG does not stimulate the heart muscle to contract like a cardiac pacemaker. Instead, it is designed to deliver specialized "cardiac contractility modulation" signals (CCM) into the wall between the two main pumping chambers (right and left ventricles) when the heart contracts. The primary effect of this therapy occurs at the cellular level in the heart muscle, naturally

[1] Trends in Heart Failure Incidence and Survival in a Community-Based Population, Véronique L. Roger MD, et al; *JAMA.* July 21, 2004; 292:344-350.

improving the efficiency and strength of cardiac contraction; i.e. more blood is pumped from the heart per heart beat.

2. THE OPTIMIZER SMART SYSTEM

The OPTIMIZER Smart System is intended for the treatment of moderate to severe heart failure. It is comprised of the following elements:

- Programmable OPTIMIZER Smart Implantable Pulse Generator
- OPTIMIZER Mini Charger

2.1 OPTIMIZER Smart Implantable Pulse Generator

The OPTIMIZER Smart Implantable Pulse Generator is an internally-powered, programmable, and telemetric device. It is typically implanted under the skin in the upper left or right chest. Connected to the OPTIMIZER Smart Pulse Generator are two implantable leads that your doctor will insert through a large vein and into the heart during the implantation process. These leads have electrodes that allow the OPTIMIZER Smart IPG to monitor the electrical activity of your heart and deliver special cardiac contractility modulation signals to the heart at a specific time during heart beats.

As mentioned, the OPTIMIZER Smart IPG is a telemetric device. That means that the device is designed with the ability to communicate through the skin with an external computer-like device called the OMNI II Programmer. The programmer is exclusively used by your doctor or his medical staff to customize the settings of the OPTIMIZER Smart IPG to your specific heart beat. It also allows your doctor to obtain important information from the device

concerning how well its programmed settings are treating your condition.

The OPTIMIZER Smart IPG has a rechargeable battery to extend its service life. Periodically it will be necessary to recharge your device. Your doctor will tell you how often. So that this process is as convenient for you as possible, you will be provided with an OPTIMIZER Mini Charger. Your doctor will instruct you in its proper use.

The expected life of the OPTIMIZER Smart IPG is limited by the expected service life of its rechargeable battery. The rechargeable battery inside the OPTIMIZER Smart IPG should provide at least fifteen years of service. Over time and with repeated charging, the battery in the OPTIMIZER Smart IPG will lose its ability to recover its full charge capacity.

Figure 1: OPTIMIZER Smart IPG

2.2 OPTIMIZER Mini Charger

The OPTIMIZER Mini Charger is also powered by a rechargeable battery. The charging wand is permanently attached to the device with a cable long enough to let you set up the charger up to almost 20 in away from you. The charging process runs automatically without requiring significant user intervention. Please refer to Section 9 of this manual for details on the proper operation of the charger.

Figure 2: OPTIMIZER Mini Charger

3. INDICATIONS[2]

The OPTIMIZER Smart System, which delivers 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, who are in normal sinus rhythm, are not indicated for CRT, and have a left ventricular ejection fraction ranging from 25% to 45%.

The OPTIMIZER Smart system delivers non-excitatory CCM™ signals to the heart and has no pacemaker or ICD functions.

4. CONTRAINDICATIONS AND PRECAUTIONS

Use of the OPTIMIZER Smart 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. POTENTIAL COMPLICATIONS

5.1 Associated with Implantation

As with any surgical procedure, the implantation of the OPTIMIZER Smart Pulse Generator involves some degree of risk. This section is intended to provide you with an

[2] The safety and performance of the OPTIMIZER Smart System is based on clinical investigations conducted with the prior generation device, the OPTIMIZER IVs and III Systems given the similarities between the Systems with regard to function, intended use, design characteristics, and the CCM™ signals. Summaries of these studies are available on Impulse Dynamics' website.

explanation of the various potential complications associated with having a device implanted. None of these complications are unique to the OPTIMIZER Smart IPG but can also appear during implantation of similar systems (like cardiac pacemakers).

Complications associated with medical device implantation reported in the medical literature include, but are not limited to:

- Irregular and/or dangerous heart rhythms caused by the pulse generator.
- Infection – This may require surgical correction.
- The skin over the device may break down (erode) exposing part of the device. This requires surgical correction.
- The device may move from its original location under the skin (migration) requiring that your doctor perform another surgery to secure it in position.
- You may bleed under the skin around the wound(s) or in the "pocket" created underneath the skin to hold the pulse generator (hematoma). This may require surgical correction.
- Fluid may accumulate in the "pocket" created underneath the skin to hold the pulse generator, which requires treatment.
- You may be sensitive to one or more of the materials used in the OPTIMIZER Smart IPG that are exposed to the tissues of the body (histotoxic reaction). Though rare, this may require removal of the device.
- Stroke.
- Collapsed lung.

