SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Stimulator, Spinal-Cord, Totally Implanted For Pain Relief

Device Trade Name: Algovita™ Spinal Cord Stimulation (SCS) System

Device Procode: LGW

Applicant's Name and Address: Algostim, LLC
10675 Naples St. NE
Blaine, MN 55449

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P130028

Date of FDA Notice of Approval: 11/13/15

II. INDICATIONS FOR USE

The Algovita™ Spinal Cord Stimulation (SCS) system is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome, intractable low back pain and leg pain.

III. CONTRAINDICATIONS

Shortwave, microwave and/or therapeutic ultrasound diathermy must not be used on SCS patients. The energy generated by diathermy can be transferred through the SCS system, causing tissue damage at the lead site which may result in severe injury or death.

Subjects who fail to receive effective pain relief during a stimulation trial.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Algovita SCS System labeling.

V. DEVICE DESCRIPTION

The Algovita SCS System is a rechargeable, 24-electrode, spinal cord stimulation system that delivers electrical stimulation to the dorsal column of the spinal cord for the treatment of chronic intractable pain of the trunk and/or limbs. The Algovita SCS System is shown in Figure 1.

Figure 1: The Algovita Spinal Cord Stimulation (SCS) System

A. Implanted Components

The implanted components of the Algovita SCS System include the following:

- Implanted Pulse Generator: Rechargeable, 24-channel implantable pulse generator (IPG or Stimulator) in two configurations:
  - 3 ports x 8 independent channels (3 leads, each with 8 electrodes)
  - 2 ports x 12 independent channels (2 leads, each with 12 electrodes)

  Both IPG models have 24 independent programmable channels, operate using identical electronics and operating values, and utilize identical hermetic enclosures. The IPG is connected, either directly or with a lead extension, to one, two, or three 8-electrode leads, or one or two 12-electrode leads. Stimulation parameters are set with the Clinician Programmer (CP), and within pre-programmed limits are adjusted by the patient using the Programmer Charger (PPC) or the Pocket Programmer (PoP). The stimulation output parameters are listed in Table 1 below:

Table 1: Stimulation Output Parameters

Number of Programs	1 to 10
Number of Channels	24
Waveform	Charged Balanced Biphasic
Pulse Shape	Rectangular
Current or Voltage Regulated	Current
Maximum Current Amplitude @ 500 Ω	0 to 15 mA per channel 30 mA total output maximum
Maximum Output Voltage @ 500 Ω	7.5 V
Pulse Width	12 to 1500 µs 4 µs resolution
Frequency	2 to 2000Hz

Current Path Options	Unipolar, Bipolar or Multipolar

- Leads: The leads provide the interface through which electrical current is delivered to the spinal cord. The following lead types are available:

  - Percutaneous leads:
    The lead specifications are depicted in Table 2 and Figure 2 below:

Table 2: Percutaneous Lead Specifications

	Percutaneous Leads
Lead Length (cm)[1]	45, 60, 75, 90
Lead Diameter (mm)	1.4
Number of Electrodes[2]	8 or 12
Electrode Material	Platinum/Iridium (90/10)
Electrode Spacing (edge-to-edge) (mm)	1, 4, 6
Array Length (mm)	8 electrode lead: 31-66 12 electrode lead: 47-102
Electrode Surface Area (mm^2)	12.7
Impedance (Ω)	20 – 60

[1] Trial leads are not available in 75 cm or 90 cm lengths
[2] Each electrode may be independently stimulated.

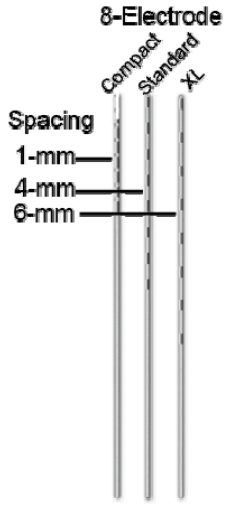

Figure 2: Algovita Percutaneous Leads

  - Surgical Paddle Leads:
    The lead specifications are depicted in

    Table 3 and Figure 3 below:

Table 3: Surgical Paddle Lead Specifications

	Percutaneous Leads
Lead Length (cm)	45 and 60
Lead Diameter (mm)	1.4
Number of Electrodes	12
Electrode Configuration	2 x 6 array 3-4-3-2 array
Paddle Thickness	1 mm at the base 2 mm at paddle ribs
Paddle Width (mm)	6.5 and 9
Paddle Length (mm)	54 and 38.35
Electrode Material	Platinum/Iridium (90/10)
Electrode Spacing (mm)	Inline: 2 Row: 2
Electrode Surface Area (mm^2)	7.16
Impedance (Ω)	18-40

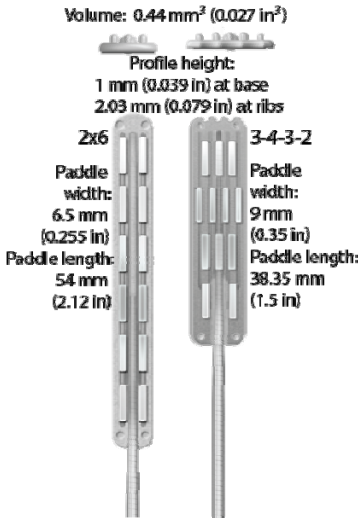

Figure 3: Algovita Surgical Paddle Leads

- Extensions: Used to provide additional length when used to connect either a trial lead to the External Pulse Generator (EPG), via a trial cable for trial stimulation, or during a system implant to connect a lead to an IPG. They are available in 1x8 and 1x12 configurations with 20, 40, and 60 cm lengths to be used according to the number of electrodes in the connecting lead.

B. External Components

- Clinician programmer (CP): Used by the clinician to program output stimulation parameters. It is a handheld, rechargeable, and has a liquid crystal display (LCD) color touch screen. The CP uses Medical Implant Communication Service (MICS) telemetry to communicate with and to program the EPG and IPG. All programming information is stored on the IPG or EPG and the CP itself. Within the CP, programming sessions are retained and stored on Secure Digital (SD) cards for review in follow-up visits. In addition, the SD cards are used to update software on the CP.

- Programmer Charger (PPC): Used to transcutaneously recharge the IPG battery and provide more advanced stimulation parameter adjustments than the pocket programmer (PoP). It is a rechargeable handheld device with a touch screen and a detachable charging paddle. The charging paddle is attached to the patient using an adhesive patch or an adjustable belt.

- Pocket Programmer (PoP): Allows patients to make adjustments to stimulation within the clinician prescribed program limits stored on the EPG during the stimulation trial, and on the IPG following implant.

- Patient Feedback Tool (PFT): An optional programming aid used by the patient during a programming session to provide confirmation of the sensation of paresthesia while settings are determined. It communicates to the CP via Bluetooth, providing one-way feedback from the patient in response to paresthesia sensation. The PFT is used during the Computer Assisted Stimulation Programming (CASP) session.

- External Pulse Generator (EPG or trial stimulator): Provides stimulation by emulating the IPG during the intraoperative test and during the stimulation trial. The EPG circuitry and stimulation parameters are the same as the IPG.

- Trial Cables: Used during intraoperative testing and stimulation trial. One end of the cable is plugged into a connector which holds the leads proximal ends, and the other end of the cable is attached to the Algovita EPG.

- Passing Elevator and Forming Tool: The Algovita Passing Elevator is used to assist with insertion of paddle leads. A forming tool is included to assist in shaping the passing elevator radius.

- Port Plug: The Algovita Port Plug is used for plugging unused ports in the IPG header.

- Torque Wrench: The Algovita Torque Wrench is used to tighten the set screws that lock the lead into the IPG and/or lead extension.

