Description of the EnteroMedics "RF2 Maestro System" for the Treatment of Obesity

Introduction

The Maestro System treats obesity by applying a high-frequency electrical current to the vagus nerve to render it unable to propagate a signal. Both signals from the brain (to the digestive tract) and toward the brain (from the digestive tract) are blocked by the application of short, biphasic, charge-balanced electrical pulses at a high pulse rate (typically, at least 1000 pulses per second). The electrodes through which the current is delivered are attached to the two branches of the vagus nerve below the diaphragm. The physiological effects produced by the blocking of the vagus nerve are expected to result in significant weight loss.

Since obesity is a major health problem in the United States, the unique therapy offered by the EnteroMedics Maestro System is expected to be beneficial to a very great number of people. EnteroMedics is therefore eager to expeditiously prove the efficacy and safety of its therapy by conducting a clinical trial of its system in the United States. This is a necessary step toward obtaining FDA approval.

System Components and Functions

The Maestro system is depicted schematically in Figure 1 below:

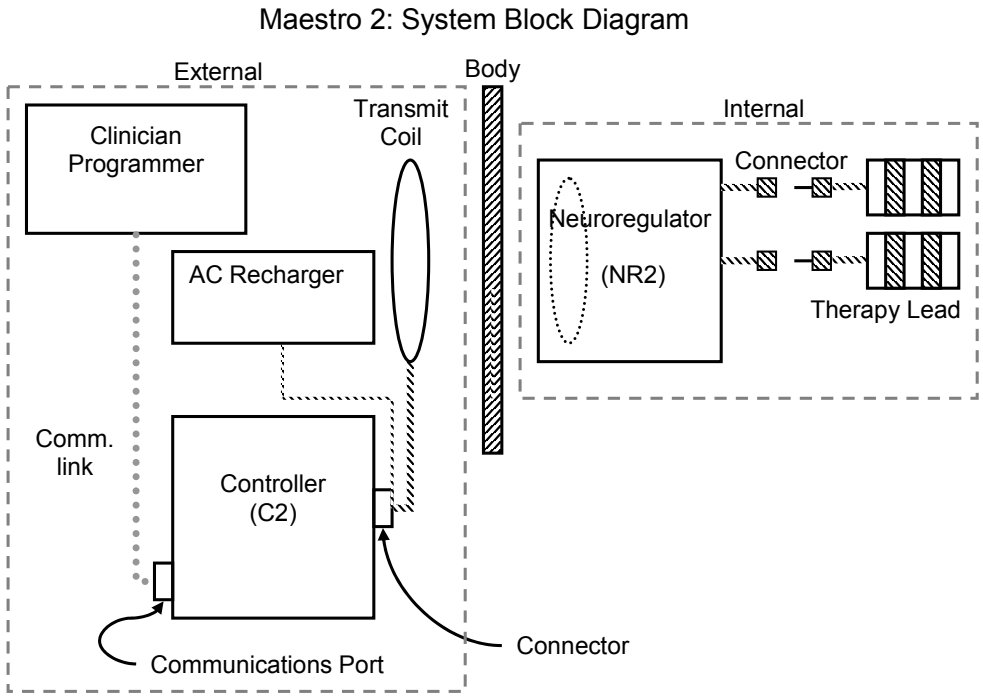

Figure 1: Block diagram of the RF-2 Maestro System

The functions of each of the system components are presented below:

- The implantable Neuroregulator (NR2) produces electrical pulses that are delivered to the vagus nerve. The NR2 also receives command signals from the external Controller and uploads data to the Controller. The NR2 is powered by RF radiated by the transmit coil and picked up by a receiving antenna on the NR2. The received RF power is used to energize the internal electronics of the NR2.
- The Maestro Controller (C2), which is worn externally by the patient, provides the electrical excitation of the transmit coil and controls the delivery of therapy by the NR2. In addition, it serves as an interface for communications between the NR2 and the Clinician Programmer. A rechargeable battery is used to power the Controller. For safety reasons, each C2 is paired with a specific NR2 and will only control that specific NR2.
- The Transmit Coil serves to transmit RF through the patient's skin from the Controller to power the Neuroregulator. It also handles bi-directional RF communications between the Controller and the Neuroregulator. Transmit coils are available in a clinician version and a patient version.
- The Clinician Programmer (a laptop computer with special software) enables the clinician to program the Controller with the treatment schedule and the amplitude and duration of the current pulses to be delivered by the NR2.

System Operation

The Neuroregulator receives power from the transmit coil at an ISM frequency of 6.78 MHz. The Neuroregulator operates according to the physician-programmed daily treatment schedule. If desired, a different schedule can be programmed for each day of the week. For example, the physician may program the device to deliver therapy between 7:00 am and 9:00 pm Monday through Friday, and 9:00 am to 11:00 pm on Saturday and Sunday. Typically, a patient's Controller is programmed to deliver between 12 and 16 hours of therapy each day. No therapy is delivered during the patient's normal sleeping hours.