- Death.

Complications associated with lead implantation reported in medical literature include:

- An implanted lead may push through the wall of the heart. On rare occasions this has led to a dangerous condition requiring surgical correction.
- If you have a very thin heart wall, you may experience a hiccup each time the device delivers a CCM signal due to stimulation of the phrenic nerve or of the diaphragm itself. This may require surgical correction.
- Although unlikely to occur (<1%), venous thrombosis (clot formation) could result from placement of leads in the venous system. This may require surgical correction.

The OPTIMIZER Smart IPG uses its leads to detect the electrical activity of your heart. Problems that can affect the lead's ability to perform this function may occur. These include:

- A lead may dislodge from where it was placed during implantation, necessitating re-operation.
- A lead may fracture or break producing a poor electrical connection, necessitating re-operation.

The lead problems described above can occur at any time during the implant life of a lead. Surgical correction is typically required.

5.2 Associated with Device/Charger Operation

- An OPTIMIZER Smart IPG may not properly sense and deliver CCM signals due to a random software or hardware problem, necessitating replacement.

- An OPTIMIZER Smart IPG may detect environmental interference and inappropriately deliver CCM signals. See Section 8.4.
- An OPTIMIZER Mini Charger may not function as designed due to a random software or hardware problem and not charge the IPG as intended. A replacement Charger will be required.

6. IMPLANTATION OF THE OPTIMIZER SMART IPG

The implantation of the OPTIMIZER Smart Pulse Generator and leads is a surgical procedure, which requires the administration of general or local anesthesia (depending on the preferences of the implanting facility). If a local anesthetic is used, it is to numb the implantation site, which is typically in the upper left or right chest just under the skin.

The OPTIMIZER Smart IPG uses two implantable leads placed in specific locations within the heart. Each lead has an electrode at its tip. Your doctor will make a small incision in the upper left or right chest area and then insert each of the leads through a large vein and into the heart. Fluoroscopy is used to aid in proper positioning. Once the leads are in place and secured, your doctor will create a "pocket" to hold the OPTIMIZER Smart Pulse Generator at the site where the initial incision for lead insertion was made.

Your doctor will then connect the implanted leads to the OPTIMIZER Smart IPG, verify that it is functioning properly, and then insert it into the pocket. The pocket is then sutured closed and the wound bandaged. X-rays will be taken of your chest to document the location of the electrodes in the heart and the orientation of the implanted pulse generator.

At the time of discharge, you will receive instructions from your doctor that will include:

- Limitations, if any, on your physical activity, until your incision has healed
- Instructions on how to bathe, taking particular care to avoid wetting the wounds as these should be kept dry
- A schedule of when the doctor wants to see you for prescribed follow-up visits.

You will also be given your OPTIMIZER Mini Charger at this time and receive instruction in its proper use. Make sure you understand these instructions. Don't be afraid to ask any questions that you may have.

Your first follow-up appointment with your doctor will be scheduled for about one to two weeks after implant. Your doctor will examine your incisions, remove any stitches or butterfly closures.

7. FOLLOWING IMPLANTATION

It is important that you become actively involved in your own recovery by following your doctor's instructions carefully, including:

- Report any redness, swelling, or drainage from your incisions to your doctor.
- Avoid lifting heavy objects until instructed by your doctor.
- Walk, exercise, and bathe according to your doctor's instructions.
- Be sure to contact your doctor if you develop a fever that persists for more than two or three days.
- Ask your doctor any questions you may have about your device, heart rhythm, or medications. Be sure to take all medications as directed by your doctor.

- Don’t wear tight clothing that could irritate the skin over the device.
- Avoid rubbing the device or the surrounding chest area.
- If directed by your doctor, limit your arm movements that could affect the lead system.
- Avoid rough contact that could result in blows to the implant site. If you fall or are in an accident that results in a blow to the implant site, contact your doctor.
- Contact your doctor if you notice anything unexpected or unusual such as new symptoms.
- Inform your doctor if you plan long distance travel or if you plan to move to another city. Ask your doctor for a referral in the area.
- Your doctor may limit your driving, at least initially, to avoid putting undue strain on your wounds.
- If given a sling, wear it as directed to limit arm movement.
- Depending on level of physical exertion required by your job, your doctor may direct you to stay home and not return to work for a period of time. Ask your doctor about the timeline for returning to work.