- Lead ID Kit (optional): Used to assist when two or three leads are being used. The kit includes a set of color lead identification flags (3), a set of color needle ID caps (3), and a drape clip to assist in identifying leads.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of chronic intractable pain of the trunk and/or limbs. Patients are typically treated on a treatment continuum with less invasive therapies prescribed first. Established non-surgical treatment options include, but are not limited to, oral medications, massage therapy, physical/occupational/exercise therapy, psychological therapies (e.g., behavior modification, hypnosis), transcutaneous electrical nerve stimulation (TENS), acupuncture, sympathetic nerve blocks, epidural blocks, intrathecal blocks, and facet joint blocks. The surgical treatment options for these patients include sympathectomy, implantable intrathecal drug delivery systems, partially implanted SCS systems (power source is external) and commercially available fully implantable SCS systems. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Algovita SCS System has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (e.g., complications) associated with the use of SCS systems. Because there is no published data on the use of this particular device, these potential adverse events have been identified from published scientific clinical studies, systematic reviews and meta-analyses of scientific literature, device labeling for currently marketed SCS systems, and post-market surveillance and safety data using complaints and (Manufacturer and User Facility Device Experience) MAUDE databases for fully implantable SCS systems similar to the Algovita system. The adverse effects include: (1) those associated with any surgical procedure, (2) those associated with the SCS system placement procedures, and (3) those associated with having an implanted SCS system to treat pain, including the Algovita SCS System. In addition to the risks listed below, there is the risk that the SCS therapy may not be effective in relieving symptoms, or may cause worsening of symptoms. Additional intervention may be required to correct some of the adverse effects.

- Risks associated with any surgical procedure: abscess; cellulitis; excessive fibrotic tissue; wound dehiscence; wound, local or systemic infection; wound necrosis; edema; inflammation; foreign body reaction; hematoma; seroma; thrombosis; ischemia; embolism; thromboembolism; hemorrhage; thrombophlebitis; adverse reactions to anesthesia; hypertension; pulmonary complications; organ, nerve or muscular damage; gastrointestinal or genitourinary compromise; seizure, convulsion,

or changes to mental status; complications of pregnancy including miscarriage and fetal birth defects; inability to resume activities of daily living; and death.

- Risks associated with SCS system placement procedures: temporary pain at the implant site, infection, cerebrospinal fluid (CSF) leakage, CSF fistula, epidural hemorrhage, bacterial meningitis, seroma, hematoma, and paralysis. Patient use of anticoagulation therapies may increase the risk of procedure-related complications such as hematomas, which could produce paralysis.

- Risks associated with the use of a SCS system: lead migration; IPG migration; allergic response or tissue reaction to the implanted system material; hematoma or seroma at the implant site; skin erosion at the implant site; persistent pain at the IPG, extension, or lead site; radicular chest wall stimulation; disturbed urination; dysesthesia; decubitus; premature battery depletion; loss of pain relief over time; and uncomfortable stimulation or ineffective pain control caused by random failure of the system components or battery, changes in electrode position, loose electrical connections, lead or extension insulation breaches or fractures.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

1. Implanted Pulse Generator (IPG)
   Testing was conducted on the Model 2408 and 2412 IPGs, including: mechanical design verification (including testing on devices subjected to accelerated aging), electrical/firmware design verification testing, electromagnetic compatibility testing, and medical procedure compatibility testing. Key testing on the IPGs is summarized in Table 4 below. Testing demonstrated the IPGs operated according to specifications after exposure to the tested conditions (i.e., passed testing).

Table 4: Summary of key testing performed and passed on the Algovita IPG

Test	Test Purpose	Acceptance Criteria
Electrical/Firmware Design Verification Testing	Testing of key functional blocks of the electrical/firmware design to demonstrate IPG operates within specification, including: Pulse generation/stimulation system, Communications/Telemetry and MICS system, Charging , Power system, Microprocessor system, Outputs, Error Handling, Bootloader mode, and Program store and retrieve.	Device operates within specifications including the following: • Leakage – 100nA Maximum leakage current per each channel. • Channel Amplitude and Crosstalk Test on all 24 channels – amplitude 1.9-2.1 mA, pulse width 487.5-512.5 microseconds, frequency 9.65-10.35 Hz, less than 1 μA cross talk on other channels. • MICS-Device communication established and maintained at a distance. • Recharge - No recharge errors (IPG status of zero). • Magnet - In storage mode, IPG is no

Test	Test Purpose	Acceptance Criteria
		longer visible/loss of telemetry session.
Dimensional Requirements	To demonstrate IPGs meet shape and profile requirements.	IPG samples must meet size specifications for IPG width, height, thickness, volume, mass, radius, and lead bore orientation.
DC Leakage Current	Verify the leakage current is in an acceptable range.	100 nA max per channel.
Environmental Conditions	Thermal Shock and Storage Exposure: To expose IPGs to thermal stress the device may encounter during storage and distribution. This test includes temperature requirements for thermal shock, storage temperature and cycling.	Device operates within specification after exposure to thermal cycling and shock from -35°C through 55°C.
	Atmospheric Pressure Exposure: To expose each IPG to pressure extremes the device may encounter during storage and distribution.	Each sterile pack is to be exposed to low pressure at 70kPA ± 5% for 60 + 5 minutes and subsequently exposed to high pressure at 150 KPa ± 5% for 60 + 5 minutes. Confirm devices continue to meet visual, hermeticity, fine leak and operate within specification after stress.
	Operating Pressure: To demonstrate the IPG remains mechanically intact and capable of normal operation during exposure to low and high pressures.	The IPG shall remain mechanically intact and capable of normal operation during exposure to low and high pressures. low pressure at 70kPA ± 5% for 60 + 5 minutes and subsequently exposed to high pressure at 150 KPa ± 5% for 60 + 5 minutes
	Operating Temperature: To demonstrate the IPG remains mechanically intact and capable of normal operation during exposure to low and high temperatures.	The IPG shall remain mechanically intact and capable of normal operation during exposure to low (10°C (- 3°C)) and high temperatures (45°C (+3°C)) for 8 hours minimum.
Mechanical Free Fall	To demonstrate the IPG remains mechanically intact and capable of normal operation following mechanical free fall drop from 18" and 12".	The IPG shall remain mechanically intact and operates within specification following mechanical free fall drop from a 12" and 18" distance.
Cyclic Deflection -Low Load	To demonstrate the IPG remains mechanically intact and continue normal operation during and after exposure to cyclic deflection.	The IPG shall remain mechanically intact and operate within specifications during and after exposure to cyclic deflection. Test devices applying a 3.0 ± 0.05 Lbf load for 300,000 cycles.
Hermetic Leak Test	To demonstrate that the IPG (including feedthroughs) maintains hermeticity after exposure to environmental testing.	The IPG enclosure is punctured, and the gas contained in the IPG is analyzed by a mass spectrometer to determine the oxygen concentration inside the IPG. The IPG shall have an oxygen concentration inside the hermetic assembly of less than 0.1000% by volume.
IPG Enclosure Deflection	To demonstrate the IPG remains mechanically intact and capable of normal operation following exposure to	The IPG shall remain mechanically intact and operate within specifications following the application of 17.2 pounds or greater force to