In practice, each morning the patient positions the transmit coil directly over the implanted Neuroregulator and attaches the coil to the skin (typically with an adhesive film). When the transmit coil is plugged into the Controller, it is energized by the Controller according to the treatment schedule programmed for that day of the week. The patient carries the Controller in a belt-attached holster or in a "fanny pack." At the end of the day, the patient removes the transmit coil from his skin and disconnects it from the Controller. The patient is expected to recharge the Controller battery every night by plugging in the AC recharger into a wall outlet.

During the programmed treatment hours, therapy is delivered as a series of ON / OFF cycles. For example, therapy may be turned on for 5 minutes, turned off for 5 minutes, turned on again for 5 minutes, etc., for the programmed duration that day. For clinical reasons, this ON/ OFF cycle never exceeds a 50% duty cycle (i.e., the OFF time is either greater than or equal to the ON time).

During therapy delivery, the Controller maintains bi-directional communication with the implanted Neuroregulator as described below. Such communications are needed to ensure that therapy is delivered safely and in accordance with the programmed treatment schedule. There are no communications outside of the programmed therapy delivery hours.

Communication from the external Controller to the implanted Neuroregulator is by modulation of the same ISM band 6.78 MHz carrier that delivers power to the Neuroregulator. The carrier is amplitude modulated by a superimposed square wave pattern that encodes information as a bit stream. The rate of modulation is 14400 bits/second, and the amplitude of the modulation is approximately 30% of the carrier amplitude. Such communications (from Controller to Neuroregulator) occur at the beginning of each ON/OFF cycle (i.e., approximately once every 10 minutes) during the hours of therapy delivery. The duration of each communication is approximately 25 ms. Thus, during the hours of therapy delivery, the duty cycle of these communications is approximately 0.004%.

Communication in the other direction, from the implanted Neuroregulator to the external Controller, is by "load key shifting," in which the Neuroregulator presents a varying load to the transmit coil. This works as though the transmit coil were the primary winding and the Neuroregulator's receive coil were the secondary winding of a transformer. Variations in the load on the secondary side appear as similarly-timed load variations on the primary side. Once again, the load variations are encoded as a bit stream carrying information at 14400 bits/second. Communications from the Neuroregulator to the Controller occur only during the ON periods, every 200 ms with a duration of approximately 12.5 ms. Thus, during the hours of therapy delivery, the duty cycle of these communications is approximately 3.1%.

Purpose of the Clinical Trial

EnteroMedics wishes to evaluate the safety and efficacy of the Maestro therapy, as delivered by the RF-2 Maestro system, in a clinical trial involving approximately 260patients in the U.S. These patients will be enrolled in the trial at approximately thirteen centers distributed throughout the continental United States. Thus, an average of approximately 20 patients will be enrolled at each trial center. Each center is a well-recognized hospital at which a skilled team of surgeons and follow-up clinicians will perform the implant surgery and then follow up the patients for a duration of 12 months.

After implantation, patients will be discharged from the hospital and will be free to go home with the device. They will wear the device each day of the 12-month follow-up period while going about their normal daily activities. Patients must return to the hospital at designated intervals for follow-up evaluations by the clinicians.

Need for an Experimental License

As described above, the current generation of the Maestro system is an RF-powered system. The implanted Neuroregulator has no internal power source. Accordingly, the transmit coil (which is attached to the skin) must transfer sufficient power to energize the implanted electronics and allow for the delivery of therapy pulses. The power transfer, considered alone, complies with the Part 18 rules. However, the carrier is modulated to permit communication between the Controller and the Neuroregulator, and the radiated emissions exceed the limits of Part 15. (All spurious emissions outside the operating bandwidth comply with Section 15.209.)

This Experimental License is requested to permit EnteroMedics Inc. to conduct its proposed clinical trial at approximately thirteen hospital sites in the United States (a necessary step to obtain FDA approval of the Maestro therapy). Each patient will participate for 12 months. Allowing 6 months to achieve enrollment of the full complement of 260 patients, with an overall uncertainty covering all aspects of the study of about 6 months, the total duration of the clinical trial is estimated to be 18 to 24 months. We request an Experimental License on a state-wide basis since the patients wearing the device are free to move about in the course of their daily activities.

The risk of harmful interference, even with state-wide licensing, should be extraordinarily low, considering both the low power involved (65 microwatts) and the use of a frequency that is centered in an ISM band and thus an unlikely choice for other users' critical communications.

The engineering development path adopted by EnteroMedics favored the RF-powered approach because it allowed for a simpler and smaller implanted device as well as a quicker pathway to establishing the safety and efficacy of the therapy. Concurrently with this study, EnteroMedics is developing a version of the Neuroregulator and Controller that will comply in all respects with the Commission's Rules.