Using neurostimulation for gastric electrical stimulation

Enterra® Therapy

Information for prescribers

Rx only
Humanitarian Device: Authorized by Federal (U.S.A.) Law for use in treatment of chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology in patients aged 18 to 70 years. The effectiveness of this device for this use has not been demonstrated.

enterra medical™

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Information available for the system:

Product manuals, such as programming guides, recharging guides, and implant manuals provide device descriptions, package contents, device specifications, product-specific warnings and precautions, and instructions for use.

The clinical summary provides information about the clinical study results for the neurostimulation system.

Indications

The Enterra® Therapy System for Gastric Electrical Stimulation (GES) is indicated for the treatment of chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology in patients aged 18 to 70 years.

Humanitarian Device: Authorized by Federal (U.S.A.) Law for use in treatment of chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology. The effectiveness of this device for this use has not been demonstrated.

Contraindications

Diathermy - Do not use shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy (all now referred to as diathermy) on patients implanted with a neurostimulation system. Energy from diathermy can be transferred through the implanted system and can cause tissue damage at the location of the implanted electrodes, resulting in severe injury or death. Refer to **Appendix B: Electromagnetic interference** on page 45 for more information.

The Enterra Therapy System is MR conditional - Patients with the Enterra System can safely have MRI examinations of some body parts under certain conditions. See the MRI Guidelines for Physicians manual for further information.

Warnings

Bowel obstruction/perforation - The lead can become entangled with or erode into the bowel, which can result in bowel obstruction and perforation. Either may lead to life threatening intra-abdominal infections and may require laparotomy, bowel resection, and system revision. Avoid excess lead slack in the abdominal cavity. Post implant, consider lead entanglement or erosion as a possible etiology in patients with bowel obstruction symptoms.

Gastric erosion/perforation - The lead(s) can erode through the stomach wall and result in gastric perforation with possible lead migration into the lumen of the intestine. Patients may experience high lead impedance measurements, decreased therapeutic effect, increased nausea, vomiting, abdominal pain, life threatening intra-abdominal infections and gastrointestinal obstruction that may require laparotomy and/or system revision or removal. Post implant, consider gastric perforation as a possible etiology for patients exhibiting these symptoms.

Electromagnetic Interference (EMI) - Electromagnetic interference is a field of energy generated by equipment found in the home, work, medical or public environments that is strong enough to interfere with neurostimulator function. Neurostimulators include features that provide protection from electromagnetic interference. Most electrical devices and magnets encountered in a normal day are unlikely to affect the operation of a neurostimulator. However, sources of strong electromagnetic interference can result in the following:

- **Serious patient injury or death,** resulting from heating of the implanted components of the neurostimulation system and damage to surrounding tissue.
- **System damage,** resulting in a loss of or change in symptom control and requiring surgical replacement.
- **Operational changes to the neurostimulator,** causing it to turn on or off (particularly in neurostimulators enabled for magnet use), or to reset to Power-on-Reset (POR) settings, resulting in loss of stimulation, return of symptoms, and in the case of POR, potentially requiring reprogramming by a clinician.

- **Unexpected changes in stimulation,** causing a momentary increase in stimulation or intermittent stimulation, which some patients have described as a jolting or shocking sensation. Although the unexpected change in stimulation may feel uncomfortable, it does not damage the device. In rare cases, as a result of the unexpected change in stimulation, patients have fallen down and been injured.

Refer to **Table 1** (page 8) and **Appendix C: Electromagnetic compatibility declaration** on page 57 for information on sources of EMI, the effect of EMI on the patient and the neurostimulation system, and instructions on how to reduce the risk from EMI.

For information about the effects of EMI on programming, refer to **Telemetry signal disruption from EMI** on page 17.

Warnings

Table 1. Potential effects of EMI from devices or procedures

Device or procedure	Serious patient injury	Device damage	Momentary increase in stimulation	Intermittent stimulation	For guidelines
Bone growth stimulators		X	X	X	Page53
CT scans			X		Page 47
Defibrillation/cardioversion	X	X	X	X	Page 47
Dental drills and ultrasonic probes		X			Page53
Diathermy, therapeutic	X	X		X	Page 45
Electrocautery	X	X			Page 48
Electrolysis		X		X	Page 53
Electromagnetic field devices: (e.g., arc welding, power stations)			X	X	Page 53
High-output ultrasonics		X			Page 49
Household items			X		Page 56
Laser procedures		X			Page 55
Lithotripsy		X			Page 49
Magnetic resonance imaging (MRI)	X	X	X	X	Page 5, Page 46
Psychotherapeutic procedures		X	X	X	Page 55
Radiation therapy		X			Page 55
Radio-frequency (RF) / microwave ablation	X	X		X	Page 50
Theft detector			X	X	Page 50
Therapeutic ultrasound	X	X		X	Page 45
Transcutaneous electrical nerve stimulation (TENS)			X		Page 55

Case damage - If the neurostimulator case is ruptured or pierced due to outside forces, severe burns could result from exposure to the battery chemicals.

Anticoagulation therapy - Patients on anticoagulation therapies may be at a greater risk for post-operative complications, such as hematomas.

Effects on other implanted devices

Neurostimulator interaction with implanted devices - When a patient's medical condition requires both a neurostimulator and an implanted device (e.g., pacemaker, defibrillator), clinicians involved with both devices (e.g., gastroenterologist, cardiologist, cardiac surgeon) should discuss the possible interactions between the devices before surgery. Defibrillation therapy from an implanted defibrillator may damage the neurostimulator. The electrical pulses from the neurostimulation system may interact with the sensing operation from a cardiac device and could result in an inappropriate response of the cardiac device. To minimize or prevent device damage or device interactions, take the following steps:

- Implant the devices on opposite sides of the body.
- Program the neurostimulator therapy output to a bipolar configuration.

- Consider using bipolar sensing on the cardiac device.
- Check for interactions.
- Careful programming and review of each system's performance is necessary to ensure safe cardiac system operation with effective gastric stimulation.

Programmer interaction with other implanted devices - When a patient has a neurostimulator and another active implanted device (e.g., pacemaker, defibrillator, neurostimulator), the Radio-Frequency (RF) signal used to program these devices may reset or reprogram the other device.

To verify that inadvertent programming did not occur, clinicians familiar with each device should check the programmed parameters of each device before the patient is discharged from the hospital and after each programming session of either device (or as soon as possible after these times).

Also, inform patients to contact their physician immediately if they experience symptoms that could be related to either device or to the medical condition treated by either device.

Precautions

Use in specific populations

Use in specific populations - The safety and effectiveness of this therapy have not been established for:

- Pregnancy, unborn fetus, or delivery.
- Pediatric use (patients under the age of 18).
- Patients over the age of 70.

Physician training

Implanting physicians - Implanting physicians should be experienced in laparoscopic procedures and should review the procedures described in the implant manual before surgery.

Prescribing physicians - Prescribing physicians should be experienced in the diagnosis and treatment of gastroparesis and should be familiar with using the neurostimulation system.

Packaging and sterilization

Component packaging - Do not implant a component if the following circumstances have occurred:

- The storage package has been pierced or altered because component sterility cannot be guaranteed, and infection may occur.
- The component shows signs of damage because the component may not function properly.
- The use-by date has expired because component sterility cannot be guaranteed and infection may occur; also, neurostimulator battery longevity may be reduced and may require early replacement.

