SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Stimulator, Electrical, Implanted, for the treatment of tremor

Device Trade Name: Vercise™ PC Deep Brain Stimulation (DBS) System
Vercise Gevia™ Deep Brain Stimulation (DBS) System
Vercise Genus™ Deep Brain Stimulation (DBS) System

Device Procode(s): PJS and MHY

Applicant's Name and Address: Boston Scientific Corporation
25155 Rye Canyon Loop
Valencia, CA 91355

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P150031/S040

Date of FDA Notice of Approval: October 20, 2021

The Vercise PC Deep Brain Stimulation (DBS) System and the Vercise Gevia™ Deep Brain Stimulation (DBS) System were originally approved on January 10, 2019 under P150031/S1. The Vercise Genus DBS System was approved on January 21, 2021 under P150031/S034. These systems are indicated for use in the following:

- Bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy in reducing some of the symptoms of moderate to advanced levodopa-responsive Parkinson's disease (PD) that are not adequately controlled with medication.

- Bilateral stimulation of the globus pallidus internus (GPi) as an adjunctive therapy in reducing some of the symptoms of advanced levodopa responsive Parkinson's disease (PD) that are not adequately controlled with medication.

The current supplement (P960009/S040) was submitted to expand the indication for the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems. The original PMA (P150031) for the Vercise DBS System was approved on December 8, 2017 and the SSED to support the indication for STN stimulation is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150031B.pdf) and is incorporated by reference here. No new clinical data were required to support the approval of the Vercise PC, Vercise Gevia and Vercise Genus Deep Brain Stimulation (DBS) Systems.

II. INDICATIONS FOR USE

The Vercise PC, Vercise Gevia and Vercise Genus DBS systems were previously indicated for use in the following:

- Bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy in reducing some of the symptoms of moderate to advanced levodopa-responsive Parkinson's disease (PD) that are not adequately controlled with medication.

- Bilateral stimulation of the globus pallidus internus (GPi) as an adjunctive therapy in reducing some of the symptoms of advanced levodopa responsive Parkinson's disease (PD) that are not adequately controlled with medication.

- Unilateral thalamic stimulation of the ventral intermediate nucleus (VIM) is indicated for the suppression of tremor in the upper extremity. The system is intended for use in patients who are diagnosed with essential tremor or parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability.

III. CONTRAINDICATIONS

The Boston Scientific Vercise PC, Vercise Gevia and Vercise Genus DBS Systems or any of its components, are contraindicated for:

- **Diathermy:** Shortwave, microwave, and/or therapeutic ultrasound diathermy should not be used on patients implanted with the Boston Scientific DBS System, or any of the system components. The energy generated by the diathermy can be transferred to the Boston Scientific DBS System, causing tissue damage in the brain resulting in severe injury or death.

- **Electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS)** The safety of these therapies in patients implanted with the DBS System has not been established. It is possible that the energy generated by these therapies can be transferred to the DBS System, causing tissue damage that may result in severe patient injury or death.

- **Magnetic Resonance Imaging (MRI).** Patients implanted with the full Vercise PC DBS System (leads, extensions and stimulator) should not be subjected to an MRI. MRI exposure may result in the following:

    - Dislodgement of implanted components
    - Heating of the contacts, or other system components, causing permanent tissue lesioning
    - Damage to the Stimulator's electronics
    - Current induction through the DBS Leads and Vercise PC DBS System causing unpredictable levels of stimulation
    - Distortion of the diagnostic image
    - Personal injury or death

    Note: Vercise DBS lead-only system (before Stimulator is implanted) is MR Conditional. An MRI examination can be conducted safely when all the instructions in the supplemental manual MRI Guidelines for Boston Scientific DBS Systems are followed. MR Conditional labeling for the DBS standard leads (Models DB-2201-30-AC, DB-2201-30-DC, DB-2201-45-BC, DB-2201-45-DC)

and DBS Directional Leads (Models DB-2202-30 and DB-2202-45) was approved in PMA Supplements P150031/S5 and P150031/S11. For the latest version of the manual go to www.bostonscientific.com/manuals.

- **Patient Incapability.** Patients who are unable to properly operate the Remote Control and Charging System should not be implanted with the Boston Scientific DBS Systems.

- **Poor Surgical Candidates.** The Boston Scientific DBS Systems are not recommended for patients who are poor surgical candidates.

- **Unsuccessful Test Stimulation.** The Boston Scientific DBS Systems should not be used in patients who experience unsuccessful test stimulation.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions are provided in the Vercise PC, Vercise Gevia and Vercise Genus DBS System labeling.

V. DEVICE DESCRIPTION

The Vercise PC, Vercise Gevia and Vercise Genus DBS Systems include non-rechargeable and rechargeable Stimulators, with DBS Leads for stimulation of selected targets (i.e., the subthalamic nucleus, globus pallidus internus and ventral intermediate nucleus of the thalamus) in the brain. DBS Extensions are used to connect the DBS Leads to the Stimulator implanted near the clavicle.

The DBS Systems utilize current steering across eight contacts per DBS Lead, which is intended to provide precise positioning of stimulation. The Stimulator is controlled by a handheld Remote Control, and can be programmed by a Clinician Programmer using the Vercise Neural Navigator Software. Periodically, the rechargeable Stimulator battery must be replenished with a radiofrequency (RF) charging device provided in the Charging Kit.

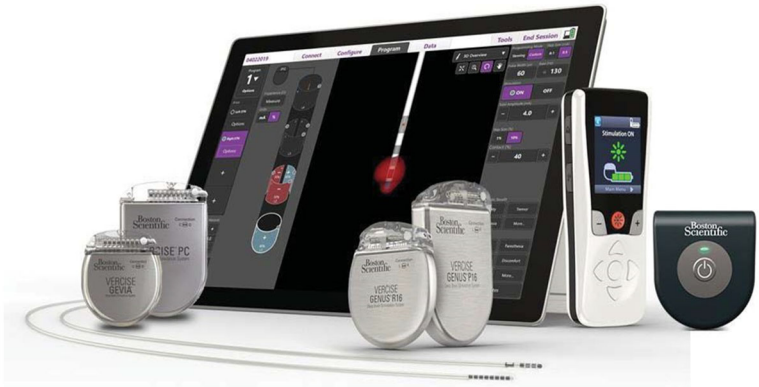

Figure 1. Vercise PC, Vercise Gevia and Vercise Genus DBS Systems

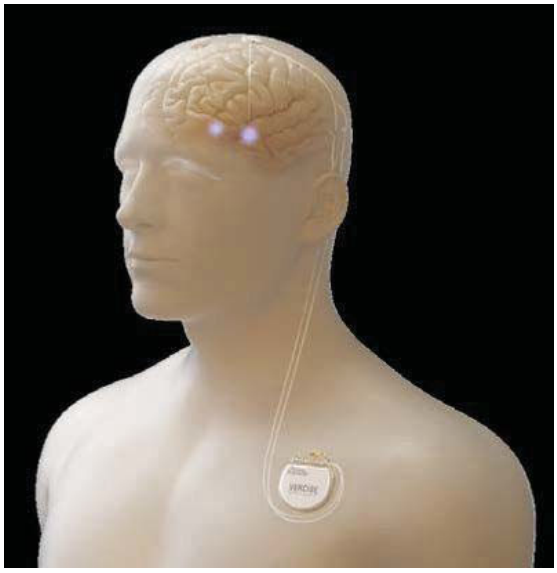

Figure 2. Typical Implant Location

A. Implanted Components

Implantable Pulse Generator (IPG, Model # DB-1140-S, DB-1200-S, DB-1216, DB-1232, DB-1408, DB-1416, DB-1432): 8, 16 and 32-contact, multi- channel, implantable pulse generators. The Vercise PC IPG Model# DB- 1140-S and the Vercise Genus IPG Model #s DB-1408, DB-1416 and DB-1432 have a non-rechargeable power source. The Vercise Gevia IPG Model# DB-1200-S and the Vercise Genus IPG Model #s DB-1216, DB-1232 have a rechargeable power source. The IPGs generate programmable electrical pulses that are conducted to targets in the brain via leads. The IPGs can support up to two 8-contact Leads. A charge density warning appears on the Clinician Programmer when stimulation settings are set to deliver ≥ 30μC/cm^2/phase. All contacts have independent current control. Table 1 below provides a summary of the programmable stimulation parameters.

Table 1: Vercise PC, Vercise Gevia and Vercise Genus DBS System Stimulation Parameters

Parameters	Range
Waveform	Charge balanced asymmetric biphasic
Pulse Shape	Rectangular
Current or Voltage Regulated	Current
Amplitude Range	0 - 12.7 mA per contact (up to 20.0 mA per Area)
Pulse Width Range	20μs - 450μs
Frequency Range[1]	2 - 255Hz
Contact Connections (i.e., Channels)	8, 16 or 32
Independent Areas of Stimulation (4 Programs with 4 Areas per Program)	16
Current Path Options	Unipolar, Bipolar, or Multipolar

[1]The rate is limited to 255 Hz for a given area. The global rate limit for each Lead is also 255 Hz.