8. LIVING WITH THE OPTIMIZER SMART IPG

8.1 General Expectations

You will be able to feel the OPTIMIZER Smart Pulse Generator beneath the skin. Normal body movement will cause no harm to it or the attached leads. However, it is important that you not try to move or turn the pulse generator. It has been implanted with a specific orientation to the skin to ensure proper communication with the OMNI II Programmer and your OPTIMIZER Mini Charger.

8.2 Effect on Your Activities

Once the wounds from your surgery are healed, you can expect to resume your normal activities, including sexual intimacy. Your implanted OPTIMIZER Smart Pulse Generator is unaffected by walking, bending over or other normal daily activities.

8.3 Medications

Prescription medications, taken as directed, have no effect upon the proper operation of your OPTIMIZER Smart IPG.

In general, the implantation of your OPTIMIZER Smart Pulse Generator should not require you to alter the use of any medication.

8.4 How Other Devices May Affect Your OPTIMIZER Smart IPG

In general, household appliances in good repair and personal communication devices held 10 in or more from the IPG will have no effect upon your OPTIMIZER Smart IPG. However, you should be cautious when in the vicinity of devices that generate electrical or magnetic fields. For example, interference may occur from some electric razors, electric power tools, and electrical ignition systems, including those used on gasoline-powered equipment. In general, gasoline-powered equipment may be operated provided that protective hoods, shrouds and other shielding are not removed.

Avoid leaning over an open automobile engine compartment, as the alternator generates a very strong electromagnetic field.

You should not use or come in close proximity to induction stoves as it may cause interference with your OPTIMIZER Smart IPG.

Any such interference detected by the OPTIMIZER Smart IPG may cause false detection of your heart beat and improper timing of CCM signal delivery.

You should avoid getting too close to equipment or devices that contain strong magnets (e.g. stereo speakers). The OPTIMIZER Smart IPG contains a magnetic switch that, when activated by placing a strong magnet near the device for 3-5 seconds, will turn your device off. If this occurs by accident, your doctor must use the OMNI II Programmer to turn your OPTIMIZER Smart IPG on again. Since the OPTIMIZER Smart IPG is not a life-sustaining device, you are unlikely to be placed at risk by such an event.

Always seek medical advice before entering an area posted with a warning for pacemaker patients (or other medical implantable devices) or where there is industrial machinery or radio transmitters, including ham radios and mobile radios.

Always inform your attending doctor that you have an implanted OPTIMIZER Smart Pulse Generator before:

- You undergo surgery where electrocautery is going to be used;
- You have a procedure involving RF Ablation;
- You have medical diathermy;
- You undergo cardioversion;
- You undergo therapeutic radiation, nuclear magnetic resonance (NMR), magnetic resonance imaging (MRI), therapeutic ultrasound, or lithotripsy;

Caution:

- The OPTIMIZER Smart IPG should either be deactivated or closely monitored prior to and during any medical treatment in which electrical current is passed through the body.
- The OPTIMIZER Smart IPG should not be directly exposed to therapeutic ultrasound or to therapeutic radiation. This type of exposure may damage the device that may not be immediately detectable.

Store anti-theft systems and airport security screening systems normally will not harm your OPTIMIZER Smart IPG. However, don't linger around the equipment. Before going through airport security screening, it is recommended that you show your OPTIMIZER Smart ID card to security personnel for review.

8.5 The Importance of Your Patient ID Card

Each OPTIMIZER Smart Implantable Pulse Generator is supplied with a Patient ID card. This will be provided to you by your doctor following the implantation of your device. In addition, the information he provides to Impulse Dynamics allows the company to register you as a recipient of a device it manufactured so that your doctor may be properly and completely notified in the event a product advisory is issued.

It is important that you carry your Patient ID card and a list of your medications with you at all times. In the event of a medical emergency, the Patient ID card contains information of great importance to an attending physician and will assist in expediting any emergency medical care you may require.

In addition, it is important to notify all of your health care providers that you have had an OPTIMIZER Smart device implanted. As such the next time you visit your doctor or dentist, show them your Patient ID card so that a copy of it may be made for their records.

9. OPTIMIZER MINI CHARGER

The OPTIMIZER Mini Charger is a charger powered by a rechargeable battery and is used to charge the battery of the OPTIMIZER Smart IPG. The device is supplied with a Battery Charger (Cell-Con Battery Charger; Input: 100–240VAC, 50-60Hz, 0.3A; Output: 8.4V, 1.3A) to recharge the internal battery.

Warning: If the OPTIMIZER Smart IPG is not charged regularly, it will shut down when the battery becomes depleted!

Caution: The OPTIMIZER Mini Charger is subject to, and/or could be the cause of, potential electromagnetic or other interference from other electrical devices operated in the vicinity. Portable and mobile RF equipment is especially prone to impair the normal function of the charger.