Sterilization - Enterra Medical, Inc. has sterilized the package contents according to the process indicated on the package label before shipment. This device is for single use only and is not intended to be resterilized.

System implant

Compatibility, all components - Follow these guidelines when selecting system components:

- **Enterra Medical components:** For proper therapy, use only Enterra Medical Neuromodulation components that are compatible or specified in an intended use statement (if present).

Components are compatible when the following conditions are met:

- Components have the same indication.
- For implanted components, the contact spacing and the number of electrode contacts at the connections for the lead and neurostimulator are the same.

For each product, refer to the indication insert(s) and the shipping label artwork for this information.

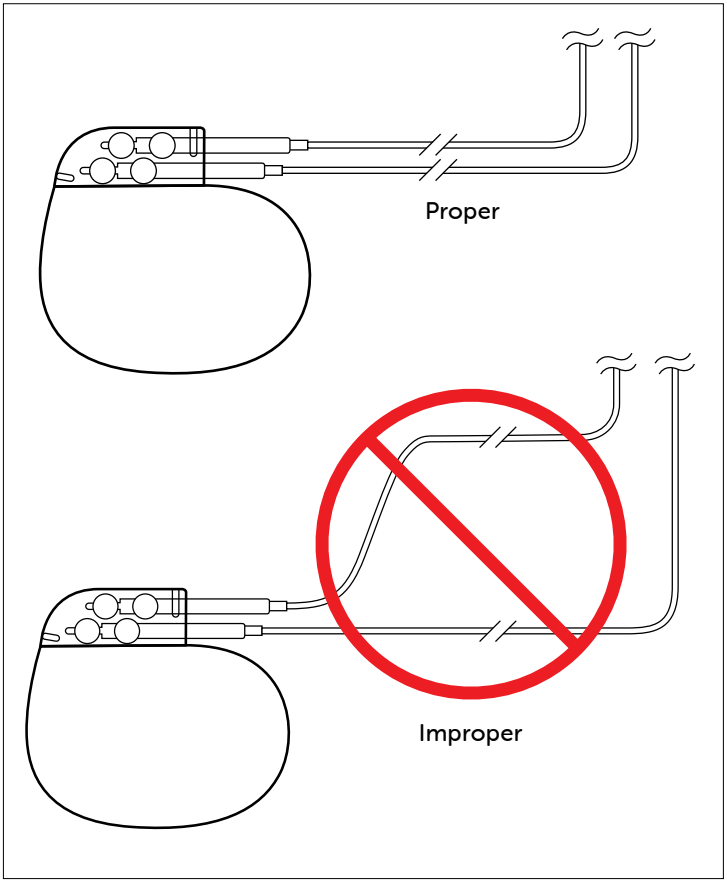
- **Non-Enterra Medical components:** No claims of safety or efficacy are made with regard to the compatibility of using non-Enterra Medical components with Enterra Medical components. Refer to the non-Enterra Medical documentation for information.

Component handling - Handle the implantable components of this system with extreme care. These components may be damaged by excessive traction or sharp instruments, which may result in intermittent or loss of stimulation, requiring surgical replacement.

Refer to the appropriate implant manual for additional instructions.

Routing for multiple leads - When multiple leads are implanted, route the leads so the area between them is minimized (**Figure 1**). If the leads are routed in a loop and the patient is exposed to some sources of electromagnetic interference (e.g., theft detectors), the patient may perceive a momentary increase in stimulation, which some patients have described as uncomfortable stimulation (jolting or shocking sensation).

Figure 1. Routing for multiple leads



Component Failures - The neurostimulation system may unexpectedly cease to function due to battery depletion or other causes. These events, which can include electrical shorts or open circuits, conductor (wire) fractures, and insulation breaches, cannot be predicted.

Patient detoxification - It is recommended that patients undergo detoxification from narcotics prior to implant so that the effects of stimulation can be properly assessed.

Clinician programming

Programmer interaction with a cochlear implant - When the patient has a cochlear implant, minimize or eliminate the potential for unintended audible clicks during telemetry by keeping the external portion of the cochlear system as far from the programming head as possible, or by turning off the cochlear implant during programming.

Programmer interaction with flammable atmospheres - The programmer is not certified for use in the presence of a flammable anesthetic mixture with air or with oxygen or nitrous oxide. The consequences of using the programmer near flammable atmospheres are unknown.

Telemetry signal disruption from EMI - Do not attempt telemetry near equipment that may generate Electromagnetic Interference (EMI). If EMI disrupts programming, move the programmer away from the likely source of EMI. Examples of sources of EMI are Magnetic Resonance Imaging (MRI), lithotripsy, computer monitors, cellular telephones, X ray equipment, and other monitoring equipment.

Patient activities

Activities requiring excessive twisting or stretching - Patients should avoid activities that may put undue stress on the implanted components of the neurostimulation system. Activities that include sudden, excessive, or repetitive bending, twisting, bouncing, or stretching can cause component fracture or dislodgement. Component fracture or dislodgement may result in loss of stimulation, intermittent stimulation, stimulation at the fracture site, and additional surgery to replace or reposition the component.

Component manipulation by patient (twiddler's syndrome) - Patients should avoid manipulating or rubbing the neurostimulation system through the skin. Manipulation may cause component damage, lead dislodgement, skin erosion, or stimulation at the implant site.

Scuba diving or hyperbaric chambers - Patients should not dive below 10 meters (33 feet) of water or enter hyperbaric chambers above 2.0 atmospheres absolute (ATA). Pressures below 10 meters (33 feet) of water (or above 2.0 ATA) could damage the neurostimulation system. Before diving or using a hyperbaric chamber, patients should discuss the effects of high pressure with their physician.

Skydiving, skiing, or hiking in the mountains - High altitudes should not affect the neurostimulator, however, the patient should consider the movements involved in any planned activity and take precaution to avoid putting undue stress on the implanted system.

Patients should be aware that during skydiving, the sudden jerking that occurs when the parachute opens may cause lead dislodgement or fractures, which may require surgery to repair or replace the lead.

Unexpected changes in stimulation - Electromagnetic interference, postural changes, and other activities may cause a perceived increase in stimulation, which some patients have described as uncomfortable stimulation (jolting or shocking sensation).

Hospital or medical environment

Effect on Electrocardiograms (ECGs) - Ensure the neurostimulator is programmed off prior to initiating an ECG. If the neurostimulator is on during an ECG, the ECG recording may be adversely affected, resulting in inaccurate ECG results. Inaccurate ECG results may lead to inappropriate treatment of the patient.

Refer to **Appendix B: Electromagnetic interference** on page 45 for information about other medical procedures that may interact with the neurostimulation system.

Individualization of treatment

Best results are achieved when the patient is fully informed about the therapy risks and benefits, surgical procedure, follow-up requirements, and self-care responsibilities.

Maximum benefits from the neurostimulation system require long-term postsurgical management.

Patient selection

Select patients carefully to ensure that:

- Their symptoms are of physiological origin.
- They are appropriate candidates for surgery.