- Leads (Model # DB-2201-xx, DB-2202-xx, xx = 30 or 45, i.e., length of 30cm or 45cm): The DBS leads deliver electrical pulses generated by the IPG to targets in the brain. The DBS Lead model DB-2201 has 8 cylindrical ring contacts at the distal end. The DBS Lead model DB-2202 has 2 ring contacts and two rows of directional

contacts that are segmented circumferentially to allow both axial and rotational stimulation selectivity. Each segmented contact covers 90 degrees of the Lead circumference. The lead specifications are provided in Table 2 below.

Table 2: DBS Lead Specifications

Feature	Description	
	DB-2201 Lead	DB-2202 Lead
Number of Contacts	8	8
Contact Length	1.5 mm	1.5 mm
Ring Contact Surface Area	6.0 mm^2	6.0 mm^2
Segmented Contact Surface Area	N/A	1.5 mm^2
Contact Spacing (axial)	0.5 mm	0.5 mm
Contact Span	15.5 mm	7.5 mm
Distal Contact to Tip Length	<1.3 mm	N/A
Diameter	1.3 mm	
Overall Length	30 cm, 45 cm	
Outer Jacket Tubing (Insulation)	Polyurethane	
Contact Material	Platinum/Iridium	
Impedance (Ω)	≤ 90 (measured from each connector to corresponding electrode contact)	

- Lead Extension (Model # NM-3138-55): The DBS Extension consists of a connector at the distal end and 8 cylindrical contacts at the proximal end. The DBS Lead may be inserted and secured into the connector, which also contains 8 contacts that align with the contacts on the DBS Lead to form electrical connections. The proximal end is inserted into the IPG.

- Implantable Accessories:
  - Burr Hole Cover: The Burr Hole Cover is used to permanently secure the DBS lead and to cover the burr hole created in the skull during the surgical implantation of the DBS lead.
  - DBS Lead Boot: The DBS Lead Boot protects the proximal end of the DBS Lead prior to the Stimulator implant surgery.
  - Suture Sleeve: The Suture Sleeve may be used to anchor the DBS Lead or DBS Extension to the fascia.
  - M8 Adaptor: The M8 Adaptor is provided to connect Medtronic Lead models (3387 and 3389) to the Boston Scientific IPG. The M8 Adaptor is compatible with the following Medtronic lead extensions models: 3708640, 3708660, 3708695, 3708540, 3708560, 3708595.

B. External Components

- ETS (Model # DB-5132-S, DB-5170): The External Trial Stimulator (ETS) is a component that may be used for intraoperative testing of stimulation. It provides the identical stimulation capabilities as the IPG.

- Remote Control (Model # DB-5250-S, DB-5270): The Remote Control is a hand-held, battery operated unit that uses telemetry to communicate with the IPG and ETS. It allows the patient to control the stimulation therapy prescribed by the clinician (e.g., turn DBS system on and off).

- Charger (Model # NM-5312): The Charger uses radiofrequency (RF) energy to inductively charge the implanted IPG battery when the Charger is placed externally over the IPG implant site.

- Base Station (Model # NM-5305): The Base Station connects to a wall-mounted power supply and is utilized to recharge the Charger.

- Clinician Programmer (Model # DB-7161, NM-7161, DB-7161R, NM-7161R, DB-7164, NM-7164, DB-7164R, NM-7164R): The Clinician Programmer is used by the clinician to program the IPG and ETS, and thus prescribe stimulation therapy for the patient.

- Non-implantable or External Accessories:
  - Tunneling Tool: used to create a path for the DBS Lead and DBS Extension in the subcutaneous tissue.
  - Lead stop: may be attached to the Lead to prevent the Lead from being advanced beyond a certain depth into the neural tissue during its initial placement.
  - Lead Stylet: inserted in the Lead to keep the Lead stiff during placement.
  - Charging Collar: used to place the Charger externally over the IPG during charging.
  - Charger Spacer: a piece of material placed behind the Charger in the pocket of the Charging Collar.
  - Adhesive Kit: for attaching the Charger to the patient's body during charging. Alternative to Charging Collar.
  - O.R. Cable and Extension: connects the Lead Extension to the ETS during intraoperative testing.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There is no cure for Parkinson's disease (PD) and essential tremor (ET). Therefore, the first-line therapy treatment is medication. The standard medical therapy for PD is levodopa combined with a peripheral decarboxylase inhibitor, such as carbidopa. Other medical therapy may be used as an adjunct to levodopa to treat the multiple symptoms of PD. In patients with ET, both primidone and propranolol reduce the magnitude of upper extremity and postural tremor. Levodopa, anticholinergic medications, dopamine agonists, and beta-blockers such as propranolol are effective drugs for rest tremor. However, these medications come with a variety of side effects. For example, chronic levodopa use can result in disabling motor fluctuations that further impair the patient's ability to function.

Surgical treatments are also available to PD and ET patients. Neurosurgical ablative procedures for the treatment of PD and ET are pallidotomy and thalamotomy. However, there is a risk of permanent neurological damage associated with the irreversible damage caused by these ablation procedures. The most disabling, permanent neurological complications reported include hemiparesis, dysarthria and dysphagia, and cognitive impairment.

Other Deep Brain Stimulation Devices are also currently marketed in the United States.

VII. MARKETING HISTORY

The Vercise PC and Vercise Gevia DBS Systems have been commercially distributed in the EU since September 2015 and June 2017 respectively. They have been commercially distributed in the US since January 2019. They have also been commercially distributed in other European countries, Canada, Australia, Japan, South America, Middle East, Russia, South Korea, and South Africa.

The Vercise Genus DBS System has been commercially distributed in the EU since May 2020. It has been commercially distributed in the US since February 2021. It has also been commercially distributed in Japan.

The device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The adverse events that may occur with the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems are among those that may occur in association with surgical complications or DBS specific complications (device-related or stimulation-related complications).

For the specific adverse events that occurred in the clinical studies, please see Section X below. Based on the technical equivalence described in Section IX below, the clinically established safety profile of the Medtronic Activa Tremor Control System which was approved under P960009 is directly applicable to the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems for treatment of tremor.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Non-clinical Studies

The Vercise PC, Vercise Gevia and Vercise Genus DBS Systems are legally marketed. Device systems were tested previously via non-clinical laboratory testing, including bench testing, biocompatibility evaluation, electromagnetic compatibility, sterilization, packaging, and shelf-life testing. Device design and system compatibility involved verification and validation of each system. The test results were found to be acceptable.

Implantable Pulse Generator (IPG)

Table 3: IPG Verification Testing

Test	Purpose	Acceptance Criteria
IPG Electronics	Verify the requirements for: • Pulse Generation • Internal IPG circuits • RF Telemetry Interface • Battery Protection Circuitry	• The IPG stimulation output parameters match the programmed parameters within the specified tolerances. • Internal IPG circuits shall function within their specified limits. • The IPG RF receiver shall function as specified. • The battery protection circuits shall function as specified.
Environmental and Mechanical Stresses	Verify the integrity and function of the IPG after exposure to environmental and mechanical stress conditions such as: • High and low storage temperature • Temperature changes • Mechanical forces • Random Vibration • High and low atmospheric pressures	The IPG shall pass device level functional tests after exposure to environmental and mechanical stresses.
	Verify the integrity of the header after mechanical stresses and suture pull.	Header shall not show visual damage.
Hermeticity	Verify that the internal moisture content of the hermetically sealed IPG case is within acceptable limits after environmental stresses.	The internal water vapor content shall be within specifications.
Immunity to Medical Procedures /Therapies	Verify that the IPG is functional after exposure to the following medical procedures/therapies: • Diagnostic Ultrasound • Monopolar and bipolar Electrocautery • External Defibrillation • X-Ray	The IPG shall pass device level functional tests after exposure.
IPG-Lead Interface	• Verify that the Lead to IPG connection meets the requirements for insertion, withdrawal and retention forces. • Verify contactresistance. • Verify electrical isolation	• The insertion, extraction and retention forces for the Lead-IPG Connector interface shall meet the specifications after multiple insertion and withdrawal cycles. • The resistance for each contact shall meetthe specifications. • The impedance between any two terminations shall be within the specifications.
Rechargeable IPG Battery	• Evaluate battery life. • Verify cell performance and integrity.	• The evaluation of battery longevity under typical use conditions shall support the labeled battery life. • After exposure to mechanical and environmental stresses, the battery cells must meet the requirements for hermeticity as well as electrical and mechanical integrity. • The battery cells must meet the requirements for self-discharge and storage loss. • After multiple discharge cycles, battery cells must meet visual, mechanical and hermeticity criteria. • The battery cells shall maintain mechanical integrity during and after application of exposure to short circuits and abnormal discharging.