9.1 OPTIMIZER Mini Charger System Components

The OPTIMIZER Mini Charger System consists of following components:

- OPTIMIZER Mini Charger (with attached charging wand) – used to charge the OPTIMIZER Smart IPG.
- Battery Charger (with Plug Adapters) – used to charge the internal battery of the OPTIMIZER Mini Charger and isolate it from the mains.
- Carrying Case – used to transport the OPTIMIZER Mini Charger system
- Patient belt – (optional) used to hold the charger around your waist while the OPTIMIZER Smart IPG is being charged.

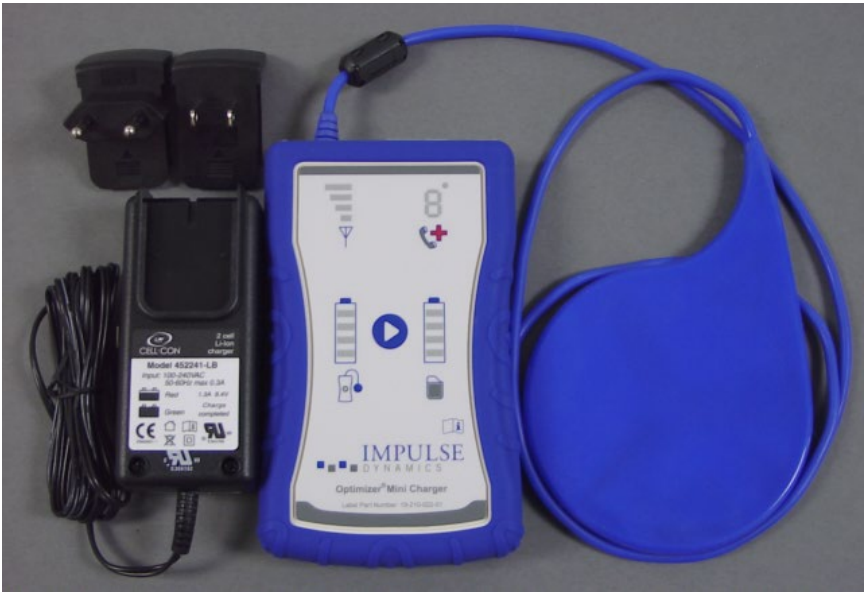

Figure 3: OPTIMIZER Mini Charger with Battery Charger and Plug Adapters

9.2 OPTIMIZER Mini Charger Features

Your OPTIMIZER Mini Charger has several features which have the following significance:

- **IPG-Charger Coupling Signal Strength Indicator:** Bar graph display depicting connection between the charger and the OPTIMIZER Smart IPG
- **"Call Doctor" Indicator:** 7-segment LED display for numerical codes
- **Charger Battery Status Indicator:** Bar graph display depicting the state-of-charge of the OPTIMIZER Mini Charger battery
- **Start Button:** Start button for the OPTIMIZER Mini Charger
- **IPG Battery Status Indicator:** Bar graph display depicting the current state-of-charge of the OPTIMIZER Smart IPG battery