Adverse events summary

In addition to the risks associated with surgery, the following adverse events may occur with implantation or use of a neurostimulation system for Enterra Therapy, which may necessitate reprogramming, medical treatment, or additional surgery:

- Lead impedance out of range
- Undesirable change in stimulation (described as a shocking, jolting, or tingling sensation), possibly related to cellular charges around the electrodes, shifts in electrode position, loose electrical connections, or lead fractures
- Loss of therapeutic effect
- Neurostimulator system ceases to function due to battery depletion, telemetry issues, or other causes
- Lead or neurostimulator erosion or migration
- Bowel obstruction, perforation, ileus, or necrosis
- Infections, including device/implant site infections, intra-abdominal infections, abscess, peritonitis, sepsis, urinary tract infections

- Stomach wall perforation
- Upper gastro-intestinal (GI) symptoms including nausea, vomiting, abdominal pain, discomfort, distention, or increased severity of gastroparesis symptoms
- Lower gastrointestinal (GI) symptoms including diarrhea and constipation
- Hemorrhage, hematoma, and possible GI complications resulting from the surgical procedure to implant the neurostimulator and leads
- Persistent pain at the neurostimulator site
- Extra-abdominal pain, bone-and joint-related pain
- Seroma at the neurostimulator site
- Allergenic or immune system response to implanted materials
- Stress incontinence
- Fever
- Feeding tube complications
- Dehydration
- Dysphagia
- Acute diabetic complications
- Cardiovascular renal related events
- Tissue damage

Patient Counseling Information

Physicians should provide patients with information about:

- The components of the neurostimulation system: lead and neurostimulator.
- The indications, contraindications, warnings, and precautions for a neurostimulation system.

Physicians should also instruct patients as follows:

- Always inform any health care personnel that they have an implanted neurostimulation system before any test or procedure is begun.
- Contact their physician if they notice any unusual symptoms or signs.

Component Disposal

When explanting a device (e.g., replacement, cessation of therapy, or postmortem), or when disposing of accessories, follow these guidelines:

- If possible, return the explanted device with completed paperwork to Enterra Medical, Inc. for analysis and disposal. See the back cover for the mailing address.
- To allow for device analysis, do not autoclave the device or expose the device to ultrasonic cleaners.

- Dispose of any unreturned components according to local environmental regulations; in some countries, explanting a battery-powered implantable device is mandatory.
  - Do not incinerate or cremate the neurostimulator. It may explode if subjected to these temperatures.

    Note: The implanted neurostimulator must be removed before cremation.
  - Do not reuse any implantable device or implantable accessory after exposure to body tissues or fluids because the functionality of the component cannot be guaranteed.

⚠ **Caution:** Follow appropriate biohazard controls for all explanted components or components coming into contact with bodily fluids. Only return such components to Enterra Medical, Inc. in the appropriate packaging supplied by Enterra Medical, Inc.

Appendix A: Enterra Therapy clinical studies

Patients with drug-refractory gastroparesis of diabetic or idiopathic etiologies were evaluated in the following clinical studies: the World Wide Anti-Vomiting Electrical Stimulation study (WAVESS), the WAVESS Compassionate Use study (WCU), and the Compassionate Use Electrical Stimulation study (CUESS).

World Wide Anti-Vomiting Electrical Stimulation Study (WAVESS)

The WAVESS study was a double-blind, randomized cross-over study that enrolled a total of 33 subjects. The study was designed to collect both safety and effectiveness information.

WAVESS study objective

The primary endpoint of the study was a reduction in vomiting frequency, as measured by patient diaries. The treatment was considered successful if a reduction in vomiting frequency by at least 80% was observed during the cross-over period of the study with the ON-mode stimulation, when compared to the OFF-mode stimulation.

The secondary endpoints in the study were quality of life (measured with the Medical Outcomes study Short-Form 36 Health Survey), body mass index, hypoglycemic attacks (diabetic group only), subjective symptoms documented by a clinical status interview, glycosylated hemoglobin, and gastric emptying documented with a gastric emptying test.

WAVESS entry criteria

The inclusion criteria for the study included:

- Symptomatic gastroparesis ≥1 year, as documented by an initial Gastric Emptying Test (GET)
- Refractory or intolerant to at least two antiemetic and two prokinetic drug classes
- On stable medical therapy, and, if applicable, stable nutritional support during the month prior to enrollment
- Frequency of vomiting >7 vomiting episodes per week, as documented with a baseline patient diary.
- Delayed gastric emptying, defined by greater than 60% retention at two hours and >10% retention at four hours, as measured by standardized gastric emptying testing.

The exclusion criteria included:

- Organ transplant
- Organic obstruction
- Pseudo-obstruction
- Prior gastric surgery
- Scleroderma
- Amyloidosis
- History of seizures
- Peritoneal or unstable dialysis
- Chemical dependency
- Pregnancy
- Primary eating or swallowing disorders
- Psychogenic vomiting
- Implanted electronic medical devices
- Age <18 or >70 years

WAVESS study enrollment

Enrollment and follow-up in the WAVESS study were as follows:

Table 2. Enrollment in WAVESS study

Number of subjects	At enrollment	Implanted >30 days	Implanted >60 days	Implanted >6 months	Implanted >12 months
(N)	33	33	33	27	24

WAVESS study demographics

A total of 33 subjects were enrolled in the WAVESS study. The demographic information on these subjects is presented in **Table 3**.

Table 3. WAVESS study patient demographics

	Diabetic (N=17)	Idiopathic (N=16)	Total (N=33)
Gender (M/F)	9/8 F	0/16 F	9/24 F
Age, mean	38.1	41.1	39.6
BMI, mean	24.7	22.9	23.7
Gastric retention (mean/median)%			
@2 hours	79.7/80.0	73.1/76.5	76.5/78.0
@4 hours	53.2/51.0	34.3/28.0	44.0/34.0

WAVESS study design

Subjects satisfying entry criteria received gastric stimulation systems that included an implanted neurostimulator connected to two unipolar leads that were implanted in the muscle wall of the stomach on the greater curvature at the limit of the corpus-antrum. All subjects received a model 7425 implantable neurostimulator and a pair of model 4300[1] leads.

The stimulation parameters used in the study were: Intensity: 5 mA, Pulse Width: 330 µsec, Frequency: 14 Hz. The neurostimulator was set to deliver a pair of pulses at these parameters every five seconds continuously 24 hours per day.

The study was conducted in two phases:

1. Phase I was a double-blind crossover study with evaluations prior to implant and at 30 days and 60 days post-implant. Subjects were randomly assigned to stimulation on and off for the first month after implant and were crossed to off and on for the second month. Subjects were blinded as to which stimulation sequence they received.
2. Phase II was an unblinded open label study with follow-up at six and twelve months. After the crossover period was complete, the subjects were asked which month of the crossover stimulation they preferred. After the selection was made, the study blind was broken. The subjects then received stimulation (on or off) consistent with their preference.

The primary and the secondary endpoints, except gastric emptying, were measured at baseline, 30 days, 60 days, six months, and twelve months postrandomization. Gastric emptying was measured at baseline, and six and twelve months postrandomization.

Primary endpoint evaluations included weekly vomiting frequency and patient preference within Phase I of the study. Secondary endpoint evaluations included gastric retention, hypoglycemic attacks, upper GI symptoms, and quality of life using the Medical Outcomes Study Short-Form 36 Health Survey.