Test	Purpose	Acceptance Criteria
Non-rechargeable IPG Battery	• Evaluate battery life. • Verify cell performance and integrity.	• The evaluation of battery longevity under typical use conditions shall support the labeled battery life. • After exposure to mechanical and environmental stresses, the battery cells must meet the requirements for hermeticity as well as electrical and mechanical integrity. • The battery cells must meet the requirements for self-discharge. • The battery swelling and capacity must meet specifications after discharge. • The battery cells shall maintain mechanical integrity after exposure to short circuits and forced discharging.
Charging (Vercise Gevia)	• Verify that the IPG can be charged at the specified charging distances and operating temperature. • Verify the requirements for heat generated during charging.	• The IPG charging current and charge time shall meet the requirements when the Charger is at a specified distance from the IPG. • The charge rate over the devices operating temperature shall meet the specifications. • The IPG case heating due to heat dissipation during charging shall be within acceptable limits.

DBS Leads, Extensions, and Accessories

Table 4: DBS Leads, Extensions, and Accessories Verification Testing

Test	Purpose	Acceptance Criteria
Physical and Mechanical Characteristics	Verify the physical and mechanical characteristics of : • Lead • Lead Extension • Stylet • Lead Boot • Lead Stop • Burr-Hole Cover	• Lead dimensions, surface finish, Lead straightness shall meet the specifications. • The distal Lead shall experience minimal movement when the proximal Lead is folded at a specified angle. • The Lead shall withstand the specified end-to-end pull force without loss of mechanical or electrical integrity. • The force required to deflect the Lead tip shall meet the requirements. • When exiting the cannula, deflection of the Lead tip shall be within specification. • The Stylet dimensions and deflection force shall meet the specifications. • The Lead Boot shall meet the requirements for fit, smooth profile, seal and retention force when connected to the lead. • The Lead Stop shall meet the dimensional and geometrical requirements and be able to resist translational forces. • The Burr-Hole Cover shall meet the requirements for dimensions, geometric specifications, lead clip placement and assembly. • The Extension shall withstand tunneling and pull forces. • The Lead and Extension shall maintain mechanical and electrical integrity after exposure to flex fatigue.

Test	Purpose	Acceptance Criteria
Electrical Tests	Verify that the Lead and Extension meets the requirements for electrical isolation and continuity of conductor paths.	• Current leakage shall be within specifications in dry and soaked states. • The electrical DC resistance of the Lead and Extension shall meet the specifications.
Interface Tests	Verify the compatibility and interface between Lead, Extension and other Lead accessories.	• The retention force for the connection between Lead, Extension and other Lead accessories shall meet the specifications. • Components shall maintain mechanical and electrical integrity following multiple connection and disconnection cycles between Lead and Lead accessories. • Lead shall maintain integrity after multiple clamp and unclamp cycles with the Burr-Hole Cover. The Lead is securely held in place by the Burr-Hole Cover. • The locking force for the connection between Extension and IPG connector shall meet the specifications.
Storage Conditions	Verify integrity of DBS Leads and Sterile Kit components after exposure to temperature conditions likely to be encountered during shipping and storage.	• Components of DBS System Sterile Kits shall be functional after temperature cycling and after storage in high and low temperatures.

Remote Control

Table 5: Remote Control Verification Testing

Test	Purpose	Acceptance Criteria
Environmental and Mechanical Stress	Verify the integrity and function of the Remote Control after exposure to environmental and mechanical stress conditions such as: • High and low storage temperature • Random Vibration • Drop • Humidity • Button presses representing years of use	The Remote Control shall pass device level functional tests after exposure to environmental and mechanical stresses.
Remote Control Functions	Verify Remote Control functions.	• Remote Control shall respond to each key press as well as typically used combinations with appropriate action and appropriate display on the LCD screen. • RF communication with stimulators shall meet the specifications at the labeled distance. • Remote Control shall display the proper battery level status. • Internal circuits shall function as specified

Charging System

The hardware design verification testing was leveraged from the Precision Charger which is the same device as the Vercise Charger.

Table 6: Charging System Verification Testing

Test	Purpose	Acceptance Criteria
Environmental and Mechanical Stress	Verify the integrity and function of the Charger and Base Station after exposure to environmental and mechanical stress conditions such as: • High and low storage temperature • Temperature changes • Mechanical forces • Random Vibration • Drop • Humidity	The Charger and Base Station shall pass device level functional tests and visual inspection after exposure to environmental and mechanical stresses.
Charger Electronics	Verify functionality of the Charger electronics.	• Protection of charging terminals against over-voltage and over- current conditions shall operate as specified. • The quiescent current, coil voltage and frequency, power dissipation and IPG charge current shall meet the specifications. • The Charger electronics shall function as specified with regards to: – indication of battery status level – charging of the Charger battery – indication of alignment with the IPG – detection of end-of-charge signal when IPG is fully charged – battery protection circuits.
Heating During Charging	Verify the requirements for heat generated during charging.	• The surface temperature of the Charger shall not exceed the acceptable limit while charging.
Base Station	Test for continuity, spring contact fatigue and connector fatigue.	• The resistance between the DC power jack and spring contact shall meet the specifications. • Spring contacts shall remain elastic after repeated deflections. • Power supply plug shall fit and not be loose after repeated • insertion/extraction cycles.

External Trial Stimulator (ETS)

Table 7: ETS Verification Testing

Test	Purpose	Acceptance Criteria
ETS Electronics	Verify the requirements for: • Pulse generation • Operation within the operating temperature range and load range • RF Telemetry Interface	• The ETS stimulation output parameters shall be within the specified tolerances across ranges of temperature and load. • The ETS RF transmitter and receiver shall function as specified.

Test	Purpose	Acceptance Criteria
Environmental and Mechanical Stress	Verify the integrity and function of the ETS after exposure to environmental and mechanical stress conditions such as: • High and low storage temperature • Random Vibration • Drop • Humidity • Button presses representing years of use	The ETS shall pass device level functional tests after exposure to environmental and mechanical stresses.
ETS - O.R. Cable Interface	• Verify that the O.R. Cable to ETS connection meets the requirements for insertion, withdrawal and retention forces.	• The insertion, extraction and retention forces for the ETS-OR Cable Connector interface shall meet the specifications. • Continuity shall be maintained after multiple cycles of insertion and extraction between the OR Cable and ETS

Software
Software testing established that the system meets the software requirements and user needs for the intended uses.

Electromagnetic Compatibility (EMC) and Wireless Technology
EMC testing was performed in accordance with the relevant clauses of the following standards and met specified acceptance criteria:

- IEC 60601-1-2: 2014, "*Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic compatibility - Requirements and tests*" (appropriate essential performance criteria were used)

- ANSI/AAMI/ISO 14708-3:2017: *Implants for surgery – Active implantable medical devices – Part 3: Implantable neurostimulators"*, Part 27

Testing to address compatibility with Radio-frequency Identification (RFID) and Electronic Article Surveillance systems was also provided.

The wireless technology of the system includes Bluetooth and inductive RF telemetry between the Remote Control and the Stimulators and wireless inductive charging of the IPG. These connections were verified to meet the range, security, data integrity and overall system functionality requirements through design verification testing.

Biocompatibility
Biocompatibility of all tissue-contacting components of the Vercise PC, Vercise Gevia and Vercise Genus Deep Brain Stimulation (DBS) System was evaluated in accordance with ISO 10993-1, *Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing within a risk management process*. The Vercise DBS Leads are considered permanent (> 30 days) implants in contact with neural tissue/bone, cerebrospinal fluid (CSF), and blood (indirect contact through CSF). The IPGs, Lead Extensions, Suture sleeves, and Burr-Hole Cover are considered permanent (>30 days)

implants in contact with tissue/bone. The Lead Boot is considered an implant device with prolonged (24 hours – 30 days) tissue/bone contact. and implanted accessories meet the biocompatibility requirements for tissue/bone contacting permanent implants per EN ISO 10993-1:2009 COR2010. The Charging Collar is considered an intact skin- contacting device with limited (≤ 24 hours) contact.