Test	Test Purpose	Acceptance Criteria
	an enclosure deflection load.	the center of the device enclosure for 10 seconds for 12 cycles.
Mechanical Shock	To demonstrates that the IPG remains mechanically intact and continues normal operation after mechanical shock	The IPG shall remain mechanically intact and operate within specifications following application of one shock in each direction at orthogonal angles (total of 6 shocks) with the following parameters: • 500 g (16100 ft/s2). Wave shape = half sine • Duration = 1.0 ms • Minimum change in velocity = 10.5 ft/s
Header Attach Fatigue and Header Channel Isolation	To demonstrate the header meets fatigue requirements the IPG maintains isolation between channels and externally.	The IPG shall remain mechanically intact and operate within specifications after 150,000 cycles of a 3.0 ± 0.1 Lbf load applied to each side of the device (300,000 cycles total) after 10 days soaked in saline. The leakage impedance between conductive elements and between any internal conductive element and the outside must exceed 50 K ohms in saline. The leakage impedance is measured periodically during soak. The specification requirement is applied after 10 days of soak have been completed.
Channel IPG Inter-channel Resistance Check	To demonstrate IPGs do not have any opens or shorts in the header.	Sample remains intact and is not damaged. The resistance for each channel must be between 18-40 Ω.
Lead Insertion and withdrawal Forces	To demonstrate that the IPG, port plug, and lead meet specified interface requirements for insertion force and withdrawal force (without setscrew engaged) when the IPG and lead are in a dry and wet conditions.	• Port plug can be fully inserted and removed. • Lead insertion force shall be less or equal to 9.0N (2.0 Lbf). • With mechanical fixation disengaged, lead withdrawal force shall be 9.0N (2.0 Lbf) or less. • With mechanical fixation engaged, lead retention force shall be 10 N (2.25 Lbf) or greater, when the header and lead are wet.
Cyclic Motion (Marching Test): Contact Impedance Charge	This test demonstrates that the IPG has minimal impedance change after 500,000 cycles of oscillatory motion upon the connected lead cycling between loaded and unloaded with the maximum IPG mass suspended in saline. This assures no effects due to micro-motion and fretting corrosion.	The resistance for each channel must be between 18-40 Ω. The maximum change in system impedance from internal side of feedthrough to lead-tip contact shall be -10 to +50 ohm. Sample remains intact and is not damaged.
Header Deflection	To show that the IPG header meets low cycle fatigue requirements related to forces applied to the geometric center of the header.	Sample remains intact and is not damaged. The resistance for each channel must be between 18-40 Ω.

Test	Test Purpose	Acceptance Criteria
Particulate matter	Verify there is no unacceptable release of particulate matter when the device is used as intended.	The excess average count of particles from the test specimen compared to a reference sample shall not exceed 100 counts/ml greater than 5.0 μm and shall not exceed 5 counts/ml greater than 25 μm.
Accelerated Aging	To demonstrate the IPGs meet mechanical and physical requirements after their labeled 2-year shelf life.	Meets requirements of testing above.
Battery	Battery Capacity Verification (Longevity).	Maintain a charge/discharge cycle of at least 24 hours for at least 123 months under worst case conditions.
	Electrical, Visual, Dimensional, Hermeticity, Short Circuit Testing, Environmental, and Forced Discharge Tests	Meet specifications.

2. Percutaneous and Surgical Paddle Lead Testing

The percutaneous and paddle leads underwent numerous testing for dimensional verification, electrical safety, environmental and mechanical conditions. Key testing on the leads is summarized in Table 5 below. Testing demonstrated the percutaneous and paddle leads operated according to specifications after exposure to the tested conditions (i.e., passed testing).

Table 5: Summary of Percutaneous and Paddle Lead Verification Testing

Test	Purpose	Acceptance Criteria
Dimensional	To ensure the leads meet dimensional requirements for Overall Lead Length Lead Body Diameter, Distal Electrode Dimensions, Lead Tip Length, Connector Dimensions.	Meets specifications.
DC Resistance	Demonstrate protection from electricity.	The DC resistance from each conductor contact to its corresponding electrode shall be less than 100 ohms. No two conductors shall be shorted to each other.
Stylet Interactions – Insertion/Removal	To demonstrate the force required to fully insert or remove each stylet into the lead	The force required to fully insert or remove each stylet into the lead shall be less than 5N. The stylet shall not damage the lead. After testing, the electrical (DC) resistance shall be within 10 ohms of baseline value (determined prior to testing) and current leakage shall be less than 2mA during Hipot testing.
Lead/Tuohy Needle Interaction - Insertion/Removal	Demonstrate lead compatibility with Touhy Needle.	The force required to fully insert and remove the lead through the needle shall be less than 9 N. The needle shall not damage the lead. Lead damage includes wire or wire insulation damage.

Test	Purpose	Acceptance Criteria
Screening Cable Interaction	Demonstrate reliability of screening cable connection.	The lead shall be able to withstand 10 connection cycles to the screening cable without damage.
Tunneling Tool Interaction	Demonstrate lead compatibility with Tunneling tool.	Three (3) leads shall be able to pass d1rough the sheath of the tunneling tool with a 6 inch minimum bend radius.
Hipot	Demonstrate the safety of the electrical insulation.	The leads must have no more than 2mA current leakage when tested to a minimum of 40 volts DC.
Insulation Resistance	Demonstrate the safety of the electrical insulation.	The minimum impedance of the insulation between each conductor and a reference electrode, and between each pair of conductors, shall be 50,000 ohms, at 100Hz.
Tensile Strength	Demonstrate the lead remains electrically and mechanically intact after a tensile load.	The tensile load shall be limited to the lesser of a) the value causing 20% elongation, or b) 5 N. The permanent elongation of the lead shall not exceed 5%. The electrical continuity shall remain intact after application of the tensile load.
Lead Retention within IPG	Demonstrate the force required to remove the lead from the IPG.	With the setscrew engaged, the force required to remove the lead from the IPG must exceed 10 N (2.25 lbs). The setscrew shall be engaged using the torque-limiting wrench provided with the lead kit.
IPG Interaction	Demonstrate the number of connection cycles with the IPG.	The lead shall withstand 10 connection cycles to the IPG without damage.
Lead Body Flex Fatigue	Demonstrate that the leads do not fatigue after flexural stressors.	The lead body shall have a flex life greater than 150,000 cycles when flexed ±90(+0/-5) degrees at a central lead body bend radius of 6 mm. Bending shall take place at a rate of approximately 2 cycles/second with the minimum tensile load needed to confom1the lead body to the fixture radius. Electrical (DC) resistance measurements during the flex testing must be 100 ohms.
Connector End Flex Fatigue	Demonstrate that the lead connector ends do not fatigue after flexural stressors.	The resistance of the lead (where the lead joins the connector body) will meet specifications and remain functionally intact after undergoing connector flex testing. A vertical load of 24 g ± 2 g will be applied and the fixture oscillated at 45°± 2° at 2 Hz for 82,000 cycles. After testing, the measured resistance of the conduction path must meet specifications and the conductor must be functionally intact.

Test	Purpose	Acceptance Criteria
Distal End Flex Fatigue	Demonstrate that the distal end of the leads do not fatigue after flexural stressors.	The lead shall undergo distal end flex testing about a 5 inch radius. A vertical load will be applied to the lead to demonstrate that the lead conforms to the fixture. The fixture shall oscillate from 0° to 90"±2° at -I Hz for150,000 cycles. After testing, d1e measured resistance of the conduction paddle must meet specifications and the lead shall remain intact.
Particulate Release	No unacceptable release of particulate matter when the lead is used as intended.	Per ISO 14708-3, Active implantable medical devices - Part 3: Implantable neurostimulators, the excess average count of particles from a test specimen compared to a reference sample shall not exceed 100 per ml greater than 5.0µm and shall not exceed 5 per ml greater than 25 µm.
Lead Tip Strength	Demonstrate the adequacy of the lead tip strength.	The force required to cause the stylet wire to protrude through the tip of the lead shall be greater than 5N.

3. Programmers

- Trial Stimulator (External Pulse Generator or EPG)
  The EPG was subjected to the following types of testing: electrical/firmware design verification, mechanical, shipping, environmental (storage and operational), product safety testing (per IEC 60601-1, Class II type BF safety classification), drop testing (per IEC 60601-1, 3rd edition), EMC testing (per IEC 60601-1-2), and FCC parts 95 and 15. All test articles met defined acceptance criteria for the defined verification tests.