[1] The model 7425G neurostimulator is identical to the model 7425 neurostimulator used in the clinical study. The model 4351 lead is similar to the model 4300 lead used in the clinical study. The model 4351 lead has a fixed electrode length of 10 mm, whereas the model 4300 lead had an adjustable electrode length.

WAVESS Compassionate Use study (WCU)

In contrast to the WAVESS study design, the WCU study was an unblinded, open label study. Upon implantation of the device within each patient, the stimulation therapy was immediately initiated without a randomized on/off cross-over period.

The WAVESS Compassionate Use study (WCU) was an open label, non-randomized study that included a total of 18 subjects. The WCU study was designed to provide safety (adverse events) information on gastric stimulation.

WCU study objective

The purpose of the WCU study was to provide treatment for patients and to evaluate adverse events of patients with drug-refractory gastroparesis who did not meet the entry criteria of the WAVESS study.

WCU entry criteria

Candidates eligible for the WCU study consisted of those subjects who did not meet the complete entry criteria for the WAVESS study, but who had documentation of drug refractory gastroparesis.

The study entry criteria:

- Did not meet the entry criteria of the WAVESS study
- Were likely to die within the next few weeks if they did not receive this therapy
- Signed an informed consent form relevant to this study

This WAVESS Compassionate Use study required:

- Documentation of life-threatening situation by an independent physician
- IRB (or IRB chairperson) approval on a case-by-case basis
- An additional informed consent form relevant to the applicable patient's condition was approved by the clinical investigator and the IRB or IRB chairperson (this varied depending on the reason(s) that the patient did not qualify for the WAVESS study)

WCU study demographics

A total of 24 subjects were enrolled in the WCU study. The demographic information on these subjects is presented in **Table 4** on page 32.

Table 4. WCU study patient demographics

	Diabetic	Idiopathic	Post-surgical
(N)	6	17	1
Gender (M/F)	1M / 5F	17 F	1 F
Age, mean	36.4	35.7	69.0
BMI, mean	20.5	23.1	18.4
Baseline:			
Vomiting severity (mean)	3.5	3.6	4.0
Nausea severity (mean)	3.3	3.6	4.0
GET 2 Hr (median)	74.0	67.0	18.0
GET 4 Hr (median)	34.0	22.0	2.0

WCU study design

Subjects satisfying entry criteria received gastric stimulation systems which included an implanted neurostimulator connected to two unipolar leads which were implanted in the muscle wall of the stomach on the greater curvature at the limit of the corpus-antrum. All subjects received a model 7425 implantable neurostimulator and a pair of model 4300 leads. The stimulation parameters used in the study were: Intensity: 5 mA, Pulse Width: 330 µsec, Frequency: 14 Hz. The neurostimulator was set to deliver a pair of pulses at

these parameters every five seconds continuously 24 hours per day. The stimulation parameters could be adjusted at any time by the physician to optimize treatment therapy.

Compassionate Use Electrical Stimulation Study (CUESS)

The Compassionate Use Electrical Stimulation Study was an open label, non-randomized study that included a total of 51 subjects. This study was designed to provide gastric stimulation safety information.

CUESS study objective

The purpose of the Compassionate Use Electrical Stimulation Study was to treat patients with drug-refractory gastroparesis who had no other medical treatment alternative.

CUESS entry criteria

The inclusion criteria for the study were:

- Symptomatic gastroparesis ≥1 year, as documented by an initial gastric emptying test (GET)
- Refractory or intolerant to at least two antiemetic and prokinetic drug classes
- On stable medical therapy during the month prior to enrollment

- Frequency of vomiting >7 vomiting or nausea episodes per week, as documented with a baseline patient diary
- Delayed gastric emptying, defined by greater than 50% retention at two hours and >6% retention at four hours, as measured by standardized gastric emptying testing

The exclusion criteria were:

- Organ transplant
- Organic obstruction
- Pseudo-obstruction
- Scleroderma
- Amyloidosis
- Peritoneal or unstable dialysis
- Chemical dependency
- Pregnancy
- Primary eating or swallowing disorders
- Psychogenic vomiting
- Implanted electronic medical devices
- Age <18 or >70 years

CUESS study demographics

A total of 50 subjects were enrolled, screened, and qualified in the Compassionate Use Electrical Stimulation Study. The demographic information on these subjects is presented in **Table 5**.

Table 5. CUESS study patient demographics

	Diabetic	Idiopathic	Post-surgical[a]
(N)	22	19	9
Gender (M/F)	10 / 12 F	1 / 18 F	1 / 8 F
Age, mean	39.8	44.5	48.8
BMI, mean	23.5	22.4	23.5
Gastric retention (median)%			
@ 2 hours	79.5	51.0	73.5
@ 4 hours	39.5	21.0	33.5

[a] Enterra Therapy System is not indicated for postsurgical gastroparesis

CUESS study design

Subjects satisfying entry criteria received gastric stimulation systems which included an implanted neurostimulator connected to two unipolar leads which were implanted in the muscle wall of the stomach on the greater curvature at the limit of the corpus-antrum. All subjects received a model 7425 implantable neurostimulator and a pair of model 4300 leads.

The stimulation parameters used in the study were: Intensity: 5 mA, Pulse Width: 330 µsec, Frequency: 14 Hz. The neurostimulator was set to deliver a pair of pulses at these parameters every five seconds continuously 24 hours per day.

The stimulation parameters could be adjusted at any time by the physician to optimize treatment therapy. In contrast to the WAVESS study design, Compassionate Use Electrical Stimulation Study was an unblinded open label study. Upon implantation of the device within each patient, the stimulation therapy was immediately initiated without a randomized on/off crossover period.

WAVESS results

The effectiveness results described below were obtained from the WAVESS study.

Primary endpoint evaluations

Weekly vomiting frequency was determined for each patient diary. These data were further analyzed by Wilcoxon signed-rank test. For the combined patient group, median weekly vomiting frequency declined 49.6% in the on period vs. the off period ($p<0.05$), see **Table 6**. Before breaking the blind at the end of Phase I, 21 patients (10 diabetic, 11 idiopathic) preferred stimulation on, while 7 (4 diabetic and 3 idiopathic) preferred stimulation off, and 5 (3 diabetic and 2 idiopathic) had no preference.

These results were analyzed by the Mainland-Gart test and were statistically significant for the idiopathic and the combined group ($p < 0.05$). At the end of Phase I, subjects were unblinded and given the option of having the device programmed on or off. At the six-month follow-up, all subjects had the device programmed on. Each patient had the option of having stimulation turned off or on at any time during the Phase II period.