Biocompatibility of the Vercise DBS non-directional Leads was demonstrated by cytotoxicity and neuroimplantation testing on the final, sterilized Vercise DBS Leads, leveraging testing previously conducted on the Linear 8 Contact Lead (Model # SC-2138 and SC-2208) approved in P030017, and leveraging biocompatibility data on U.S. marketed devices with direct blood contact. An ISO MEM elution cytotoxicity test was conducted on the Vercise DBS Lead with passing results. A neuroimplantation study was conducted in a swine model to assess the safety of the Vercise DBS Leads at approximately 30 and 180 days post-implantation. Implantation of the Vercise DBS Leads was not associated with any unexpected adverse effects. Both cytotoxicity and implantation studies on the Vercise DBS Leads were conducted in compliance with Good Laboratory Practices (GLP) regulations (21 CFR Part 58). The sensitization, intracutaneous reactivity, systemic toxicity (acute, subchronic, and chronic toxicity), material-mediated pyrogenicity, genotoxicity, and carcinogenicity endpoints for the Vercise DBS Leads were assessed by leveraging biocompatibility information on the Linear 8 Contact Lead (P030017). This was appropriate because the Vercise DBS Leads and Linear 8 Contact Lead are identical in terms of the tissue-contacting materials and are manufactured and sterilized by the same processes. Hemolysis (indirect contact) endpoint was assessed by leveraging hemocompatibility data on the U.S. marketed devices (approved in P010012/S274 and P050046/S012) with identical tissue-contacting materials as the Vercise DBS Leads.

Biocompatibility of the Vercise Cartesia DBS Directional Leads was based on similarity with the Vercise DBS non-Directional Leads. Both Directional and non-directional Leads have the same tissue-contacting materials and are manufactured and sterilized by the same processes. ISO MEM Elution cytotoxicity and particulate matter release tests were performed on the Vercise Cartesia DBS Directional Leads with passing results. In addition, a neuroimplantation study was conducted in a swine model to assess the safety of the Vercise Cartesia DBS Directional Leads at approximately 90 days post-implantation. Implantation of the Vercise Cartesia DBS Directional Leads was not associated with any unexpected adverse effects.

Biocompatibility of the Vercise PC, Vercise Gevia and Vercise Genus IPGs was demonstrated by leveraging testing previously conducted on the Precision Novi, Precision Spectra and Precision Montage SCS System IPG Models SC-1140 (P030017/S217, S287), SC-1132 (P030017/S134, S245) and SC-1200 (P030017/S235) respectively. Leveraging this testing information was appropriate because the Vercise PC, Vercise Gevia and Vercise Genus IPGs are identical to the Precision SCS System IPGs in terms of the tissue-contacting materials, manufacturing including sterilization processes, and the nature and duration of tissue contact.

The Vercise Lead Extensions are the same lead extensions used in the Precision SCS

System (P030017).

Biocompatibility of the Vercise Suture Sleeves was demonstrated by appropriately leveraging testing previously conducted on Linear 8 Contact Lead (Model # SC-2138 and SC-2208) approved in P030017. The Vercise Suture Sleeves are made of the identical silicone material that is present in the Linear 8 Contact Lead and both devices have permanent (> 30 days) contact with tissue/bone. In addition, an ISO MEM elution cytotoxicity test was conducted on the finished, sterilized 4.0 cm Vercise Suture Sleeve with passing results.

The Burr Hole Cover consists of a Base, Retaining Clip, Cap and two Screws. Biocompatibility of the Base, Retaining Clip, and the Cap was demonstrated by testing conducted on these components in their finished, sterilized forms and by leveraging data in the device master file and in the US marketed devices with identical material. The MEM elution cytotoxicity, guinea pig maximization sensitization, intracutaneous reactivity, intramuscular implantation (13 weeks), acute systemic toxicity, rabbit pyrogenicity, and genotoxicity (Ames, in vitro chromosomal aberration, and mouse micronucleus) tests were conducted on the Base, Retaining Clip, and Cap. All biocompatibility tests were conducted in compliance with GLP regulations (21 CFR Part 58). All pre-specified test acceptance criteria were met for all tests and all tests passed. The data in the device master file and the US marketed devices were leveraged for the assessment of subchronic/chronic toxicity and carcinogenicity endpoints.

Biocompatibility of the Screws was demonstrated by appropriately leveraging biocompatibility data on Precision SCS System IPG Model SC-1110 (P030017) with identical material and nature and duration of tissue contact. In addition, the final, sterilized Burr Hole Cover was used in the swine neuroimplantation study (30 and 180 days) and no device material related adverse findings were noted in the study.

Biocompatibility of the Vercise Lead Boot was demonstrated by leveraging testing previously conducted on the Precision SCS System 55cm 8 Contact Lead Extension (Model SC-3138-55) approved under P030017. Leveraging this testing information was appropriate since the Vercise Lead Boot is identical to the Precision SCS System 55cm 8 Contact Lead Extension (Model SC-3138-55) in terms of the tissue-contacting materials, manufacturing and sterilization processes. In addition, an ISO MEM elution cytotoxicity assay was conducted on the finished, sterilized Vercise Lead Boot with passing results.

Biocompatibility testing was conducted on the finished DBS Charging collar in accordance with GLP regulations (21 CFR Part 58). The agarose overlay cytotoxicity assay, primary skin irritation, and repeated patch dermal sensitization tests were conducted on the DBS Charging Collar, All pre-specified test acceptance criteria were met for all tests and all tests passed.

Sterilization

The IPGs, DBS Lead, Extension, OR Cable, Burr Hole Cover and other implanted accessories are sterilized using a validated EO sterilization cycle to achieve a minimal sterility assurance level of 10^{-6}. Validation of the EO sterilization process for these

devices was done in accordance with EN ISO 11135:2014 *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*. EO residual levels found on these devices following EO sterilization process are shown to be below the maximum allowable limits of EO and Ethylene chlorhydrin (ECH) residual levels specified in EN ISO 10993-7:2008(Cor) 2009 *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals.*

The bacterial endotoxin levels on these device, determined using Limulus Amebocyte Lysate (LAL) testing in accordance with the USP Chapter <161> *Transfusion and Infusion Assemblies and Similar Medical Devices*, and ANSI/AAMI ST72:2011 *Bacterial endotoxins - Test methods, routine monitoring and alternatives to batch testing*, comply with the bacterial endotoxin limits specified in the and FDA's Guidance for Industry - Pyrogen and Endotoxins Testing: Questions and Answers (June 2012).

Packaging and Shelf Life

Packaging performance and stability testing results demonstrated that the packaging system for the sterile components of the BSN Vercise PC, Vercise Gevia and Vercise Genus DBS Systems can withstand the environmental and mechanical stresses likely to be encountered during transportation and storage and maintain its sterile barrier up to two years of the established shelf-life.

B. Technological Comparison

In lieu of providing a clinical data set for treatment of tremor with the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, the sponsor provided a technological comparison (including a comparison of the technology, and instructions for use) of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems to the Medtronic Activa Tremor Control System which was approved under P960009 for the requested indications for use. The purpose of the technological comparison was to establish sufficient similarity of the Boston Scientific and Medtronic DBS devices such that FDA could apply Section 216 of the Food and Drug Modernization Act (FDAMA), i.e., the "six-year rule," to assess the effectiveness profile of Vercise PC, Vercise Gevia and Vercise Genus DBS Systems.

According to FDA's "Guidance on Section 216 of the Food and Drug Modernization Act of 1997" available at: https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073709.pdf, FDA may choose to utilize the publicly available detailed SSED of a previously approved device to support approval of a PMA for a new device if the applicant provides "a detailed justification of how the information in the earlier SSED applies to the applicant's device" and if the applicant is able "to describe how the devices are similar enough to allow for the data from the earlier device to apply to the new device."

For the purposes of establishing sufficient similarity of the Vercise PC/Vercise Gevia/Vercise Genus DBS Systems and the Medtronic Activa Tremor Control System,

the sponsor provided a technical comparison of the devices. The comparisons are summarized as follows:

1. Volume of Tissue Activation (VTA)

   Deep brain stimulation (DBS) systems work by sending electrical stimulation from an implanted neurostimulator to leads in the brain where the current is dispersed through electrodes into the brain tissue in order to activate neurons in specific brain regions. The clinical response of stimulation varies depending on the brain target and the orientation of the DBS lead within the target. As part of DBS programming, the clinician can adjust the combination of parameters, including amplitude, pulse width, frequency and electrode configuration, to tailor the stimulation field to the needs of each patient. By comparing the VTA of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems to the Medtronic Activa Tremor Control System it was determined that the Vercise DBS Systems stimulate, and thus activate, neurons with volume of brain tissue equivalent to that which was shown to be safe and effective for the Medtronic Activa Tremor Control System approved in P960009.