- Clinician Programmer (CP)
  The CP was subjected to the following types of testing: functional verification, mechanical, shipping, environmental (storage and operational), battery charging, product safety testing (per IEC 60601-1, Class II type BF safety classification), and drop testing (per IEC 60601-1, 3rd edition). All test articles met defined acceptance criteria for the defined verification tests.

- Programmer Charger (PPC) and Pocket Programmer (PoP)
  The PPC and PoP were subjected to the following types of testing: functional verification, mechanical, shipping, environmental (storage and operational), battery charging, product safety testing (per IEC 60601-1 for power supply classification Type B Applied Part and protection against electric shock: internal powered equipment), and drop testing (per IEC 60601-1, 3rd edition). All test articles met defined acceptance criteria for the defined verification tests.

- Patient Feedback Tool (PFT)
  The PFT was subjected to the following types of testing: functional verification, mechanical, shipping, environmental (storage and operational), battery properties, product safety testing (per IEC 60601-1, Class II type BF safety classification), and drop testing (per IEC 60601-1, 3rd edition). All test articles met defined acceptance criteria for the defined verification tests.

4. Electromagnetic Compatibility Testing
   EMC testing for the implanted components per 14708-3:2008(E): Implants for surgery – Active implantable medical devices – Part 3: Implantable neurostimulators," Part 27, and EN 301 839-2 and 489-17 (Emissions), EN 301 489-27 (Emissions & Immunity), and EN 489-2 (Emissions). External components were tested per IEC 60601-1-2. All test articles met defined acceptance criteria for the defined tests.

5. Wireless Coexistence
   Wireless technology, quality of service (QOS), coexistence, and security of wireless transmissions testing was also performed and all acceptance criteria were met.

6. System Testing
   Testing to verify that system-level design requirements were met for interactions between Algovita SCS System components was performed. All test articles met defined acceptance criteria for the system integration tests conducted. System validation testing consisting of the following was conducted on the Algovita system components: evaluating the compatibility, interaction and functional operation of the system components when used together as a system. All validation steps passed. System validation testing demonstrated that the system operated as expected and has been validated for safe and effective use.

7. IPG Medical Compatibility Testing
   The Algovita IPG was tested for compatibility with external defibrillation, Electrocautery (high power electric fields) diagnostic ultrasound, and diagnostic x-ray exposure (see Table 6 below). The implanted SCS system (IPG and leads) was evaluated for effects on its function and programming by exposure to the medical therapies that may occur on a patient during or after implantation of an Algovita SCS System. Functional testing was performed on each IPG before exposure to confirm that it meets all of its performance requirements, and where appropriate, each was monitored during exposure. Functional testing was then performed post exposure to confirm that the IPG still met all functional requirements, and that the exposure to medical therapy had no effect on device performance, program, or stored calibrations. All samples met all functional requirements of the testing after exposure to medical therapy conditions, verifying that the IPG meets requirements for compatibility with these therapies

Table 6: IPG Medical Compatibility Testing

Test	Acceptance Criteria
External Defibrillator Test	Verify that the device meets functional electrical test requirements after exposure to external defibrillation per EN 45502-1.
Electrocautery (High Power Electrical Fields) Test	Exposure was performed at an external test facility, Intertek. Leads were attached to the IPG and the IPG was stimulating on all electrodes to an external load. Exposure was conducted on one device per EN 45502-2-1 Clause 21.2, with the exception of outputting current on all channels simultaneously, and a pulse frequency of 2 Hz versus 1 Hz per the cardiac standard. Acceptance criteria is that the device meets all functional requirements post exposure
Diagnostic Ultrasound Test	Exposure was performed at an external test facility, Acertara Acoustic Laboratories (subcontract by Intertek). Leads were attached to the IPG and the IPG placed in storage mode. Exposure was conducted on one device per EN 45502-1 Clause 22.1, with the exception that the actual ultrasonic energy used was 575 W/m^2 instead of the required 500 W/m^2. Acceptance criteria is that the device meets all functional requirements post exposure
X-Ray Compatibility Test	Exposure was performed at an external test facility, North Star Imaging. IPG was placed in storage mode during the exposure. Exposure was conducted on one device to deliver an x-ray dosage of 150 rads minimum, using 120 kVP and 8.5 mA x-ray tube current. Acceptance criteria is that the device meets all functional requirements post exposure

B. Animal Studies

Two GLP *in vivo* studies were conducted to validate system functionality of the Algovita SCS System. A summary of the studies is provided in Table 7.

Table 7: Summary of *In Vivo* Animal Studies

Test Name: Purpose	Method	Objective	Results/ Conclusion
Algovita Spinal Cord Stimulation's (SCS) System Animal Study: To evaluate the functionality of the Algovita SCS System in an *in vivo* setting over an extended period of time.	This chronic GLP animal study evaluated the Algovita SCS System, Model 2412 and Model 2408 in 6 sheep. The systems were comprised of an intraoperative EPG, implanted IPG, paddle leads or percutaneous leads, surgical accessories, and external programmers and components. The sheep were implanted with the system using a sterile surgical procedure.	The primary objective of this chronic study was to validate, in an in vivo setting, Algovita (SCS) system component function, both intraoperatively and postoperatively, as defined by the System Validation Test Protocol. Intraoperative System Function: • Algovita SCS System implantability • External device (Pocket Programmer (PoP), Clinician Programmer (CP) and Programmer Charger (PPC) communication with the IPG and EPG • Lead functionality and Anchors • Initial Programming of the EPG and IPG Postoperative Ongoing System Function: • External device communication with the IPG, including the CP, PPC and PoP • Lead functionality • Programming of the IPG • Recharging of the IPG	The results of the Algovita SCS System animal study demonstrate that the system performs safely and reliably as expected, in an *in vivo* model over an extended period of time.

Test Name: Purpose	Method	Objective	Results/ Conclusion
IPG Recharging Study: To demonstrate *in vivo* that the Algovita SCS System's IPG functionality performs safely under all recharge conditions.	In this GLP study, a total of 8 temperature probes attached to the IPG, PPC, and in surrounding tissue, were used to monitor IPG temperature recharging behavior in 3 acute procedure days, covering 24 charge cycles under these different conditions. Three (3) male sheep were implanted with a model 2408 and 2412 IPG. One pocket was formed on the left and right posterior caudal side of each animal to hold the IPGs. The temperature of tissue facing the surface of the PPC charging paddle, the charging coil temperature, and the surface IPG temperature distributions were collected during recharge for 4 cases: • IPG Implant Normal (label facing out), Charging Coil aligned. • IPG Implant Normal, Charging Coil Offset • IPG Implant Flipped (label facing in), Charging Coil Aligned • IPG Implant Flipped, Charging Coil Offset	The primary objective of this study was to demonstrate that the Algovita SCS IPG and PPC charging system remains within a safe temperature range during recharging. The Algovita SCS System was designed with a safety feature which reduced the charge rate at an IPG temperature of 41 °C.	The Algovita SCS System performed as designed, and all temperatures were below the defined safety temperature limit, under all recharge conditions. The results of the study demonstrate that the IPG recharge functionality for each IPG orientation performs safely in an *in vivo* model.