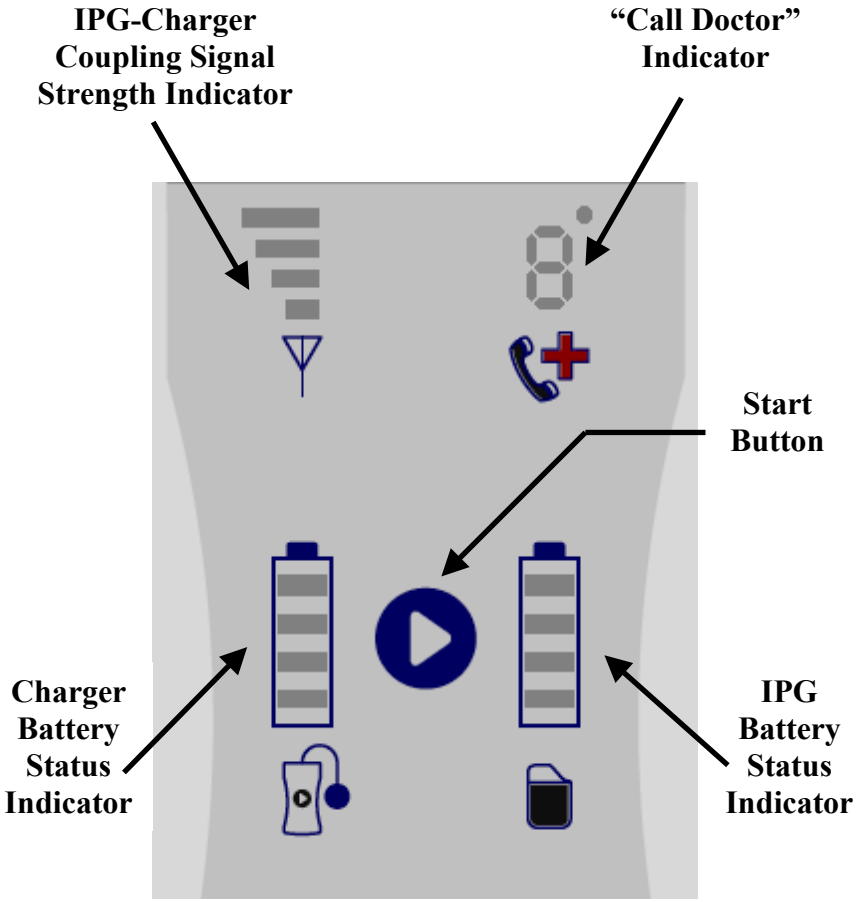

Figure 4: OPTIMIZER Mini Charger Features

9.3 Operating Your OPTIMIZER Mini Charger

The OPTIMIZER Mini Charger is used to charge the battery of the OPTIMIZER Smart IPG. It is especially designed to properly control the charging process with minimal intervention and to ensure your safety.

Warning: The OPTIMIZER Mini Charger shall not be used on board aircraft. The OPTIMIZER Mini Charger shall not be used on board a ship without prior consent from the ship's crew.

Note: Consult local regulations if using the Mini Charger outside of the country where it was purchased.

Warning: Do not attempt to connect any equipment to the I/O port of the OPTIMIZER Mini Charger. This port is solely for factory or service personnel use.

Using the OPTIMIZER Mini Charger to charge your OPTIMIZER Smart IPG consists of 2 steps:

- Charging of the internal battery of the OPTIMIZER Mini Charger
- Charging of the battery of your OPTIMIZER Smart IPG

Note: Charging the internal battery of your OPTIMIZER Mini Charger and charging your OPTIMIZER Smart IPG CANNOT be done at the same time. You FIRST have to charge the battery of your OPTIMIZER Mini Charger and THEN you can charge your OPTIMIZER Smart IPG.

1. Plug the DC output connector of the Battery Charger into the power input connector located on the top left of the charger and then plug in the Battery Charger to the mains to begin charging the internal battery of the charger.

Note: Inspect the Battery Charger for any damage before each use. Contact your physician if a replacement Battery Charger is needed.

Warning: Only use the Battery Charger provided with the OPTIMIZER Mini Charger to charge the battery in the OPTIMIZER Mini Charger.

Caution: Do not touch the DC contacts of the Battery Charger. However it poses no significant risk if inadvertent contact is made.

2. The **Charger Battery Status Indicator** will show the current state-of-charge of the charger's internal battery. As this charging process is fully automatic, you can for example recharge the battery over night.
3. When all 4 bars of the **Charger Battery Status Indicator** are continuously illuminated, the battery in the OPTIMIZER Mini Charger is fully charged.
4. Disconnect the Battery Charger from the OPTIMIZER Mini Charger. The OPTIMIZER Mini Charger can now be used to charge OPTIMIZER Smart IPG.

Note: The OPTIMIZER Mini Charger can not be used to charge the OPTIMIZER Smart IPG until the Battery Charger is disconnected from the charger.

5. To charge your OPTIMIZER Smart IPG, first assume a stationary, comfortable position, ideally reclining at a 45° angle (sofa, armchair). The accessory belt may be used to hold the charger in a convenient position while charging.
6. Position the charging wand directly over your OPTIMIZER Smart IPG implant site. If you wish, you may to drape the wand cable around your neck so that the charging wand rests on your chest over your clothes.

Note: The charger should not be operated close to other electronic equipment. If sufficient spatial separation cannot be maintained, the charger needs to be monitored to ensure normal function.

7. Start the charging process by pressing the **Start Button** and holding it down for about 3-4 seconds.
8. Slowly move the charging wand over the implant site while observing the **IPG-Charger Coupling Signal Strength Indicator**, which depicts the connection status between OPTIMIZER Smart IPG and charging wand. Reposition the charging wand as needed until the most number of bars are illuminated on the **IPG-Charger Coupling Signal Strength Indicator**. The charger will automatically search for the location of the strongest signal from the OPTIMIZER Smart IPG.
9. Once the charging wand has established a link with the OPTIMIZER Smart IPG, the OPTIMIZER Mini Charger will begin the charging process.