   VTA modeling has been used to estimate the degree of neuronal activation and by extension the degree of stimulation efficacy [1]. Thus, the sponsor provided comparative modeling of the VTA between the stimulation produced by Vercise PC/Vercise Gevia/Vercise Genus DBS System IPGs and the associated non-directional (DB-2201) and directional (DB-2202) leads and the Medtronic Activa Tremor Control System using the Soletra IPG Model 7426 approved in P960009/S009 with the same tremor indication and the Medtronic lead (Model 3387) that was approved in P960009. The Model 7424 Itrel II IPG was original IPG used in the clinical trials for the approval of the treatment of tremor under P960009. The Model 7424 Itrel II IPG was updated and rebranded as the Soletra IPG model 7426 under PMA Supplement P960009/S009 with the same Tremor indication. No significant waveform differences were measured among the Soletra or Itrel II IPGs [2]. Thus, the VTA model provided for the Model 7426 Soletra IPG is directly applicable to the Model 7424 Itrel II IPG.

   The electric fields generated during stimulation by the DBS electrodes were calculated from the Poisson equation with a finite element model (FEM) solver to determine space-dependent voltage within the tissue medium [1, 2]. Finite element models were constructed to calculate the electric fields produced by DBS leads in a homogenous tissue medium, and the calculated voltages in space were applied to non-linear axon models in accordance with methods described in the literature for evaluation of DBS electrode design and characterization of field shape [1,2]. There are no differences in assumptions and boundary conditions between the previous modeling papers and the modeling data presented by the sponsor.

   The Boston Scientific Vercise PC, Vercise Gevia and Vercise Genus IPG waveform includes a current regulated stimulation phase and is passively charged balanced, while the Medtronic Model 7426 Soletra IPG waveform is voltage regulated. The waveform was accounted for in this modeling. Both waveforms

were measured from their respective IPGs [2] and the components of the waveform were fed into the model, in addition to appropriate electrode geometry, including edge-to-edge spacing, array length, electrode surface area, and electrode configuration. The following output stimulation parameters were used as the basis for the input parameters for the model: amplitude, pulse width, frequency, and stimulation mode (monopolar or bipolar). The sponsor consulted literature (Koller et al, 2001) and data reported for clinical trials for the Medtronic Activa Tremor Control System as described in the SSED for P960009 and chose values representative of the ranges of parameters reported. The sponsor chose combinations of parameters to create low and high nominal values as typically used parameters for VIM stimulation in Tremor (i.e., 1.5 – 5.0 V, 30 – 120 μs, and 130–185 Hz). The following scenarios were modeled for the Medtronic leads and the Boston Scientific 8 channel non-segmented (DB-2201) and segmented (DB-2202) leads, where current was titrated to achieve a comparable VTA:

Table 8: Parameters Used in Models of the Medtronic Model 7426 Soletra VTAs

Lead	Configuration	Voltage	Pulse Width[§]	Frequency
Medtronic 3387	Monopolar	1.5 V	60 μs	130 Hz
Medtronic 3387	Monopolar	5 V	120 μs	185 Hz
Medtronic 3387	Bipolar	1.5 V	60 μs	130 Hz
Medtronic 3387	Bipolar	5 V	120 μs	185 Hz

[§] 60 μs is the minimum programmable pulse width available for the Medtronic Soletra

A total of 14 unique VTAs were modeled in combination for both Medtronic and Boston leads. For the Medtronic lead, 6 unique VTAs result from the 4 settings listed in Table 8; the Monopolar configurations were modeled for both MDT electrode '0' and electrode '1'. For each Boston Scientific lead, 4 unique VTAs were modeled, corresponding to Table 8 settings, resulting in 8 total Boston Scientific VTAs. These VTAs represented relevant output parameters, configurations, and lead types (non-directional (non-segmented) and directional (segmented)). The scenarios were created to demonstrate the capability of both the Boston Scientific Vercise 8-contact non-directional lead (DB-2201) and the Boston Scientific Vercise Cartesia 8-contact directional lead (DB-2202) to produce a VTA comparable to that produced by the Medtronic 3387 4-contact lead. Then for each Medtronic VTA, amplitude was titrated with the Boston Scientific DB-2201 and DB-2202 leads to achieve a VTA comparable to that achieved by the Medtronic lead.

Results:
The modeled Boston Scientific leads were able to achieve a comparable VTA volume and shape when compared the Medtronic lead.

In all the scenarios above the percent deviation of the VTAs of the Boston Scientific leads from the VTA of the Medtronic lead ranged between **0.61%** (meaning greater coverage for Boston Scientific leads) and **-3.26%**.

Conclusions:
The results show that parameters of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems can be varied to achieve a VTA comparable to that achieved by the Medtronic Activa Tremor Control System approved in P960009; the range of deviation is acceptable. These results also demonstrate that a desired VTA can be achieved by adjusting stimulation parameters on any of the lead models (Boston Scientific lead models DB-2201 and DB-2202, Medtronic lead model 3387).

The clinical response to stimulation varies depending on the brain target and the position and orientation of the DBS lead within the target. As part of DBS programming, the clinician can adjust the combination of parameters, including amplitude, pulse width, frequency and electrode configuration, to tailor the stimulation field to the needs of each patient. Parameters can be adjusted to achieve a desired VTA, with shaping customized on a patient by patient basis.

2. Output Parameters

Table 9: Device Comparison Summary Table of Medtronic Activa Tremor Control System Model 7424 IPG to Vercise PC, Vercise Gevia and Vercise Genus DBS System IPGs

	Vercise PC/ Gevia/Genus	7424 Itrel II	Safety	Efficacy
Amplitude (settings)	0 - 12.7 mA per contact (max 20.0 mA per area)	1 – 10.5V	Both confined by charge density limit (30 μC/cm^2). Parameters verified via Boston Scientific Parkinson's study to be safe for use in the STN which is also relevant to the VIM.	Can be programmed within clinically relevant parameter ranges, wider ranges that are available through BSN IPGs provide additional programming flexibility.
Frequency (settings)	2 - 255 Hz	2 – 185 Hz	Parameters verified via the Boston Scientific Parkinson's Study to be safe for use in the STN which is also relevant to the VIM.	Can be programmed within clinically relevant parameter ranges, wider ranges that are available through BSN IPGs provide additional programming flexibility.
Pulse width (settings)	20 – 450 μsec	60 – 450 μsec	Both confined by charge density limit (30 μC/cm^2).	Can be programmed within clinically relevant parameter ranges, wider ranges that are available through BSN IPGs provide additional programming flexibility.
Number of Programs	4	1	All programs created must be within the available safe parameters.	Can be programmed within clinically relevant parameters, additional parameters provide programming flexibility

	Vercise PC/ Gevia/Genus	7424 Itrel II	Safety	Efficacy
Independent Frequency/ Hemisphere	Yes	No	All programs created must be within the available safe parameters.	Can be programmed within clinically relevant parameters, additional parameters provide programming flexibility
Stim on/off	1 seconds – 90 minutes	IPG has a Cycling Mode (cycling period not stated)	BSN Stimulators ensure charge balance condition for all settings.	Can be programmed within clinically relevant parameters.
Output waveform	Rectangular	Rectangular	Same	Same
Charge balance	Passive discharge	Active discharge	System requirements have been incorporated into the product design to ensure that stimulation pulses are balanced with appropriate discharge.	Waveform shown to be effective in eliciting and inhibiting action potentials as shown in approval for STN stimulation which is also grey matter.
Pulse delivery modes	Continuous and Cycle	Continuous	System requirements have been incorporated into the product design to ensure that stimulation pulses are balanced with appropriate discharge.	Continuous and cycling effective in eliciting and inhibiting action potentials cycling can help prevent habituation
Current distribution to electrodes	Stimulators control the amount of current at each electrode independently during a stimulation pulse	Single voltage source. Impedance dictates the amount of current at each electrode	Stimulation is delivered at clinician prescribed stimulation settings over time.	Impedance changes do not affect stimulation delivery. The prescribed current is maintained at each electrode regardless of impedance changes.

The table above demonstrates that the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems have the capability to replicate at least the same output as the Medtronic Activa Tremor Control System indicating it can provide at least a comparable level of efficacy. Though the waveforms of Vercise PC/Gevia/Genus and Model 7424 Itrel II/Model 7426 Soletra differ in their method of charge balancing they all have the capability to inhibit and excite action potentials. The degree of neuronal activation with DBS is proportional to the amount of charge delivered. The intensity of the charge delivered (charge density) also has implications for clinical safety. For parameters that differ between the devices, Table 9 above shows that the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems ensure safety by providing a charge density limit (30 $\mu C/cm^2$) and preventing charge imbalance conditions. As the electrode surface area of the

Boston Scientific DBS Leads is less than or equal to that of the Medtronic Leads, the maximum charge at the charge density limit is less than or equal to the Medtronic system. The maximum power and power density is limited by the charge density limit.