C. <u>Biocompatibility</u>

Biocompatibility testing was performed for all patient-contacting components of the Algovita™ Spinal Cord Stimulation System in accordance with ISO 10993-1 Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process, on the finished sterilized devices. All biocompatibility studies were conducted in compliance with Good Laboratory Practices (GLP), 21 CFR Part 58. The implanted components of the Algovita™ Spinal Cord Stimulation System are considered permanent (> 30 days) implants in contact with tissue/bone. The Algovita™ Spinal Cord Stimulation System also contains external communicating and skin-contacting components with both prolonged (> 24 hours – 30 days) and

limited (≤ 24 hours) tissue/bone contact. The biocompatibility test data are summarized in Table 8 below. All pre-specified test acceptance criteria were met and all tests passed.

Table 8: Biocompatibility Test Data on the Implantable, External Communicating, and Skin-Contacting Components of the Algovita Spinal Cord Stimulation System*

Biological Effect (Applicable Standard)	Test Method	Acceptance Criteria	Results
Implanted[a], External Communicating[b], and Skin-contacting[c] Components:			
Cytotoxicity (ISO 10993-5)	ISO MEM (minimum essential medium) Elution Assay	Reactivity grade is not greater than mild reactivity (Grade 2)	PASS
	ISO Agar Overlay Test	Reactivity grade is not greater than mild reactivity (Grade 2)	
Sensitization (ISO 10993-10)	ISO Guinea Pig Maximization Sensitization Test	Grades of <1 in the test group provided grades of < 1 are observed on the control animals. (If grades of ≥ 1 are noted on the control animals, then the reactions of the test animals which exceed most severe control reaction are presumed to be due to sensitization).	PASS
	Buehler Dermal Sensitization Test	Grades of <1 in the test group provided grades of < 1 are observed on the control animals. (If grades of ≥ 1 are noted on the control animals, then the reactions of the test animals which exceed most severe control reaction are presumed to be due to sensitization).	PASS
Irritation/Intracutaneous Reactivity (ISO 10993-10)	ISO Intracutaneous Reactivity Test	The difference between the test article and the control mean score is ≤ 1.0.	PASS
	ISO Primary Skin Irritation Test	The Primary Irritation Index is calculated and the response is characterized as Negligible (score of 0.0 – 0.4) / Slight (score of 0.5 – 1.9) / Moderate (score of 2.0 – 4.9) / Severe (score 5.0 – 8.0)	PASS – Primary Irritation Index is 0.0 (Negligible)
Implanted[a] and External Communicating[b] Components			
Systemic Toxicity (ISO 10993-11)	ISO Acute Systemic Injection Test	None of the test animals show a significantly greater	PASS

Biological Effect (Applicable Standard)	Test Method	Acceptance Criteria	Results
		biological reaction than the animals treated with vehicle control.	
	Materials Mediated Rabbit Pyrogen Test	No rabbit shows an individual rise in temperature of 0.5°C or more above the baseline temperature.	PASS
	Subacute Toxicity (14 Day Intravenous Toxicity Study in Mice)* (* testing conducted for implanted[a] components only)	The correlation of all data for patterns of toxicity, including death of > 1 animal/group, mean body weight loss for each group, clinical signs of toxicity in > 1 animal/group, hematological and clinical chemistry values, and histopathology of tissues in the test and control groups.	PASS
Implanted[a] Components			
Genotoxicity (ISO 10993-3)	Bacterial Reverse Mutation Assay (Ames Test)	There is less than 2-fold increase in the number of revertants when compared to the solvent controls in strains TA97a, TA100, and TA102 and less than 3-fold increase in the number of revertants when compared to the solvent control in strains TA98 and TA1535.	PASS
	In Vitro Chromosome Aberration Assay	There is no statistically significant increase in aberrations between the test group and the negative control.	PASS
	In Vivo Mouse Micronucleus Assay	There is no statistically significant increase in the number of micronucleated polychromatic erythrocytes (PCEs) in the test group as compared to the concurrent negative control.	PASS
Implantation (ISO 10993-6)	13 Week Rabbit Intramuscular Implant Test	The test results are considered acceptable based on an overall interpretation of the degree of biocompatibility exhibited by the test article based on gross and microscopic analysis comparing test to control article (USP high density	PASS

Biological Effect (Applicable Standard)	Test Method	Acceptance Criteria	Results
		polyethylene reference standard), as well as clinical observations.	
Chronic Toxicity (ISO 10993-11)	An adequate chronic toxicity risk assessment was provided.		
Carcinogenicity (ISO 10993-3)	An adequate carcinogenicity risk assessment was provided.		

* Testing conducted for implanted[a] components only

[a] Components tested: IPG, Percutaneous and Paddle Leads, Port Plugs, Anchor

[b] Components tested: Tunneling Tool and Sheath, Introducer Needle, Guidewire, Lead Stylet

[c] Components tested: Trial Cable, Adhesive Patches

D. Packaging and Shelf Life

Packaging and shelf- life validation tests were completed in compliance with ISO 11607:2006 *Packaging for Terminally Sterilized Medical Devices.* A shelf-life of two years is established for sterile system components.

E. Sterility

The Algovita components that are provided sterile are terminally sterilized using a 100% ethylene oxide (EO) sterilization cycle. Validation of the sterilization process demonstrates a Sterility Assurance Level (SAL) of 10^{-6} and is in compliance with ANSI/AAMI/ISO 11135-1:2007. *Sterilization of health care products – Ethylene oxide – Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices*. Sterilant residuals conform to the maximum allowable limits of EO) and Ethylene Chlorohydrin (ECH) residuals specified in ISO 109937: 2008. *Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals*. The product bacterial endotoxin limits were chosen based on FDA's *Guidance for Industry - Pyrogen and Endotoxins Testing: Questions and Answers (*June 2012) and were verified using Limulus Amebocye Lysate (LAL) testing.

F. Additional Studies

1. System Usability Testing

   Patient and clinician usability testing was conducted to verify those tasks for which failure to properly perform them could lead to death or serious injury or those tasks required for the overall safe and effective use of the device, but not posing serious risk to the user can be performed by patients and health care providers. System usability testing was completed successfully with no critical user errors identified in any of the use environments.

2. Perfusion Phantom Temperature Study
   In vitro testing was conducted on the Models 2408 and 2412 IPGs and the Model 4200 Programmer Charger to demonstrate that while charging the IPG, unsafe temperature rise does not occur. Testing was conducted using a perfusion phantom model to simulate the thermal environment of an IPG implanted into a human fat layer (fat presents worst case thermal environment). All test cases passed and no unsafe conditions were observed and no temperature readings exceeded the acceptance criteria during any of the testing.

X. SUMMARY OF CLINICAL DATA

A. Study Design

The safety and effectiveness of the Algovita SCS System was based on a systematic review and meta-analysis of published clinical studies that evaluated the safety and/or effectiveness of commercially available, fully implantable SCS systems in treating chronic intractable pain of the trunk and/or limb. The Algovita SCS System is similar in design, technology, performance, intended use, and patient population to the SCS systems evaluated in these studies. The literature review strategy was conducted according to the guidelines outlined in the PRIMSA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement.[1]

A total of 23 studies (see references in Section XV(A) below), representing a total of 1670 patients with specific inclusion and exclusion criteria were identified by the meta-analysis for inclusion in the safety analysis. T Five studies representing a total of 202 patients were included in the effectiveness analysis.

The Algovita SCS System is similar to the SCS systems reported in the published literature in intended use, target patient population, device design and output characteristics. Based on these similarities the primary objective of the literature search was to provide clinical evidence of the effectiveness of the Algostim device, for the relief of failed back surgery syndrome, intractable low back, and limb pain.

Effectiveness was demonstrated by the following:

1. A reduction of pain as demonstrated by a clinically significant reduction in the Visual Analog Scale (VAS) score;

2. A 50% reduction in pain using either a 3 or 4 point scale in at least 30% of patients included in that study; and/or

3. A clinically significant difference in pain reduction as measured by a VAS score when compared to a control group.

[1] Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Safety of the Algostim SCS System was established using literature articles, for the relief of failed back surgery syndrome, intractable low back, and limb pain. This was accomplished by examining the incidence of complications of the SCS systems used in the published literature.