Appendix A: Enterra Therapy clinical studies

Table 6. Vomiting frequency, WAVESS phase I, all subjects (N=33)

Vomiting episodes per week	Baseline	On	Off	Difference (off-on)	% difference
Mean (N ± SD)	37.3 ± 45.1	15.9 ± 25.0	23.6 ± 35.6	7.7	32.6
Median (N)	17.3	6.8	13.5	6.7	49.6

Table 7. Vomiting frequency, WAVESS phase II, all subjects

All patients combined	Baseline	6 months	% difference	Baseline	12 months	% difference
(N)	33	27	—	33	24	—
Mean number of episodes ± SD	37.3±45.1	13.7±30.2	-63	37.3±45.1	8.5±16.3	-77
Median number of episodes	17.3	2.6	-85	17.3	4.8	-72
Patients with >50% vomiting reduction vs baseline, N(%)	—	16/27 (59)	—	—	18/24 (75)	—
Patients with >80% vomiting reduction vs baseline, N(%)	—	13/27 (48)	—	—	13/24 (54)	—

Although 33 patients completed the two-month crossover period of the study (through Phase I), data at six months is provided for only 27 patients. Of these 27 patients, some patients had the device turned to the on mode immediately at the end of the Phase I period, while others had the device turned on later. By the end of the fourth month postrandomization, all 27 patients had the device turned on. As a result, the vomiting frequency at six months was obtained from patients who received continuous stimulation for at least two months, see **Table 9**.

Vomiting frequency results at 6- and 12-months post-implantation are shown in **Table 7**, **Table 8**, and **Table 9**. **Table 7** includes data for all subjects, while **Table 8** and **Table 9** include data for the idiopathic and diabetic gastroparesis groups, respectively. The vomiting frequency at 6 and 12 months was significant compared to baseline.

Appendix A: Enterra Therapy clinical studies

Table 8. Vomiting frequency, WAVESS phase II, idiopathic gastroparesis subjects

All patients combined	Baseline	6 months	% difference	Baseline	12 months	% difference
(N)	16	14	—	16	13	—
Mean number of episodes ± SD	44.3±55.5	12.1±25.1	-73	43.3±55.5	11.8±21.2	-73
Median number of episodes	26.8	3.0	-88	26.8	4.5	-83
Patients with >50% vomiting reduction vs baseline, N(%)	—	9/14 (64)	—	—	10/13 (77)	—
Patients with >80% vomiting reduction vs baseline, N(%)	—	8/14 (57)	—	—	7/13 (54)	—

Table 9. Vomiting frequency, WAVESS phase II, diabetic gastroparesis subjects

All patients combined	Baseline	6 months	% difference	Baseline	12 months	% difference
(N)	16	13	—	16	11	—
Mean number of episodes ± SD	30.3±31.9	15.7±36.4	-48	30.3±31.9	4.2±3.9	-87
Median number of episodes	13.4	2.6	-80	13.4	4.9	-63
Patients with >50% vomiting reduction vs baseline, N(%)	—	7/12 (58)	—	—	8/11 (73)	—
Patients with >80% vomiting reduction vs baseline, N(%)	—	5/12 (42)	—	—	6/11 (55)	—

WAVESS secondary endpoint evaluations

The results of secondary endpoint evaluations indicate that many patients experienced improvements in quality of life (73%) and ability to tolerate solid meals (73%).

Additionally, there was a trend in improvement for gastric retention, subjective symptoms, and hypoglycemic attacks.

Adverse events

The adverse events information (**Table 10**) was obtained from the WAVESS study (N=27), the WAVESS Compassionate Use study (N=24), and the CUESS study (N=49). Adverse events were reported at each follow-up visit or at interim periods as appropriate in both studies. **Table 10** summarizes those system related adverse events reported through May 22, 2003.

Table 10. Summary study of system related adverse events[a]

Event description	WAVESS N=27			WAVESS compassionate use N=24			CUESS N=49		
	Events	Patients	% of patients	Events	Patients	% of patients	Events	Patients	% of patients
Device infections	10	7	26	4	4	17	5	5	10
Device erosion	1	1	4	0	0	0	0	0	0
Extrusion of neurostimulator through incision	1	1	4	0	0	0	0	0	0
Hematoma at pocket	1	1	4	0	0	0	1	1	2
Infection in wound incision/abdominal wall	1	1	4	0	0	0	0	0	0
Neurostimulator migration	1	1	4	2	1	4	1	1	2
Lead penetration	4	4	15	1	1	4	0	0	0
Lead revision	1	1	4	0	0	0	0	0	0
Lead impedance out of range	3	3	11	5	5	21	3	2	4
Irritation/inflammation over neurostimulator site	5	4	15	5	5	21	3	2	4
Pain at neurostimulator site	5	4	15	0	0	0	2	2	4
Concomitant stimulation of abdominal rectus muscle	1	1	4	0	0	0	2	2	4
Seroma at pocket	2	2	7	1	1	4	0	0	0
Surgical removal of system due to discomfort	0	0	0	2	2	8	0	0	0
Inability to program device/programming difficulty	0	0	0	1	1	4	1	1	2
Tingling sensation	0	0	0	1	1	4	0	0	0
Failure of wound healing	0	0	0	0	0	0	1	1	2
Extra-abdominal pain	0	0	0	0	0	0	4	4	8
Epigastric pain	0	0	0	0	0	0	1	1	2
Surgical removal of IV access	0	0	0	0	0	0	1	1	2
Electrical shocks with discomfort	0	0	0	0	0	0	1	1	2
Patient "can't eat as well as before therapy"	0	0	0	0	0	0	1	1	2
Left side nerve rib pain	0	0	0	0	0	0	1	1	2
Uncomfortable neurostimulator location	0	0	0	0	0	0	2	2	4
Fluid collection at neurostimulator site with erythema over RLQ	0	0	0	0	0	0	1	1	2

[a] Refer to the notes following this table for more information.

Adverse event table notes

The decline in the rate of device-related adverse events from the WAVESS to the CUESS protocols may be related to several factors:

- During patient enrollment in the WAVESS study, the protocol was modified to require intraoperative endoscopy to ensure that neither stimulating lead perforated the stomach.
- During the WAVESS study, the physicians were encouraged to administer perioperative antibiotics to minimize the potential for infections at the implant site.
- At one center, the majority of the 39 total cases implanted in the three protocols were done by one surgeon, and 4 infections (10.3%) were reported.
- At another center, 11 systems were implanted in the three protocols and 5 infections (45.5%) were reported. All implant procedures in the WAVESS study and WAVESS Compassionate Use study were done by laparotomy, whereas 5 (10.2%) of the 49 in CUESS were done by laparoscopy.

CUESS (N=49): Two diabetic patients who were implanted but did not qualify for the CUESS protocol were excluded from this summary table.

Appendix B: Electromagnetic interference

Please review **Electromagnetic Interference (EMI)** under **Warnings** on page 5 and **Table 1. Potential effects of EMI from devices or procedures** on page 8.

Before any medical procedure is begun, patients should always inform any health care personnel that they have an implanted neurostimulation system. The potential for the following effects results from an interaction of the neurostimulation system and equipment—even when both are working properly.

Contraindications

Diathermy - Do not use shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy (all now referred to as diathermy) on patients implanted with a neurostimulation system. Energy from diathermy can be transferred through the implanted system and can cause tissue damage at the location of the implanted electrodes, resulting in severe injury or death.

Diathermy can also damage the neurostimulation system components, resulting in loss of therapy and requiring additional surgery for system explantation

and replacement. Advise your patient to inform all their health care professionals that they should not be exposed to diathermy treatment.

Injury to the patient or damage to the device can occur during diathermy treatment when:

- The neurostimulation system is turned on or off.
- Diathermy is used anywhere on the body—not just at the location of the neurostimulation system.
- Diathermy delivers heat or no heat.
- Any component of the neurostimulation system (lead or neurostimulator) remains in the body.