The Boston Scientific INTREPID Parkinson's study of STN stimulation provides further assurance of the safety of the additional parameters provided by the Vercise PC, Vercise Gevia and Vercise Genus devices. The study was used to support the safety of DBS at therapeutic levels for Parkinson's disease. Although patients in the study were implanted in the STN, both STN and VIM are grey matter nuclei that can be stimulated to treat some of the symptoms of Parkinson's disease.

3. Leads

See VTA analysis in Section IX(B)(1) above. Table 10 below provides an additional comparison of Lead attributes.

Table 10: Comparison between Vercise PC, Vercise Gevia and Vercise Genus DBS System Leads and Medtronic Activa Tremor Control System Lead

	Boston Scientific DBS Leads		**Medtronic DBS Lead Models 3387**	**Clinical Equivalence**
	Standard 8-contact DBS Lead Model DB-2201	**Directional 8-contact DBS Lead Model DB-2202**		
Electrode configuration	1-1-1-1-1-1-1-1  8 electrode configuration, no active tip	1-3-3-1  8 electrode configuration, active tip	1-1-1-1  4 electrode configuration, no active tip	See VTA analysis in Section IX(B)(1). Additionally, the Directional Lead has the same stimulation output capabilities with additional programming options. 1st and 4th contact rows provide omnidirectional stimulation. 2nd and 3rd rows can use all 3 segments to provide omnidirectional stimulation that is clinically equivalent or use segmented electrodes

	Boston Scientific DBS Leads		Medtronic DBS Lead Models 3387	Clinical Equivalence
	Standard 8-contact DBS Lead Model DB-2201	**Directional 8-contact DBS Lead Model DB-2202**		
Active tip	No	Yes	No	The presence of Active Tip at the tip of the Directional array (contact 1), results in one contact (tip) with the same larger surface area as the other ring contacts. From a stimulation efficacy perspective, the clinical response of stimulation varies depending on the brain target and the orientation of the DBS lead within the target. See VTA analysis in Section IX(B)(1).
Electrode material	Platinum/Iridium	Platinum/Iridium	Platinum/Iridium	Same
Conductor Wire	Nickle based alloy with platinum core	Nickle based alloy with platinum core	Platinum/Iridium	Conductor material facilitates delivery of stimulation current with minimal loss. From a stimulation perspective they are clinically equivalent.
Lead Body	55D Polyurethane	55D Polyurethane	80A Urethane	All leads are made up of biocompatible materials. The minor differences in materials have no impact on the biological safety or function of these leads.
Electrode Surface area	6 mm^2	Ring electrodes: 6 mm^2 Segmented electrodes: 1.5 mm^2	5.98 mm^2	See VTA analysis in Section IX(B)(1).
Number of electrodes	8	8	4	See VTA analysis in Section IX(B)(1).
Contact length (mm)	1.5	1.5	1.5	Same
Contact spacing (mm)	0.5	0.5	1.5	See VTA analysis in Section IX(B)(1).

	Boston Scientific DBS Leads		Medtronic DBS Lead Models 3387	Clinical Equivalence
	Standard 8-contact DBS Lead Model DB-2201	Directional 8-contact DBS Lead Model DB-2202		
Array length (mm)	15.5	7.5	10.5	See VTA analysis in Section IX(B)(1).
Leads length (cm)	30, 45	30, 45	28, 40	Lead length does not impact the delivery of stimulation to the targets.
Lead diameter (mm)	1.3	1.3	1.27	See VTA analysis in Section IX(B)(1).

As outlined in Table 10 above, the Vercise PC, Vercise Gevia and Vercise Genus DBS System and the Medtronic Activa Tremor Control System Leads are clinically equivalent. Although there are differences in some physical aspects of the Leads, those differences have been demonstrated not to impact the safe and efficacious delivery of the stimulation to the targeted location.

4. Extensions

The table below shows a comparison between attributes of the Boston Scientific DBS Extension and the Medtronic Extension.

Table 11: Comparison between Boston Scientific DBS System Extension and Medtronic Activa Tremor Control System Extension

	Boston Scientific DBS 8-contact Extension Model NM-3138	**Medtronic DBS Extension Model 7495**	**Clinical Equivalence**
Body diameter (mm)	1.35	2.6	The diameter does not impact the delivery of electrical stimulation to the target location through the lead contacts.
Body construction	Continuous	Continuous	The body construction for both extensions is continuous and therefore they are clinically equivalent.
Lengths (cm)	55	51	The additional lengths offered for the Boston Scientific Extensions are available for physicians to use as appropriate for different patient anatomies and do not impact safety and effectiveness of the system as the delivery of effective stimulation is not impacted by the length of the Extension.
Number of distal (lead) contacts	8	4	The variance in the number of contacts is a function of the actual Lead with which the Extension is used. For example, an 8-contact Lead would require 8 distal contacts in order to adequately connect to the Extension and deliver therapy from the IPG to the target location. The difference is the number of contacts does not impact safety and effectiveness because the stimulation can be effectively transmitted along the Extension regardless of the number of contacts.
Wiring	Straight, not coiled	Coiled	Conductor facilitates delivery of stimulation current with minimal loss. From a stimulation perspective they are clinically equivalent.
Locking mechanism	1 setscrew	4 setscrews	Locking mechanisms are designed and tested to provide adequate retention force of the Lead within the Extension header. Although the Boston Scientific Extension has fewer setscrews, testing establishes that a single setscrew provides sufficient retention force of 14 N or greater for its safe and efficacious use which is a force greater than what would occur clinically.

	Boston Scientific DBS 8-contact Extension Model NM-3138	Medtronic DBS Extension Model 7495	Clinical Equivalence
Patient Contacting Materials			
Extension Header	Silicone: Nusil MED 4860 Nusil MED 4870 Nusil MED 1137 Nusil MED1-161	Silicone rubber	The Extension is made up of biocompatible materials. The minor differences in materials have no impact on the biological safety or function of the Extension.
Extension Body	55D Polyurethane	Silicone Rubber and polyurethane	The Extension is made up of biocompatible materials. The minor differences in materials have no impact on the biological safety or function of the Extension.

As outlined in Table 11 above, the Vercise PC, Vercise Gevia and Vercise Genus DBS System and the Medtronic Activa Tremor Control System Extensions are clinically equivalent. Although there are differences in some physical aspects of the Extensions, those differences have been demonstrated not to impact the safe and efficacious delivery of the stimulation to the targeted location.

5. Accessories

Since IPGs, Leads and Extensions play a direct role in the delivery of therapy to patients, detailed equivalence assessments (technical, biological and clinical) are provided. However, the assessment of PMA approved system accessories is focused on how each accessory functions and contributes to the effective delivery of therapy, including how its dimensions, materials and mechanical properties allow it to safely perform that function. Table 12 below provides this comparison and establishes that there are no differences that impact the safety and effectiveness of the respective systems during use for a VIM target location.

Table 12: Comparison between Vercise PC, Vercise Gevia and Vercise Genus DBS System accessories and Medtronic Activa Tremor Control System accessories

Accessories Name	Vercise PC/ Gevia/Genus	Activa	Function	Clinical Equivalence
IPG Implant Accessories				
Torque Wrench	Yes	Yes	Secure the Extensions in the IPG	The mechanical properties and dimensions are compatible with the IPG/Lead to safely ensure system performance (e.g. lead connection to IPG)

Accessories Name	Vercise PC/ Gevia/Genus	Activa	Function	Clinical Equivalence
Port Plug	Yes	Yes	Prevent tissue and fluid ingress into unused ports	The mechanical properties and dimensions are compatible with the IPG to safely ensure system performance (e.g. IPG port enclosure). From a material perspective, port plugs are considered biocompatible for their intended use per ISO 10993.
Pocket Adapter	Yes	Yes	To adapt Medtronic extensions to the neurostimulator	Boston Scientific provides the M8 Adapter to connect Medtronic Extensions to the Boston Scientific IPG. The mechanical properties and dimensions are compatible with the IPG/extensions to safely ensure system performance (e.g. via electrical connection). From a material perspective the adapters are considered biocompatible for their intended use per ISO 10993. The Boston Scientific Extensions connect directly to the IPG. The absence of a pocket adapter does not impact clinical safety or performance.
Patient Magnet	No	Yes	Used to perform magnet enabled functions on the IPG	The Vercise PC, Gevia and Genus IPGs do not have any magnet enabled functions. The absence of a patient magnet does not impact clinical safety or performance.
Pocket Template	Yes	Yes	Create an IPG implant site that is appropriate for the IPG size	The dimensions match the dimensions of the IPG for use during the implant procedure. From a materials perspective the Pocket Templates are considered biocompatible for their intended use per ISO 10993.
External Trial Stimulator Accessories				
OR Cable	Yes	Yes	Connects Lead or Extension to an External Stimulator to evaluate lead placement location and integrity during the procedure	The dimensions and mechanical properties are compatible with the External Stimulator and Leads to safely ensure system performance (e.g. via electrical connection). From a material perspective the OR Cables are considered biocompatible for their intended use per ISO 10993.