B. Literature Search Strategy

A literature search strategy consisted of seven primary steps:

1. Search of Medline database for indexed articles using MeSH terms (Medical Subject Headings, National Library of Medicine) relevant for SCS systems and treatment of trunk and/or limb pain (213 abstracts).

2. Search of non-indexed PubMed database using broad SCS terms (260 abstracts).

3. Identification of literature from other sources (4 abstracts).

4. Clinical review for inclusion by two independent reviewers using pre-defined criteria (79/477 abstracts selected).

5. Final selection of eligible articles by a clinical and statistical reviewer (27/79 articles).

6. Determination of studies with safety endpoints appropriate for the safety summary (23/27 studies).

7. Determination of studies appropriate for the efficacy summary (5/27), which required efficacy endpoints and excluded studies with (1) retrospective designs, (2) device features or waveforms not offered by Algovita, (3) subjects with ischemic pain, or (4) subjects with pain etiologies for which SCS has not demonstrated effectiveness such as Complex Regional Pain Syndrome Type I (CRPS I) and diabetic neuropathy.

C. Safety and Effectiveness Results

1. Safety Results

   Standard summary statistics are provided for each adverse event type and surgical intervention. In cases where data for a particular event was reported in at least 4 studies, a random-effects model was used to estimate a pooled rate. Two additional models stratified by the ≤1 year time period and the >1 year time period were conducted if the event was reported by at least 4 studies in each time period. In the case the number of events was reported in the article, instead of the number of subjects experiencing an event, it was assumed that each event was experienced by a unique subject.

   In total, 23 articles reported data on 20 subject populations (3 articles reported on the same subjects at later time point) which included a total of 1670 enrolled

subjects eligible for inclusion in the qualitative safety review and meta-analysis. Of the 20 study populations, 8 were from retrospective case series, 7 from prospective case series, 2 from randomized trials, 2 from prospective studies, and 1 from a crossover trial.

Of the 20 study populations, the median sample size was 38 (range, 11 to 707), and 894 (53.5%) of the patients were female. The median average age was 52 years (range, 38 to 70). The median follow-up time was 2.0 years (range, 0.3 to 5.0). The studies enrolled patients between 1983 and 2010. Five of the 20 samples were patients from the United States, representing 921 (55.1%) of the subjects in the safety meta-analysis.

The safety profile was based on adverse events reported for subjects with failed back surgery syndrome (FBSS) and chronic pain of the trunk and limbs. Safety was assessed by analyzing the surgical interventions and adverse events reported in the clinical studies.

- Surgical Interventions
  Three categories of surgical intervention were analyzed:
  - *System explant* was defined as definitive removal of the SCS system without subsequent replacement with a new system, and was typically associated with infection or inadequate pain relief.
  - *System explant with replacement* was defined as temporary removal of the entire SCS system (i.e., IPG and leads) with eventual replacement with a new system, usually secondary to an infection.
  - *Revision* was defined as any surgical procedure required that did not involve complete explant of the system for adverse events such as lead failure/fracture, battery replacement, or IPG change-out.

  A summary of the surgical intervention results in provided in Table 12.

Table 9: Results of Surgical Intervention Meta-Analysis

Procedure Type	N samples (N patients)*	N Interventions**	Median (Range) Follow-up Years	Pooled Rate (95% CI)	Median Rate (IQR) [Range]
System explant (overall)	13 (1401)	62	2.7 (0.3 to 5.0)	5.2% (3.4 to 7.5)	6.2% (2.6 to 8.3) [0.0 to 16.7]
Explant with replacement (overall)	8 (284)	12	1.8 (0.9 to 5.0)	5.1% (2.6 to 8.2)	4.9% (4.1 to 5.9) [0.0 to 12.5]
Revision (overall)	18 (1395)	314	2.0 (0.3 to 5.0)	25.8% (13.7 to 40.1)	23.6% (11.8 to 36.5)

Procedure Type	N samples (N patients)*	N Interventions**	Median (Range) Follow-up Years	Pooled Rate (95% CI)	Median Rate (IQR) [Range]
					[0.0 to 100]
Revision (≤1 year)	7 (340)	N/A	1.0 (0.3 to 1.0)	15.5% (7.3 to 26.1)	19.0% (10.8 to 25.9) [1.3 to 33.3]
Revision (>1 year)	13 (1143)	N/A	2.7 (1.1 to 5.0)	31.8% (15.4 to 50.9)	30.4% (12.5 to 41.7) [0.0 to 100]

* Refers to the number of subject populations and patients for which this outcome measure was assessed. For example, in the first row of the table, 13 of the 20 total subject populations, comprising 1401 patients, had data for the outcome measure "System explant".

** The number of interventions reflects the total number of interventions for the reported patient population. A patient may have experienced more than one intervention.

The reasons for system explant, system explant with replacement, and revision are summarized in
Table 10 below.

Table 10: Summary of Reasons for Surgical Intervention

Reasons for Surgical Intervention*	N
System Explant (N=62)	
Infection	39
Lack of efficacy	6
Subject decision for morphine pump	3
Surgery	3
Reason unspecified	2
Allergy	1
Concomitant surgery	1
Dehiscence	1
Epidural abscess	1
Infection before permanent implant	1
Pregnancy	1
Recurrent rejection	1
Relapsing ulcerative colitis	1
Subject decision	1
System Explant with Replacement (N=12)	

Reasons for Surgical Intervention*	N
Infection (including generator pocket infection)	9
Replacement of system (unspecified)	2
Skin problems at implant site	1
Revision (N=314)	
Lead migration	128
Lead connection failure	50
Lead repositioning	36
Lead fracture	35
Adverse event	11
Pulse generator pocket	8
Inadequate paresthesia coverage	6
Lead replacement	6
Non-specific complications	5
Addition of second lead	4
Migration of electrodes and loss of paresthesia	4
Pain at incision site	4
Lead migration or lead added	3
Connection between lead and extension cable inadequate	2
Lead idiopathic failure	2
Lead repositioning due to technique issue	2
Loss of paresthesia	2
Defective lead	1
IPG migration	1
IPG repositioning	1
Lack of efficacy	1
Lead revision	1
Pocket revision	1

* The reasons for surgical intervention are associated with the surgical interventions presented in the meta-analysis in Table 5 above.

- Adverse Events
  Ten adverse event types, reported in at least four studies, were formally meta-analyzed: stimulation issues, pain over implant site, lead migration, ineffective pain control, lead fracture/failure, infection, skin erosion/problem at implant site, IPG malfunction, CSF leak, and seroma. Table 11 shows an overall summary, sorted by the overall frequency of the adverse event.