Note: If the charging wand positioning is poor or if the charging wand has been displaced, the OPTIMIZER Mini Charger will display a decreasing number of illuminated bars on the **IPG-Charger Coupling Signal Strength Indicator**. In addition, you will hear an audio signal sounding approximately once per second. If this occurs, please move the charging wand back into the correct position.

Note: If the position of the charging wand with respect to the OPTIMIZER Smart IPG remains poor, the charging process is automatically suspended. When this occurs, a new charging session must be initiated by pressing the **Start Button** again.

10. The **IPG Battery Status Indicator** depicts how the charging process of your OPTIMIZER Smart IPG is progressing.

Note: Aim to fully recharge the device during the charging session. Charging the battery of the OPTIMIZER Smart IPG may take longer than one hour if the battery is significantly depleted. If the device cannot be completely recharged in one session, repeat the charging process. If the battery is severely depleted, several daily sessions may be required to fully charge the OPTIMIZER Smart IPG.

11. When the battery of the OPTIMIZER Smart IPG is completely charged, a long audible signal will sound and all 4 bars of the **IPG Battery Status Indicator** will be illuminated. The charging process will then be automatically terminated and the charger will shut off.

To terminate a charging session before it has been completed, remove the charging wand from the implant site. The charger will then automatically halt the charging process. Alternatively, you may shut down the charger by pressing and holding the **Start Button** once again.

The charger monitors the temperature of your implanted OPTIMIZER Smart IPG so that its temperature rises only minimally. If you wish to resume the charging session after a pause, please wait for approximately 10 minutes before initiating a new charging session to allow the temperature of your implanted OPTIMIZER Smart IPG to return to normal.

9.4 Frequency of Charging Sessions

Optimal performance of the rechargeable battery in the OPTIMIZER Smart IPG can only be ensured if the battery is fully recharged on a weekly basis. It is not important which day or time you choose to charge your OPTIMIZER Smart IPG, but it is recommended that you should not let more than one week pass between the charge sessions.

If the charge level of the OPTIMIZER Smart IPG battery drops below a certain threshold, therapy delivery is automatically suspended. If this occurs, your OPTIMIZER Smart IPG battery will need to be recharged before it resumes delivering therapy. Once the charging session has been completed, your OPTIMIZER Smart IPG will automatically resume therapy delivery with its previously programmed parameters. You should always conduct a recharge session whenever you are not feeling well to ensure that your device is working. Contact your doctor immediately if you are unable to recharge the device.

9.5 Numerical Codes

The OPTIMIZER Mini Charger was designed to provide you with certain warnings regarding the status of the OPTIMIZER Smart IPG as well as the OPTIMIZER Mini Charger.

If the charger detects a situation that requires action, a code digit will appear on the **"Call Doctor" Indicator** of the OPTIMIZER Mini Charger

If a numerical code appears, take note of the numeral code that is displayed and then use the information listed in this section to determine your next course of action.

- For numerical codes "0", "1", "2", "3", "4", and "8", please contact your doctor to schedule a prompt OPTIMIZER Smart IPG check-up.

Note: Remember you should always conduct a recharge session when you are not feeling well to ensure that your device is working.

- When Numerical Code 5 is displayed, it means that the charger has detected a temporary issue regarding body temperature and has terminated the charging process. Please repeat the charging process at a later time. If this numerical code is displayed repeatedly by the charger over the course of several days, please contact your doctor to schedule a prompt OPTIMIZER Smart IPG check-up.
- When Numerical Code 6 is displayed, it means that the OPTIMIZER Mini Charger has detected an internal error and discontinued the charging process. Please contact your doctor to obtain a replacement charger.
- When Numerical Code 7 is displayed, it means that the OPTIMIZER Mini Charger has determined that the implanted device is not an OPTIMIZER Smart IPG and has terminated the charging process. Please contact your doctor to obtain an appropriate charger.

9.6 OPTIMIZER Mini Charger Cleaning

Warning: Always unplug the Battery Charger from the OPTIMIZER Mini Charger prior to cleaning.

The exterior surface of the OPTIMIZER Mini Charger should be cleaned as needed with only a soft cloth simply **dampened** with water (wrung out completely).

Caution: DO NOT use solvents or cleaning cloths impregnated with chemical cleaning agents.

Warning: DO NOT attempt to clean the electrical connectors of the OPTIMIZER Mini Charger.

Warning: DO NOT submerge any part of the OPTIMIZER Mini Charger in water. Damage to the unit may result.

9.7 OPTIMIZER Mini Charger Maintenance

The OPTIMIZER Mini Charger does not contain any user serviceable parts. If the OPTIMIZER Mini Charger is not operational, please contact your doctor to obtain a replacement charger.