Accessories Name	Vercise PC/ Gevia/Genus	Activa	Function	Clinical Equivalence
Lead Surgical Accessories				
Lead Stop	Yes	Yes	To mark the depth of the Lead during implantation.	The mechanical properties and dimensions are compatible with the Leads to safely ensure system performance (e.g. marking a specific position on the Lead). From a material perspective, the Lead Stop is considered biocompatible for its intended use per ISO 10993.
Lead Boot	Yes	Yes	To protect the electrodes from damage.	The mechanical properties and dimensions are compatible with the Leads to safely ensure system performance (e.g. isolation and protection of the Lead). From a material perspective, the Lead protection boot is considered biocompatible for its intended use per ISO 10993.
Burr Hole Cover	Yes	Yes	To permanently secure the DBS Lead and to cover the burr hole created in the skull during the surgical implantation of the DBS Lead.	The mechanical properties and dimensions are compatible with the Leads to safely ensure system performance (e.g. secure the Lead). From a material perspective, the Burr Hole Cover is considered biocompatible for its intended use per ISO 10993.
Suture Sleeves	Yes	No	Used to protect the Lead when using a miniplate. May also be used to anchor the DBS Lead or DBS Extension to the fascia.	The mechanical properties and dimensions are compatible with the Leads to safely ensure system performance (e.g. secure the Lead). From a material perspective, the Suture Sleeves are considered biocompatible for its intended use per ISO 10993

6. Remote Control/Therapy Controller capabilities

The patient Remote Control for Vercise PC/Gevia/Genus IPGs and the Patient Magnet for the Medtronic 7424 Itrell II IPG can turn Stimulation On/Off.

Vercise PC/Gevia/Genus Remote Control has the additional ability to:

- Check status of Stimulation On/Off
- Switch between up to 4 programs, as set by the physician in the Clinician Programmer.
- Adjust amplitude within limits set by the physician in the Clinician Programmer.

These additional capabilities do not affect the therapy as prescribed by the physician.

7. Labeling

The instructions for use are equivalent regarding implant procedures, stimulation related device programming (see Table 9 above) and other instructions for use. The devices also have equivalent labeling for contraindications, warnings, precautions, and adverse events.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

A. Summary of Study to Support Approval of the Medtronic Activa Tremor Control System approved in P960009

Because of the technological similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems to the Medtronic Activa Tremor Control System approved under P960009, as described in Section IX above, the clinical studies used to provide evidence of the reasonable assurance of the safety and effectiveness of the Medtronic Activa Tremor Control System under P960009 apply equally well to the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems. The clinical studies used to establish reasonable assurance of the safety and effectiveness of the Medtronic Activa Tremor Control System are summarized as follows. Additional details of these studies are provided in the SSED for P960009 that is available on the CDRH website.

Tremor was studied in two multicenter trials (US and European Tremor Trials) using the Medtronic Activa Tremor Control System. These clinical studies used the Unified Parkinson's Disease Rating Scale (UPDRS) and the Tremor Rating Scale (TRS) to assess the effect of stimulation on tremor of the upper extremity in patients with Parkinson's disease and essential tremor, respectively. The DBS Lead was implanted in the ventral intermediate nucleus of the thalamus after a preimplant evaluation

US Tremor Trial

This was a prospective, controlled, multicenter clinical study with a randomized assessment at three months. The suppression of tremor due to essential tremor or Parkinson's disease was evaluated at 1, 3, 6, 9, and 12 months post-implant. At the 3 month visit, patients were randomized to stimulation ON or OFF, and tremor assessment was done in a randomized, controlled manner. Effect of the tremor suppression (with stimulation ON vs. OFF) was assessed by the investigator using the Tremor Rating Scale (TRS) for essential tremor (0 to 4), and the Unified Parkinson's Disease Rating Scale (0 to 4). Activities of daily living (secondary outcome measure) were evaluated with the stimulation ON.

European Tremor Trial

This study was designed as a prospective, clinical investigation of the treatment of tremor using the Activa System.

The UPDRS was used to evaluate patients with Parkinson's Disease, and the TRS was used to evaluate essential tremor patients. Patients were assessed at 3, 6, and 12 months with stimulation ON and stimulation OFF. Therapy adverse event and system complication profiles were collected prospectively.

B. Results Used to Establish Reasonable Assurance of Safety of Vercise PC, Vercise Gevia and Vercise Genus Systems for Treatment of Tremor

1. Safety Results for P960009

   The most common adverse events reported in the US trial (≥ 5% of patients) were postoperative pain, lead repositioning. stimulation not effective, paresthesia, dysarthria, disequilibrium, and paresis. Details of the safety results are provided in the SSED for P960009 that is available on the CDRH website.

   The adverse events attributed to the therapy (deep brain stimulation) which occurred in more than one patient were paresthesia, dysarthria, disequilibrium, paresis, dystonia, gait disorder, initial jolt, headaches, pain, discomfort, local stress, attention deficit, dysphasia, initial tingling, insufficient therapeutic effect, ataxia, dyskinesia and sensory deficits. Adverse events attributed to the therapy which occurred in in one patient each included facial weakness, fatigue, intention coordination, loss of energy, numbness, other speech deficits, rebound, and transient heaviness in arm. The number and percentage of patients with adverse events (any one or more) in the US and European Tremor Trials for patients with essential tremor was 43 of 78 (55%) compared to 33 or 111 (30%) for patients with Parkinson's disease. The number and percentage of adverse events (any one or more) in the European Tremor Trial for all patients implanted bilaterally was 4 of 27 (15%) compared to 10 of 85 (12%) of patients implanted unilaterally.

   Most (70%) of the therapy-related adverse events were tolerated by the patients and involved no clinical intervention. Stimulation parameters were adjusted in 22% of the cases. Other interventions included: patient education; adjustment of concomitant medications; and instructions to discontinue stimulation. Nine patients required lead repositioning to regain therapeutic effect.

   Five essential tremor patients had their Activa Tremor Control Systems explanted. Four patients were explanted due to loss of effectiveness. One patient was explanted due to infection.

   Of the 114 Parkinson's disease patients (US and Europe), disease progression was reported in ten patients, exacerbation of tremor in three patients (both occurred in one patient). These events were listed as adverse events, but attributed by the investigator to disease progression.

   Three suicides were reported during the clinical studies. One patient implanted in the periventricular gray in a DBS for Pain clinical trial reported suicidal ideation present at high stimulation amplitudes. The suicide ideation was resolved when the stimulation parameters were decreased. Depression was reported in two patients in the tremor clinical studies. The depression was judged by the investigators to be related to disease progression and not to the therapy and procedure.

Ten patients died during the clinical studies. One patient suffered significant neurological decline resulting from a postoperative intracranial hemorrhage, and died two weeks after surgery. Two patients died from perioperative myocardial infarctions. The other seven patient deaths were judged unrelated to the therapy and procedure.

An autopsy report in one patient using a different lead showed histopathological changes within 2 mm of the implanted lead. There was no report of an associated change in the patient's neurologic status or the therapeutic effect of the stimulation.

A total of 11 leads were explanted during the US and European Clinical Studies. Of these leads, six were replaced once. No patients had leads removed and replaced more than once, and no leads were left in place while a second lead was implanted on the same side.

2. Safety Results for P150031

INTREPID Study

The INTREPID Study is a multi-center, prospective, double-blind, randomized, controlled study performed by Boston Scientific that was design to evaluate the safety and effectiveness of the Vercise DBS System for bilateral stimulation of the STN as an adjunctive therapy for improving dyskinesia and other symptoms in adults with advanced, levodopa-responsive bilateral Parkinson's disease which is not adequately controlled with medication. This study was used to support approval of the Vercise DBS System under P150031. Additional details of this study is provided in the SSED for P150031 that is available on the CDRH website. The Vercise PC, Vercise Gevia and Vercise Genus DBS Systems were approved under P150031/S001 and P150031/S034 based on a similarity of technological characteristics to the Vercise DBS System. Although the data were used to support the safety of DBS at the STN, findings have applicability to the safety of stimulation at the VIM since the STN and VIM are both grey matter nuclei and the technological characteristics are similar. Stimulation related adverse effects typically can be resolved at either of the grey matter locations by adjustments to stimulation parameters.

The initial epoch of the study was a period of 12 weeks during which subjects remained blinded to their treatment assignment, and during which a blinded assessor (who was unaware of the subject assignment) completed all study assessments (i.e., double blind study design). Subjects were randomized in a 3:1 ratio to either receive Active or Control settings. Subjects in the Active group received therapeutic settings titrated by the treating neurologist to best clinical effect. Subjects in the Control group received sham stimulation where the stimulation was not set to therapeutic levels. At the Week 12 post-randomization visit, all subjects began an open-label period, with a follow-up period up to 5 years.

The primary safety endpoint of the study included the rates of occurrence of pre-specified adverse device effects at 52 weeks post-randomization. Additional safety parameters evaluated in the study included the rates of occurrence of all serious adverse events and all adverse device effects, including serious adverse device

effects and unanticipated adverse device effects at 5 years post-randomization.

The data used in consideration of PMA P150031 reflected data collected through December 31, 2016, and included 292 patients from 23 investigational sites. A total of 788 adverse events in 143 subjects were reported at the time of the data snapshot. Of these, 74 events were reported as serious adverse events. Of 74 serious adverse events, 19 were related to hardware, 2 related to stimulation, and 31 related to procedure. Infection has been the most commonly reported serious adverse event associated with device-hardware/procedure (8 events, representing 2.7% of subjects). There were three events (each) of device-hardware/procedure- related serious adverse events of peri-operative intracranial hemorrhage (representing 1% of subjects) and seizure (representing 1% of subjects). These events are comparable to published reports.

C. Results Used to Establish Reasonable Assurance of Effectiveness of Vercise Gevia and Vercise Genus Systems for Treatment of Tremor

1. Effectiveness Results for P960009:US Tremor Trial

   A modified Mini Mental Status Examination completed by the patients in the US Tremor Study showed no cognitive effects related to the tremor control therapy.

   Activities of daily living (AOL) showed statistically significant improvement in seven scales for essential tremor patients. In patients with Parkinsonian tremor, ADL scores showed a trend in improvement in four scales, but only the tremor-specific AOL showed statistically significant improvement. Patients' assessment (subjective evaluation) of their disability was improved in both groups when compared to a preimplant assessment. During the clinical trial, 17 Parkinson's disease patients increased use and eight decreased use of levodopa. Six patients decreased use of anticholinergics.

   Rebound is a phenomenon in which a patient's tremor appears clinically exaggerated (compared to baseline tremor) after turning off the stimulator. The exaggerated tremor generally stabilizes (returns to normal) within approximately 30 minutes. In the US clinical study, a maximum of 29% of Parkinson's disease patients, and 28% of essential tremor patients experienced rebound lasting for a mean duration of 17 minutes and 22 minutes, respectively.

2. Effectiveness Results for P960009: European Tremor Trial
   Activities of daily living and other functional improvements were statistically significant in both essential tremor and Parkinson's disease patients.

   During the clinical trial, 17 Parkinson's disease patients increased use and 11 decreased use of levodopa. Two patients decreased use of anticholinergics.

D. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation.

The pivotal clinical study for the Boston Scientific Vercise DBS System included 48 investigators of which none were full-time or part-time employees of the sponsor and only one had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: none
- Significant payment of other sorts: one investigator
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: none

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

The pivotal clinical studies for Medtronic Activa Tremor Control System under P960009 included 23 investigational sites. The SSED does not provide any information with respect to Financial Disclosures since this information was not required to be placed in the SSED at the time of that PMA approval.

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

In accordance with the provisions of section 515(c)(3) 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. Conclusions Drawn from Nonclinical Studies

The Vercise PC and Vercise Gevia DBS Systems were approved for stimulation of the STN in P150031/S001 and stimulation of the GPi in P150031/S028. The Vercise Genus DBS System was approved for stimulation of the STN and GPi in

P150031/S034. The pre-clinical studies provided to support approval in P150031/S001 and P150031/S034 are directly applicable to this PMA because the only requested change is to the indications for use to include treatment of tremor, and this change would not affect the non-clinical testing.

B. Effectiveness Conclusions

In this PMA Supplement, the sponsor provided adequate evidence of the sufficient similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems with regard to its technological characteristics as described in Section IX(B). Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Tremor Control System approved under P960009, in support of the reasonable assurance of its effectiveness, is directly applicable towards establishing reasonable assurance of the effectiveness of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems for treatment of tremor.

As detailed in the SSED for the Medtronic Activa Tremor Control System, in the prospective US Tremor Study of the Medtronic Activa Tremor Control System, activities of daily living showed statistically significant improvement in both essential tremor and Parkinson's disease patients. For the prospective European Tremor Study, activities of daily living and other functional improvements were statistically significant in both essential tremor and Parkinson's disease patients.

C. Safety Conclusions

In this PMA Supplement the sponsor provided adequate evidence of the sufficient similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems to the Medtronic Activa Tremor Control System with regard to its technological characteristics, as described in Section IX(B). Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Tremor Control System approved under P960009 is directly applicable towards establishing reasonable assurance of the safety of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems for treatment of Tremor.

As detailed in the SSED for the Medtronic Activa Tremor Control System, the frequency of adverse events reported in the US and European Tremor Trials did not differ markedly from the frequencies reported for DBS in the European Basic Study and DBS for Pain Study that were performed to generate a safety profile for the Activa System.

Boston Scientific also performed a multi-center, prospective, double-blind, randomized, controlled study (INTREPID Study) that was design to evaluate the safety and effectiveness of the Vercise DBS System for bilateral stimulation of the STN as an adjunctive therapy for improving dyskinesia and other symptoms in adults with advanced, levodopa-responsive bilateral Parkinson's disease which is not adequately controlled with medication. This study was used to support approval of the Vercise

DBS System under P150031. Additional details of this study are provided in the SSED for P150031 that is available on the CDRH website. The Vercise PC, Vercise Gevia and Vercise Genus DBS Systems were approved under P150031/S001 and P150031/S034 based on a similarity of technological characteristics to the Vercise DBS System. Although the data were used to support the safety of DBS at the STN, findings have applicability to the safety of stimulation at the VIM because of similarity of the technological characteristics. Location of the stimulation is different, but stimulation related adverse effects can be resolved at either of the grey matter locations by adjustments to stimulation parameters.

D. Benefit-Risk Determination

The probable benefits of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems are based on data collected in the clinical study conducted to support PMA approval of the Medtronic Activa Tremor Control System. As described above, the sponsor also provided adequate evidence of the sufficient similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems with regard to its technological characteristics as described in Section IX(B) such that FDA could apply Section 216 of the FDAMA and cite safety and effectiveness data presented in the SSED for the Medtronic Activa Tremor Control System in support of a determination of reasonable assurance of the effectiveness of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems for treatment of tremor.

The probable risks and safety profile of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems are the same as for the Medtronic Activa Tremor Control System due to similarity of the technological characteristics.

As documented in the SSED for the Medtronic Activa Tremor Control System, "Clinical studies using the Activa™ System demonstrated that in patients with essential tremor and Parkinson's disease, tremor was suppressed. Furthermore, in patients with essential tremor, the therapy had a positive impact on their activities of daily living and need for medication. The majority of adverse events consisted of paresthesia (33%) followed by dysarthria (9%). These adverse effects can be minimized by changing stimulation parameters, if necessary. An alternative therapy for tremor which is not adequately controlled by medications is thalamotomy. Since the effects produced by deep brain stimulation are reversible in most cases, surgery is still an option if stimulation becomes ineffective. Therefore, it is reasonable to conclude that the benefits of use of the Activa ™ System for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use."

Patient Perspectives:

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information identified above and its applicability to the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, the data support that

for the requested indications for use the probable benefits for the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems outweigh its probable risks.

E. Overall Conclusions

The data in this application and its applicability to the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems for treatment of tremor support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

With regard to reasonable assurance of effectiveness of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, the sponsor provided adequate evidence of the sufficient similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems and the Medtronic Activa Tremor Control System with regard to technological characteristics. Because of this, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Tremor Control System is directly applicable towards establishing reasonable assurance of the effectiveness of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems.

With regard to reasonable assurance of the safety of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, the sponsor provided adequate evidence of the sufficient similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems and the Medtronic Activa Tremor Control System with regard to technological characteristics. Because of this, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Tremor Control System is directly applicable towards establishing reasonable assurance of the safety of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems.

In conclusion, given the available information identified above and its applicability to the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, the data support that for the requested indications for use the probable benefits for the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems outweigh its probable risks.

XIII. CDRH DECISION

CDRH issued an approval order on 10/20/2021.

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

1. Butson CR, McIntyre CC. *Tissue and electrode capacitance reduce neural activation volumes during deep brain stimulation.* Clin Neurophysiol. 2005;116(10):2490-2500. doi:10.1016/j.clinph.2005.06.023
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3. Koller WC, Lyons KE, Wilkinson SB, Troster AI, Pahwa R. *Long-term safety and efficacy of unilateral deep brain stimulation of the thalamus in essential tremor. Mov Disord. 2001 May;16(3):464-8. doi: 10.1002/mds.1089. PMID: 11391740*