Table 11: Summary of Meta-Analyzed Adverse Events

Adverse Event Type	N samples (N patients)*	Median (Range) Follow-up Years	Pooled Rate (95% CI)	Median Rate (IQR) [Range]
Stimulation issue (overall)	4 (225)	1.0 (0.3 to 2.0)	41.1% (4.2 to 85.8)	25.2% (12.2 to 53.6) [11.9 to 100]
Pain over implant site (overall)	8 (1284)	2.0 (0.3 to 3.7)	29.2% (10.5 to 52.6)	9.7% (5.9 to 17.6) [0.8 to 95.5]
Pain over implant site (≤1 year)	5 (277)	0.9 (0.3 to 1.0)	8.3% (4.1 to 13.8)	6.1% (6.0 to 8.3) [5.3 to 21.4]
Pain over implant site (>1 year)	5 (1095)	2.0 (2.0 to 3.7)	22.3% (0.4 to 63.2)	11.9% (7.5 to 16.3) [0.8 to 95.5]
Lead migration (overall)	14 (1514)	2.0 (0.3 to 3.7)	10.2% (7.0 to 14.1)	8.0% (7.2 to 15.8) [2.4 to 25.0]
Lead migration (≤1 year)	7 (319)	1.0 (0.3 to 1.0)	9.3% (5.6 to 13.7)	9.1% (7.5 to 12.9) [2.4 to 25.0]
Lead migration (>1 year)	8 (1247)	2.9 (2.0 to 3.7)	10.7% (6.4 to 15.9)	7.8% (7.2 to 14.9) [4.3 to 22.6]
Ineffective pain control with permanent implant (overall)	6 (255)	2.0 (1.0 to 3.1)	9.4% (4.7 to 15.7)	11.5% (6.5 to 14.6) [2.4 to 22.2]
Lead fracture/failure (overall)	9 (1284)	2.7 (0.9 to 3.7)	5.7% (3.4 to 8.5)	7.1% (4.3 to 8.3) [1.9 to 25.0]
Lead fracture/failure (≤1 year)	4 (198)	1.0 (0.5 to 1.0)	3.7% (1.5 to 6.8)	3.3% (2.4 to 5.2) [2.4 to 8.2]
Lead fracture/failure (>1 year)	7 (1174)	3.1 (2.0 to 3.7)	6.0% (3.2 to 9.5)	7.1% (5.3 to 8.3) [1.9 to 25.0]
Infection (overall)	17 (1547)	2.0 (0.9 to 5.0)	5.3% (4.0 to 6.6)	6.1% (2.5 to 9.5) [0.0 to 12.5]
Infection (≤1 year)	6 (261)	1.0 (0.5 to 1.0)	6.3% (3.7 to 9.6)	6.5% (4.3 to 8.3) [2.4 to 12.5]
Infection (>1 year)	13 (1374)	2.7 (1.1 to 5.0)	5.2% (3.8 to 6.8)	6.1% (2.5 to 9.5) [0.0 to 11.1]

Adverse Event Type	N samples (N patients)*	Median (Range) Follow-up Years	Pooled Rate (95% CI)	Median Rate (IQR) [Range]
Skin erosion/problem at implant site (overall)	5 (515)	2.0 (0.3 to 3.7)	3.2% (0.6 to 7.7)	2.5% (2.4 to 3.6) [0.4 to 11.8]
CSF leak (overall)	4 (406)	1.0 (0.5 to 3.7)	3.0% (0.6 to 7.2)	4.3% (2.0 to 6.7) [0.8 to 8.3]
IPG malfunction (overall)	5 (484)	2.9 (0.9 to 3.7)	2.3% (0.7 to 4.7)	4.1% (2.4 to 4.8) [0.8 to 6.2]
Seroma (overall)	8 (1304)	2.6 (0.3 to 3.7)	1.4% (0.5 to 2.8)	1.4% (0.9 to 2.1) [0.0 to 7.1]

- Refers to the number of subject populations and patients for which this outcome measure was assessed. For example, in the first row of the table, 4 of the 20 total subject population, comprising 225 patients, had data for the outcome measure "Stimulation issue".

All other adverse events had fewer than 4 studies reporting on the rate over follow-up. Therefore, each reported adverse event is summarized using standard summary statistics in Table 12 below.

Table 12: Summary of Other Adverse Events

Adverse Event Type	N studies (N patients)*	Median (Range) Follow-up	Median Rate (IQR) [Range]**
Allergy	1 (30)	1.6	3.4%
Bacterial meningitis	1 (30)	2.9	0.0%
Battery depletion	1 (84)	3.1	1.2%
CSF fistula	1 (260)	3.7	0.4%
Death (non-device related)	2 (289)	3.4 (3.0 to 3.7)	10.9% (9.5 to 12.4) [8.1 to 13.8]
Decubitus	1 (260)	3.7	3.8%
Disturbed urination	1 (36)	2.0	18.2%
Dysesthesia	1 (260)	3.7	0.4%
Epidural abscess	2 (278)	2.4 (1.0 to 3.7)	3.5% (2.1 to 4.9) [0.8 to 6.2]
External component failure	3 (194)	1.0 (0.9 to 3.1)	6.1% (3.7 to 6.6) [1.2 to 7.1]
Hematoma	2 (35)	3.1 (2.7 to 3.4)	2.2% (1.1 to 3.3) [0.0 to 4.3]
Hemorrhage (requiring surgery)	1 (260)	3.7	0.0%
Implant difficulty	1 (45)	1.0	4.8%
Implant technique complications	1 (52)	1.0	4.8%
Inflammation at implant site	1 (45)	1.0	11.9%
Lead revision	3 (118)	2.0 (1.6 to 5.0)	7.1% (5.3 to 39.0) [3.4 to 70.8]

Adverse Event Type	N studies (N patients)*	Median (Range) Follow-up	Median Rate (IQR) [Range]**
Loose connection	2 (752)	2.2 (1.0 to 3.4)	8.3% (7.7 to 8.9) [7.1 to 9.5]
Lumbar site problem	1 (45)	1.0	4.8%
Meningism	1 (260)	3.7	0.8%
More pain in other body parts	1 (36)	2.0	31.8%
Paraplegia	1 (260)	3.7	0.0%
Presumed epidural pneumocephalus headache	1 (260)	3.7	3.5%
Programming error	1 (45)	1.0	4.8%
Radiculopathy	1 (260)	3.7	0.8%
Recurrent rejection	1 (36)	5.0	4.2%
Revision of pulse generator pocket	1 (36)	5.0	33.3%
Spinal cord injury	1 (30)	2.9	0.0%
Ulcerative colitis	1 (36)	5.0	4.2%
Unable to operate patient programmer	1 (84)	3.1	3.6%

* Refers to the number of subject populations and patients for which this outcome measure was assessed. For example, in the first row of the table, 1 of the 20 total subject population, comprising 30 patients, had data for the outcome measure "Allergy".

** For reports occurring in multiple studies

2. Effectiveness Results

There were an insufficient number of studies to perform an efficacy meta-analysis; however, a qualitative summary of efficacy findings for each eligible study is provided.

Five (5) articles from the systematic review of SCS systems reporting on four (4) subject populations (1 article reported on the same subjects at a later time point) were used to summarize the effectiveness of the Algovita SCS System (de Vos et al. 2012, Kumar et al. 2007, Kumar et al. 2008, Oakley et al. 2007, and Ohnmeiss et al. 1996). These studies included a total of 202 enrolled patients permanently implanted with a SCS system. These study populations were followed prospectively for a median of 1.5 years (range, 0.9 to 2 years), 119 (58.9%) were female, and the median average age was 51 years. The primary treated disease was failed back surgery syndrome or intractable lower extremity pain for all subjects. These characteristics are consistent with the patient population for which the Algovita SCS System is indicated.

- De Vos et al. (2012) conducted a prospective case series from 2008 to 2009 among 45 subjects (21 female) with a mean age of 56 years. Forty-three (43)

subjects were ultimately implanted following test stimulation. At one year, the mean visual analog scale (VAS) score (on a scale of 0 to 10) for leg pain was significantly reduced from 8 to 3.2; the mean VAS score on lower back pain was also significantly reduced from mean of 7.5 to 4.2. Subject's mean quality of life rating (0 = most miserable, 100 = best possible) increased from 34 to 70 at one year. The proportion of patients with a 50% or greater reduction in pain according to VAS was 71% for leg pain and 51% for back pain.