The Enterra Therapy System is MR conditional — Patients with the Enterra System can safely have MRI examinations of some body parts under certain conditions. See the MRI Guidelines for Physicians manual for further information.

Warnings

EMI from the following medical procedures or equipment may damage the device, interfere with device operation, or cause harm to the patient. If these procedures are required, follow the guidelines below:

CT scans - Prior to the patient undergoing a CT scan, program the neurostimulator to 0 V and turn the neurostimulator off. If these guidelines are not followed, the patient may experience a momentary increase in stimulation, which some patients have described as uncomfortable stimulation (jolting or shocking sensation).

Defibrillation or cardioversion - When a patient is in ventricular or atrial fibrillation, the first consideration is patient survival. External defibrillation or cardioversion can damage a neurostimulation system and cause induced currents in the lead portion of the neurostimulation system that can injure the patient. Minimize the current flowing through the neurostimulation system by following these guidelines:

- Position defibrillation paddles as far from the neurostimulator as possible.
- Position defibrillation paddles perpendicular to the neurostimulation system.
- Use the lowest clinically appropriate energy output (watt seconds).

After defibrillation, confirm the neurostimulation system is functioning as intended.

Electrocautery - If electrocautery is used near an implantable device, or contacts a device or insertion needle, the following effects may occur:

- The tissue surrounding the insertion-needle (during placement of a percutaneous lead) may be damaged.
- The insulation on the lead may be damaged, resulting in component failure, or induced currents into the patient that may damage tissue, or stimulate or shock the patient.
- The neurostimulator may be damaged, output may be temporarily suppressed or increased, or stimulation may stop because parameters were changed to power-on reset settings (e.g., output off, amplitude 0.0 V).

When electrocautery is necessary, follow these precautions:

- Before using electrocautery, turn off the neurostimulator.
- Disconnect any cable connecting the lead to a screener or external neurostimulator.
- Use only bipolar cautery.

- If unipolar cautery is necessary:
  - Use only a low-voltage mode.
  - Use the lowest possible power setting.
  - Keep the current path (ground plate) as far from the neurostimulator and lead as possible.
  - Do not use full-length operating room table grounding pads.
- After using electrocautery, confirm that the neurostimulator is functioning as intended.

High-output ultrasonics - Use of high-output ultrasonic devices is not recommended for patients who have an implanted neurostimulation system. If high-output ultrasonics must be used, do not focus the beam within 15 cm (6 in) of the neurostimulator.

Lithotripsy - Safety has not been established. Lithotripsy is not recommended for patients with an implanted neurostimulation system. If lithotripsy must be used, do not focus the beam on the neurostimulator, which may damage the device.

Radio-frequency or microwave ablation - Safety has not been established for Radio Frequency (RF) or microwave ablation in patients who have an implanted neurostimulation system. Induced electrical currents may cause heating, especially at the lead electrode site, resulting in tissue damage.

Theft detectors and security screening devices - Advise patients to use care when approaching theft detector and security screening devices (such as those found in airports, libraries, and some department stores). When approaching these devices, patients should do the following:

1. If possible, patients should request to bypass these devices. Patients should show the security personnel their patient identification card for the neurostimulator and request a manual search. Security personnel may use a handheld security wand but patients should ask the security personnel not to hold the security wand near the neurostimulator any longer than is absolutely necessary. Patients may wish to ask for another form of personal search.

2. If patients must pass through the theft detector or security screening device, they should approach the center of the device and walk through normally (Figure 2).

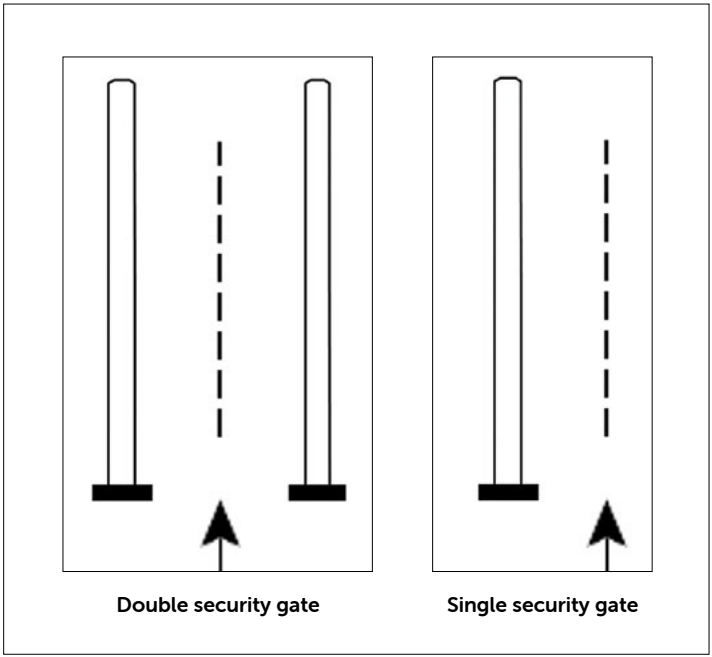
    a. If two security gates are present, they should walk through the middle, keeping as far from each gate as possible.

    b. If one gate is present, they should walk as far from it as possible.

    Note: Some theft detectors may not be visible.

3. Patients should proceed through the security screening device. They should not linger near or lean on the security screening device.

Figure 2. Approaching security gates



Precautions

EMI from the following equipment is unlikely to affect the neurostimulation system if the guidelines below are followed:

Bone growth stimulators - Keep external magnetic field bone growth stimulator coils away from the neurostimulation system. When using either an implantable or external bone growth stimulator, ensure that both the bone stimulator and neurostimulator are working as intended.

Dental drills and ultrasonic probes - Keep the drill or probe 15 cm (6 in) away from the neurostimulator.

Electrolysis - Turn off the neurostimulator. Keep the electrolysis wand away from the neurostimulator.

Electromagnetic field devices - Patients should exercise care or avoid the following equipment or environments:

- Antenna of citizens band (CB) radio or ham radio
- Electric arc welding equipment
- Electric induction heaters used in industry to bend plastic
- Electric steel furnaces
- High-power amateur transmitters

- High-voltage areas (safe if outside the fenced area)
- Linear power amplifiers
- Magnetic degaussing equipment
- Magnets or other equipment that generates strong magnetic fields
- Microwave communication transmitters (safe if outside the fenced area)
- Perfusion systems
- Resistance welders
- Television and radio transmitting towers (safe if outside the fenced area)

If patients suspect that equipment is interfering with neurostimulator function, they should do the following:

1. Move away from the equipment or object.

2. If possible, turn off the equipment or object.

3. Inform the equipment owner or operator of the occurrence.

If the above actions do not resolve the effects of the interference, or the patients suspect that their therapy is not effective after exposure to EMI, they should contact their physician.

Laser procedures - Turn off the neurostimulator. Keep the laser directed away from the neurostimulation system.

Psychotherapeutic procedures - Safety has not been established for psychotherapeutic procedures using equipment that generates electromagnetic interference (e.g., electroconvulsive therapy, transcranial magnetic stimulation) in patients who have an implanted neurostimulation system. Induced electrical currents may cause heating, especially at the lead electrode site, resulting in tissue damage.

Radiation therapy - High-radiation sources should not be directed at the neurostimulator. High-radiation exposure may temporarily interfere with neurostimulator operation and may damage the neurostimulator. Damage may not be immediately apparent. To limit device exposure, use appropriate shielding or other measures, such as making beam angle adjustments to avoid the device.

Transcutaneous Electrical Nerve Stimulation (TENS) - Do not place transcutaneous electrical nerve stimulation electrodes so that the TENS current passes over any part of the neurostimulation system. If patients feel that the TENS may be interfering with the implanted neurostimulator, patients should discontinue using the TENS until they talk with their doctor.

Notes

Household items - Most household appliances and equipment that are working properly and grounded properly will not interfere with the neurostimulation system. The following equipment is generally safe if patients follow these guidelines:

- **Induction range:** Keep the neurostimulator away from the burners while the burners are turned on.
- **Power tools:** Keep the motor away from the neurostimulator and lead.

Other medical procedures - EMI from the following medical procedures is unlikely to affect the neurostimulation system:

- Diagnostic ultrasound (e.g., carotid scan, doppler studies)
  Note: To minimize potential image distortion, turn off the neurostimulator and keep the transducer 15 cm (6 in) away from the neurostimulation system.
- Diagnostic X-rays or fluoroscopy
  Notes:
  – To minimize potential image distortion, turn off the neurostimulator.

– Tight pressure such as that used during mammography may damage the neurostimulator or disconnect the neurostimulation system components, which may require surgery to reconnect or replace components. During X-ray procedures that require external compression around implanted components, the X-ray equipment should be adjusted to limit the amount of pressure exerted on the neurostimulator.

- Magnetoencephalography (MEG).
- Positron Emission Tomography (PET) scans.

Appendix C: Electromagnetic compatibility declaration (60601-1-2)

Wireless quality of service

Proximal telemetry, also known as Telemetry N or Tel-N, is the main communication medium between Enterra Medical Neuromodulation external instruments and neurostimulators. Successful programming requires close proximity between the programmer and the neurostimulator. A connection is established only through direct inductive coupling with no dependence on a network. If the wireless connection is lost without

warning, the user should reposition the programmer to reestablish the connection. Interrupted or partial messages are invalid and must be resent.

Wireless security

A model-specific device access code is used to initiate a programming session. The Tel-N link between a programmer and a neurostimulator is limited to a maximum distance of approximately 9 cm (3.5 in), and inadvertent programming, malicious programming, and eavesdropping are mitigated by close contact with the patient for any communication.

Electromagnetic compatibility declaration

Table 11, **Table 12A**, **Table 12B** and **Table 13** apply to Enterra Medical neuromodulation in-line powered and battery powered external devices.

Table 11. Electromagnetic emissions

The N'Vision model 8840 Clinician Programmer is intended for use in the electromagnetic environment specified below. The customer or the user of this device should ensure that it is used in such an environment.		
Emissions test	**Compliance**	**Electromagnetic environment – guidance**
Radio-frequency (RF) emissions CISPR 11	Group 1	The model 8840 uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The model 8840 is suitable for use in all establishments, including domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions EN 61000-3-2	Not applicable (Battery powered device)	The device is suitable for use in all establishments, including domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Voltage fluctuations/ flicker emissions EN 61000-3-3	Not applicable (battery powered device)	

Appendix C: Electromagnetic compatibility declaration (60601-1-2)

Appendix C: Electromagnetic compatibility declaration (60601-1-2)

Table 12A. Electromagnetic immunity

The N'Vision model 8840 Clinician Programmer is intended for use in the electromagnetic environment specified below. The customer or the user of this device should ensure that it is used in such an environment.

Immunity test	EN 60601 test level	Compliance level	Electromagnetic environment – guidance
Electrostatic discharge (ESD): EN 61000-4-2	±6 kV contact ±8 kV air	±2 kV, ±4 kV, ±6 kV contact ±2 kV, ±4 kV, ±8 kV air	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Electrical fast transient/burst: EN 61000-4-4	±2 kV for power supply lines ±1 kV for input/ output lines	Not applicable (Battery powered device)	Mains power quality should be that of a typical home health care environment.
Surge: EN 61000-4-5	±1 kV differential mode ±2 kV common mode	Not applicable (Battery powered device)	Mains power quality should be that of a typical home health care environment.
Voltage dips, short interruptions and voltage variations on power supply input lines: EN 61000-4-11	<5% U_T (>95% dip in U_T) for 0,5 cycle 40% U_T (60% dip in U_T) for 5 cycles 70% U_T (30% dip in U_T) for 25 cycles <5% U_T (>95% dip in U_T) for 5 sec	Not applicable (Battery powered device)	Mains power quality should be that of a typical home health care environment. If the user of the device requires continued operation during power mains interruptions, it is recommended that the device be powered from an uninterruptible power supply or a battery.
Power frequency (50/60 Hz) magnetic field: EN 61000-4-8	3 A/m	3 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical home health care environment.

Table 12B. Electromagnetic immunity

The N'Vision model 8840 Clinician Programmer is intended for use in the electromagnetic environment specified below. The customer or the user of this device should ensure that it is used in such an environment.			
Immunity test	**EN 60601 test level**	**Compliance level**	**Electromagnetic environment – guidance**
NOTE: U_T is the a.c. mains voltage prior to application of the test level.			
Portable and mobile RF communications equipment should be used no closer to any part of the device, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.			
			Recommended separation distance:
Radiated RF EN 61000-4-3	3 V/m 80 MHz to 2,5 GHz	3 V/m	d=4 √P 80 MHz to 800 MHz d=7,7 √P 800 MHz to 2,5 GHz where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey,[a] should be less than the compliance level in each frequency range.
NOTE 1: At 80 MHz and 800 MHz, the higher frequency range applies.			
NOTE 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects, and people.			
[a] Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast, and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the device is used exceeds the applicable RF compliance level above, the device should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the device.			

Appendix C: Electromagnetic compatibility declaration (60601-1-2)

Table 13. Recommended separation distances between portable and mobile radio-frequency (RF) communications equipment and the device

The N'Vision model 8840 Clinician Programmer is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of this device can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and this device as recommended below, according to the maximum output power of the communications equipment.

Rated maximum output power of transmitter (W)	80 MHz to 800 MHz (m) d=1,2√P	800 MHz to 2,5 GHz (m) d=2,3√P
0,01	0,12	0,23
0,1	0,38	0,73
1	1,2	2,3
10	3,8	7,3
100	12	23
For transmitters rated at a maximum output power not listed above, the recommended separation distance d in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where *P* is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.		
NOTE 1: At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.		
NOTE 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects, and people.		
⚠ **Caution:** Do not use non-Enterra Medical components with Enterra Medical battery-powered external devices. The use of non-Enterra Medical components may result in damage to Enterra Medical components, increased emissions, or decreased electromagnetic immunity of the Enterra Medical devices or systems.		
⚠ **Caution:** Do not use Enterra Medical battery-powered external devices adjacent to, or stacked with, other electronic devices. Using Enterra Medical devices in these configurations may result in decreased electromagnetic immunity of the Enterra Medical devices or systems.		