Warning: No modification of this equipment is allowed.

The battery inside the OPTIMIZER Mini Charger is expected to have a service life of 5 years. If your OPTIMIZER Mini Charger is unable to fully charge your OPTIMIZER Smart IPG after the charger battery has been fully charged, please contact your doctor to obtain a replacement charger.

9.8 OPTIMIZER Mini Charger Storage and Handling

Once you receive your OPTIMIZER Mini Charger it should not be exposed to excessively hot or cold conditions. Store the OPTIMIZER Mini Charger in a cool, dry place. Do not to leave the devices in your car or outdoors for extended periods of time. The sensitive electronics can be damaged by temperature extremes, particularly high heat. For proper operation, the OPTIMIZER Mini Charger should not be used if the ambient temperature is above 80°F. If necessary, move to a cool location where the ambient temperature is below 80°F prior to initiating a charging session.

In addition, your OPTIMIZER Mini Charger should be kept in normal environmental conditions: 1) relative humidity between 20% and 75%; and 2) atmospheric pressure between 700 hPa and 1060 hPa.

9.9 OPTIMIZER Mini Charger Disposal

If the OPTIMIZER Mini Charger is no longer needed, you may return it to your doctor's office.

Warning: DO NOT discard the OPTIMIZER Mini Charger in the trash. The OPTIMIZER Mini Charger contains Lithium batteries as well as non-RoHS components. If disposal of the OPTIMIZER Mini Charger is necessary, properly dispose of it in accordance with local regulations governing the disposal of such material.

10. REPLACEMENT OF YOUR OPTIMIZER SMART IPG

Your OPTIMIZER Smart Pulse Generator contains a rechargeable battery and the need to replace the device because the battery is unable to hold a charge is **not** expected within the warranty period as long as it is charged on a weekly basis. Implantable devices which use **non-rechargeable** batteries always need to be replaced when their battery's useable charge capacity has been depleted. Nevertheless, there still remain reasons why the device or one of its leads may not function in accord with expectations. In that event, your doctor will explain the reason(s) to you and schedule you for a replacement surgery.

This procedure is typically more limited in scope and may not require you to stay overnight in the hospital. In general, the post-surgical care associated with replacement surgery is no different than what you experienced during your initial surgery.

11. CLINICAL SUMMARY

OPTIMIZER® System in Subjects with Moderate-to-Severe Heart Failure with Ejection Fraction between 25% and 45%: FIX-HF-5C Study[3]

This study was designed to show that that cardiac contractility modulation (CCM) improved exercise tolerance (ET) and quality of life in patients with ejection fractions between 25% and 45%. CCM therapy for New York Heart Association (NYHA) functional class III and IV heart failure (HF) patients consists of nonexcitatory electrical signals delivered to the heart during the time when the heart does not contract. A total of 160 patients with NYHA functional class III or IV symptoms, QRS duration <130 ms, and ejection fraction greater than or equal to 25% and less than or equal to 45% were randomized to continued medical therapy (control, n = 86) or CCM (treatment, n = 74) for 24 weeks. Peak oxygen consumption (primary endpoint), Minnesota Living With Heart Failure questionnaire (Quality of Life), NYHA functional class, and 6-min hall walk were measured at baseline and at 12 and 24 weeks. Safety was assessed by the percentage of patients free of device-related adverse events with a pre-specified lower bound of 70%. The difference in peak oxygen consumption between groups was 0.84ml O2/kg/min (CI: 0.12, 1.55), satisfying the primary endpoint. Minnesota Living With Heart Failure questionnaire ($p < 0.001$), NYHA functional class ($p < 0.001$), and 6-min hall walk ($p = 0.02$) were all better in the treatment versus control group. Method of imputation affected the results and the VO2 estimate varied from 0.48 to 0.84 depending on method. The treatment effect can be seen to be a result of a significant decrease in VO2 for the control group with relatively little increase in VO2 for the treatment group. There

[3]Abraham, W. T., Kuck, K., Goldsmith, R. L., Lindenfeld, J., Reddy, V. Y., Carson, P. E., Hasenfuß, G. (2018). A Randomized Controlled Trial to Evaluate the Safety and Efficacy of Cardiac Contractility Modulation.

were 7 device-related events, yielding a lower bound of 80% of patients free of events, satisfying the primary safety endpoint. The composite of cardiovascular death and HF hospitalizations was reduced from 10.8% to 2.9% (p = 0.048).