- Kumar et al. (2007) conducted a randomized controlled trial of SCS versus conventional medical management for failed back surgery syndrome (FBSS). The trial enrolled 100 subjects from 2003 to 2005 and reported six-month efficacy results. Forty-nine (49) subjects were female and the mean age was 50 years. Fifty-two (52) subjects were randomized to the SCS group and forty-eight (48) to the conventional medical management (CMM) group. Forty-eight (48) of the subjects randomized to the SCS group were ultimately implanted. At six months, 48% of SCS subjects had a 50% or greater reduction in leg pain compared to 9% in the CMM group; 22% of SCS subjects had an 80% or greater reduction in leg pain compared to 7% of subjects who received CMM. At six months, mean back and leg pain as measured by the VAS, improved significantly greater among subjects in the SCS group than those who received CMM.

- Kumar et al. (2008) reported an update of the subjects randomized to receive SCS treatment for failed back surgery syndrome in the randomized controlled trial reported in Kumar et al. (2007). Forty-two (42) of the fifty-two (52) randomized subjects had two-year follow-up data. At two years, 69% had at least 30% leg pain relief, 40% had at least 50% leg pain relief, and 14% had at least 80% leg pain relief.

- Oakley et al. (2007) conducted a prospective trial of SCS in the US primarily among subjects with chronic, intractable pain of the trunk and/or limbs, primarily for FBSS. Sixty-five (65) subjects (40% female) with a mean age of 52 years were enrolled between 2003 and 2004. Sixteen (25%) did not experience at least 50% pain relief with test stimulation and were not implanted. Due to the rolling enrollment, efficacy data were available for 47 subjects at 2 weeks, 38 at 3 months, 33 at 6 months, and 12 at 1 year, for a mean follow-up of 0.9 years among the 49 implanted subjects. The percentage of subjects reporting a 50% or greater improvement in pain was 85%, 63%, 55%, and 75% at each time point, respectively. The mean pain score as measured by the VAS (0-10 scale) was 8.0 baseline and was reduced to 2.5, 3.2, 3.9, and 2.2, respectively.

- Ohnmeiss et al. (1996) conducted a prospective study of SCS among subjects with intractable leg pain. In total, 40 subjects were implanted with a SCS system and were assessed at 6 weeks, 12 months, and 24 months post-implant. The baseline observation carried forward method was used to impute missing

data for subjects with missing follow-up data in an intention-to-treat (ITT) analysis. Mean VAS scores for leg pain were 7.4 pre-operatively, and were reduced significantly to 4.2, 5.6, and 6.3 at 6 weeks, 12 months, and 24 months, respectively, in ITT analyses. At 24 months, leg pain, pain when walking, standing pain, pain's effect on lifestyle, and total VAS scores were significantly improved on average from pre-operative values.

C. Financial Disclosure

A clinical study was not performed and thus, the Financial Disclosure by Clinical Investigators regulation (21 CFR 54) is not applicable to this PMA.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Neurological Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The evaluation of efficacy was conducted using prospective studies relevant to Algovita SCS System features and indications. A total of five (5) studies based on 4 subject populations (1 article reported on the same subjects at a later time point) and 202 patients were qualitatively reviewed. The majority of patients had either intractable limb pain or FBSS and SCS treatment was demonstrated to be effective in each of the five studies. The results of the review support the effectiveness of SCS therapy in treating patients who suffer from chronic, intractable pain of the trunk and/or limbs.

B. Safety Conclusions

The clinical evidence provided to support safety of the Algovita SCS System includes 1) a systematic literature review of clinical research conducted on comparable devices, 2) a qualitative evaluation of the peer-reviewed published clinical research relevant to fully implantable SCS systems, 3) a quantitative meta-analysis of safety and efficacy using relevant clinical studies, and 4) post-market surveillance and safety assessment analysis using complaints and MAUDE databases for fully implantable SCS systems similar to the Algovita system.

The risks of the device are based on nonclinical laboratory and animal studies as well as a meta-analysis included 23 studies with 20 subject populations (3 articles reported on the same subjects at later time points) and a total of 1670 subjects. The majority of patients in the safety meta-analysis had either FBSS or CRPS I.

The findings with respect to surgical interventions were reported with ranges in Table 8. Revisions were the most common surgical intervention and occurred at a rate of 25.8% (13.7% to 40.1%). Revisions were most often secondary to lead migration, followed by lead-related events, such as lead connection failure and lead fracture. Though smaller in number, IPG revisions required for battery replacement or IPG repositioning also contributed to the revision rate. System explants (without replacement), occurred at 5.2% and were typically due to infection, and to a lesser extent, inadequate pain relief. Finally, system explants (with replacement) occurred at 5.1% and were most often the result of infection.

The rates of occurrence for the ten adverse events appropriate for meta-analysis correspond to the surgical intervention rates determined by the meta-analysis and are consistent with trends reported in large systematic literature review of 2520 patients (Cameron, 2004) stimulation issues 41.1%, pain over implant site 29.2%, lead migration 10.2%, ineffective pain control with the permanent implant 9.4%, lead fracture/failure 5.7%, infection 5.3%, skin problems at the implant site 3.2%, CSF leak 3.0%, IPG malfunction 2.3%, and seroma 1.4%. (The range for these adverse events can be found in Table 10.) In any cases where there was statistical evidence of publication bias, with one exception, the bias was in the more conservative direction where larger studies reported lower rates of adverse events than studies with smaller sample sizes.

The rates of occurrence for adverse events from the meta-analysis corresponded to the surgical intervention results and are consistent with trends reported in the literature. The most common complications were stimulation issues, pain at implant site, lead migration, and ineffective pain control. Additionally, the results of the Medical Device Reporting (MDR) analysis of patient events, IPG events, and system events were consistent with the results above, and indicate relatively stable reporting of these well-known events.

The results of the systematic review and meta-analysis support the safety of SCS therapy in treating patients who suffer from chronic, intractable pain of the trunk and/or limbs. The Algovita system is similar to SCS systems approved by the FDA.

C. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a systematic literature review conducted to support PMA approval as described above. Five (5) articles based on four (4) subject populations (1 article reported on the same subjects at a later time point) were used to demonstrate the effectiveness of the Algovita SCS system for the treatment of chronic intractable pain of the trunk and/or limbs. Effectiveness was demonstrated by an improvement in pain using a VAS score. The magnitude of literature reported pain relief ranged from 30 to 50%. In the Kumar 2008 article, pain relief lasted through two years. It would be expected that subjects with chronic pain would experience a similar benefit.

As described above, the risks were evaluated in a systematic literature review and meta- analysis. This resulted in safety information on 1670 patients implanted with SCS systems. The safety information provided was consistent with the well-known safety profile of SCS systems.

Additional factors to be considered in determining probable risks and benefits for the Algovita device included the open label design of the clinical studies during FDA review. In some of the studies reviewed, open label studies may cause an overestimation of the treatment effect in investigator and subject ratings. Also, open label studies do not assess the magnitude of the placebo response, regression to the mean, the effect of changes in medications or other treatments to alleviate pain or changes in the underlying severity of the pain disorder. SCS is an option for patients who do not have adequate pain relief from medications and/or other treatments for pain.

In conclusion, given the available information above, the data support that for the use of the Algovita SCS as an aid in the management of chronic intractable pain of the trunk and/or limbs the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The results from the clinical evaluation support reasonable assurance of the safety and efficacy of the Algovita SCS System, as well its long-term performance, when used in a manner consistent with its labeling and intended use. The evidence supporting the safety and effectiveness of the Algovita SCS System is based on a foundation of 30 years of clinical research and experience as documented in the literature with fully implantable SCS systems and the similarities of the Algovita system to market-released implantable SCS systems. The results from comprehensive pre-clinical testing show that the Algovita SCS System performs as intended. The analyses also support a clinical benefit to risk determination that is favorable

XIII. CDRH DECISION

CDRH issued an approval order on 11/13/15.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XV. REFERENCES

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B. Additional References

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