Appendix D: Enterra II Neurostimulator model 37800 communications regulations

The following communications regulations apply to the model 37800.

United States Compliance

FCC ID: LF537602

This device complies with part 15 of the FCC Rules.

Operation is subject to the following two conditions: (1) This device may not cause harmful interference, and (2) this device must accept any interference received, including interference that may cause undesired operation.

IMPORTANT: Changes or modifications to this product not authorized by Enterra Medical, Inc., could void the FCC Certification and negate your authority to operate this product.

Enterra Medical Neurostimulation System limited warranty[2] (U.S. Customers Only)

A. This limited warranty provides the following assurance to the patient who receives an Enterra Medical Neurostimulation System. The Neurostimulation System includes neurostimulators, permanent leads, single-use accessories, and disposable tools, hereafter referred to as "components", unless specifically noted.

(1) Should the components fail to function within normal tolerances due to a defect in materials or workmanship within a period of one (1) year, commencing with the date of implantation or use of the components, Enterra Medical will at its option: (a) issue a credit to the purchaser of the replacement component equal to the Purchase Price, as defined in Subsection A(3), against the purchase of any same component requested as its replacement, or, (b) provide a functionally comparable replacement component at no charge.

(2) Neurostimulator battery cell depletion will occur with time and is not considered to be a defect in materials or workmanship. The batteries have a specified capacity that may deplete at different rates depending on settings and individual requirements for neurostimulation functions. Therefore, no representation is made that the neurostimulator will last the entire term of this limited warranty.

(3) As used herein, "purchase price" shall mean the lesser of the net invoiced price of the original or current functionally comparable, or replacement component.

B. To qualify for this limited warranty, these conditions must be met:

(1) The components must be implanted prior to its "Use By" date.

(2) The components must be used in conjunction with components compatible with the Enterra Medical Neurostimulation System.

(3) All device registration materials must be completed and returned to Enterra Medical within thirty (30) days of implantation of the neurostimulator.

(4) Replaced neurostimulators must be returned to Enterra Medical within thirty (30) days of explantation and shall be the property of Enterra Medical. For all other components, the component, or portion thereof, must be returned to Enterra Medical within thirty (30) days after discovery of the defect and shall be the property of Enterra Medical, and if not explanted, the serial number or lot number must be provided to Enterra Medical instead.

(5) The components must be used in accordance with the labeling and instructions for use provided with the components.

C. This limited warranty is limited to its express terms. In particular:

(1) Except as expressly provided by this limited warranty, ENTERRA MEDICAL IS NOT RESPONSIBLE FOR ANY DIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES BASED ON ANY DEFECT, FAILURE OR MALFUNCTION OF THE NEUROSTIMULATOR TO FUNCTION WITHIN NORMAL TOLERANCES WHETHER THE CLAIM IS BASED ON WARRANTY, CONTRACT, NEGLIGENCE, STRICT LIABILITY, OR OTHER TORT OR OTHERWISE.

(2) This limited warranty is made only to the patient in whom the components were implanted. AS TO ALL OTHERS, ENTERRA MEDICAL MAKES NO WARRANTY, EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, WHETHER ARISING FROM STATUTE, COMMON LAW, CUSTOM OR OTHERWISE. NO SUCH EXPRESS OR IMPLIED WARRANTY TO THE PATIENT SHALL EXTEND BEYOND THE PERIOD SPECIFIED IN A(1) ABOVE. THIS LIMITED WARRANTY SHALL BE THE EXCLUSIVE REMEDY AVAILABLE TO ANY PERSON.

(3) The exclusions and limitations set out above are not intended to, and should not be construed so as to contravene mandatory provisions of applicable law. If any part or term of this limited warranty is held to be illegal, unenforceable or in conflict with applicable law by a court of competent jurisdiction, the validity of the remaining portions of the limited warranty shall not be affected, and all rights and obligations shall be construed and enforced as if this limited warranty did not contain the particular part or term held to be invalid. This limited warranty gives the patient specific legal rights. The patient may also have other rights that vary from state to state.

(4) No person has any authority to bind Enterra Medical to any representation, condition, or warranty, except this limited warranty.

[2] This Limited Warranty is provided by Enterra Medical, Inc., 5353 Wayzata Boulevard, Suite 400, St. Louis Park, MN 55416-9906. It applies only in the United States. Areas outside the United States should contact their local Enterra Medical representative for exact terms of the Limited Warranty.

Appendix E: Patient MRI Eligibility Checklist

This checklist is provided as an optional resource to support MRI centers in conducting an MRI of a patient implanted with the Enterra System.

Prior to performing a scan, verify all information with the patient's pain management physician, the referring medical facility, the implanting physician or a Enterra Medical representative.

Patient Name: _____

☐ **Step 1: Confirm that the patient has brought their patient ID card.**

☐ **Step 2: Verify model numbers of implanted Enterra System components.**

Component	Model Number	Head/Neck & Extremity Eligible (1.5T)
Enterra II IPG	37800	☐
Enterra Unipolar Leads	4351-35	☐

☐ **Step 3: Check if the patient has any other medical device implants.**

The most restrictive MRI exposure requirements must be used if the patient has multiple medical device implants. For patients with other implanted devices in addition to the Enterra System, consult the appropriate device manufacturers for MRI eligibility of those devices.

☐ **Step 4: Confirm that all implanted leads are connected to the IPG.**

☐ **Step 5: Document the patient's current amplitude, frequency (rate), on/off time, and pulse width.**

Amplitude	Frequency (rate)	On/off	Pulse width

☐ **Step 6: Perform an impedance check using the Model 8840 programmer.**

Note, the Model 8840 programmer is not MRI safe. **Do NOT** perform an MRI scan if any impedance is out of range.

☐ **Step 7: Stimulation is turned off using the 8840 programmer.**

☐ **Step 8: Verify the following MR scanner requirements and perform scans per the table below.**

Monitor the patient both visually and audibly. Discontinue the MRI examination immediately if the patient reports any problems.

MRI Safety Information

A person with the Enterra Medical Enterra II System may be safely scanned under the following conditions. Failure to follow these conditions may result in injury.

Device Name	Enterra II
Device Configuration	Stimulation OFF
Static Magnetic Field Strength (Bo)	1.5T
MR Scanner Type	Cylindrical
Bo Field Orientation	Horizontal
Maximum Spatial Field Gradient	20 T/m (2,000 gauss/cm)
Maximum Gradient Slew Rate	200 T/m/s per axis
RF Excitation	Circularly Polarized (CP)
RF Transmit Coil Type	Head or Extremity Coils Only
RF Receive Coil Type	Any
Operating Mode	Normal Operating Mode
Maximum Whole-Body SAR	2 W/kg
Maximum Head SAR	3.2 W/kg
Scan Duration	Scan for up to 60 minutes of continuous RF (a sequence or back to back series/scan without breaks).
Scan Regions	Only head or extremity scanning allowed.
MR Image Artifact	The presence of this implant may produce an image artifact.

☐ **Step 9: After scan is completed, turn stimulation back on using the 8840 programmer.**

Ensure the settings are the same as recorded in step 5. Verify that the patient has not experienced any adverse effects as a result of the MRI. Contact Enterra Medical, Inc. if the patient has experienced any adverse effects.

Manufacturer

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