FIX-HF-5C2: Evaluation of the Safety and Efficacy of the 2-lead OPTIMIZER® Smart System in Subjects with Moderate-to-Severe Heart Failure with Ejection Fraction between 25% and 45%

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. This study was designed to show that cardiac contractility modulation (CCM) therapy delivered by the 2-Lead OPTIMIZER Smart device could improve peak VO2 (exercise tolerance) while maintaining effective CCM delivery. Sixty patients were enrolled and implanted with the OPTIMIZER Smart System 2-Lead configuration.

The primary effectiveness endpoint was an improvement in exercise tolerance as measured by peak VO_2 obtained on cardiopulmonary exercise testing (CPX). 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. 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.

After implantation of the 2-Lead OPTIMIZER Smart, 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, exercise test, NYHA assessment, and an assessment of adverse events. Data collection for assessment of the study endpoints was concluded with the 24-week visit.

Peak VO2 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.

Mean, SD of Peak VO2 by Group and Time

	Mean		Standard Deviation	
	Control	**Device**	**Control**	**Device**
Baseline	15.36	15.01	2.81	2.94
12 Weeks	14.59	16.01	4.29	3.34
24 Weeks	14.34	16.22	4.69	3.09

In total, we observed an improvement in peak VO2 for the device subjects in the FIX-HF-5C2 study which was not dependent on a decrease in VO2 for the control group. The total CCM delivery at 24 weeks was equivalent between the OPTIMIZER groups of the FIX-HF-5C2 and FIX-HF-5C studies. Both the primary and secondary effectiveness endpoints of the study were met.

The complication rate in FIX-HF-5C2 study ITT group was 1.7% (1/60). The rate of complications in the FIX-HF-5C2 study was nominally lower than seen in the previous study although not statistically significant. The primary safety endpoint of the FIX-HF-5C2 study was met and that delivery of CCM through a 2-Lead device was 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.

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.

12. FREQUENTLY ASKED QUESTIONS

1. Why has my doctor recommended that I have an OPTIMIZER Smart Pulse Generator implanted?

Your doctor has diagnosed your condition as a form of heart failure that may be treated with an OPTIMIZER Smart Implantable Pulse Generator. To date you have not been successfully treated using standard medical treatments. Therefore, your doctor believes that you are a good candidate for implantation of an OPTIMIZER Smart IPG as a means of treating your condition.

2. What does the OPTIMIZER Smart IPG do?

The OPTIMIZER Smart IPG monitors your heart rhythm and delivers cardiac contractility modulation signals at a very specific time when the heart contracts. These signals are intended to increase the strength of each contraction, thus improving your heart failure symptoms. The OPTIMIZER Smart IPG is programmed to your specific requirements by your doctor using an external programmer and a wand placed over your pulse generator.

3. Will I need to be put to sleep (general anesthesia) during the implant procedure?

The use of general anesthesia versus local anesthesia with mild sedation for the implant procedure is dependent on the preferences of the particular implant facility. To find out which method of anesthesia will be used for your implant procedure, consult your doctor.

4. What are the risks associated with this type of surgery?

There is a risk of infection, as is the case with any invasive procedure. There is a risk that the heart muscle may be perforated (a hole is made in the heart wall) or other complications, some of which may require follow-up surgery. A more detailed list of Potential Complications may be found in Section 5.

5. How long will I need to be in the hospital?

Typically, you will arrive at the hospital the day of the procedure, and then depending on the facility, go home that same day or spend the night and then go home the next day.

6. Will I still be able to do the things I do now?

Yes, unless you are involved in contact sports or other activities or have an accident that can damage your implanted system or interfere with its operation. Your doctor will discuss this matter with you in detail.

7. Will the OPTIMIZER Smart IPG ever need to be replaced?

Your OPTIMIZER Smart IPG is powered by a rechargeable battery. Your doctor will show you how to recharge your device and tell you how often to recharge. Your doctor will need to assess the condition of the battery during your routine checkup visits. In order to help facilitate this battery assessment, please fully charge your OPTIMIZER Smart IPG 7 days before your doctor visit.

In addition, there is a risk that a problem will develop with a component or a lead necessitating replacement or re-operation. Since the OPTIMIZER Smart IPG is not a life-sustaining device, you are unlikely to be placed at risk if your device should not operate as expected.

IMPORTANT INFORMATION:

Electrophysiologist:	
Address:	
City:	
Country:	Postal Code:
Telephone No.:	

Cardiologist:	
Address:	
City:	
Country:	Postal Code:
Telephone No.:	

Hospital:	
Address:	
City:	
Country:	Postal Code:
Telephone No.:	

Medications:

OPTIMIZER Smart Implantable Pulse Generator

Model No.:

Serial No.:

Lead 1 Model No.:	S/N
Lead 2 Model No.:	S/N

NOTES: