SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Stimulator, Electrical, Implanted, For Parkinsonian Tremor

Device Trade Name: Abbott Infinity™ DBS System

Device Procode: MHY

Applicant's Name and Address: Abbott Medical, Inc.
6901 Preston Road
Plano, TX 75024

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P140009/S039

Date of FDA Notice of Approval: 1/02/2020

The Abbott Infinity™ DBS System was approved on September 19, 2016 under P140009/S001 and is indicated for:

- Bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy to reduce some of the symptoms of advanced levodopa-responsive Parkinson's disease that is not adequately controlled by medications.

- Unilateral or bilateral stimulation of the ventral intermediate nucleus (VIM) of the thalamus for the suppression of disabling upper extremity tremor in adult essential tremor patients whose tremor is not adequately controlled by medications and where the tremor constitutes a significant functional disability.

The current supplement (S039) was submitted to expand the indication for the Abbott Infinity™ DBS System. The original PMA (P140009) for the Brio Neurostimulation System was approved on June 12, 2015 and the SSED to support the indication is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf14/P140009b.pdf) and is incorporated by reference here. No new clinical data were required to support the approval of the Abbott Infinity™ DBS System in P140009/S001.

II. INDICATIONS FOR USE

The Abbott Infinity™ DBS System is indicated for use in the following:

- Bilateral stimulation of the subthalamic nucleus (STN) or the internal globus pallidus (GPi) as an adjunctive therapy to reduce some of the symptoms of advanced levodopa-

responsive Parkinson's disease that is not adequately controlled by medications.

- Unilateral or bilateral stimulation of the ventral intermediate nucleus (VIM) of the thalamus for the suppression of disabling upper extremity tremor in adult essential tremor patients whose tremor is not adequately controlled by medications and where the tremor constitutes a significant functional disability.

III. CONTRAINDICATIONS

The Infinity DBS System is contraindicated for patients who are unable to operate the system or who have unsuccessful test stimulation.

The following procedures are contraindicated for patients with a deep brain stimulation system. Advise patients to inform their healthcare professional that they cannot undergo the following procedures:

* Diathermy
    - short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy
* Electroshock therapy and transcranial magnetic stimulation (TMS)

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Infinity DBS System labeling.

V. DEVICE DESCRIPTION

The Infinity DBS System is a non-rechargeable system designed to deliver low-intensity electrical pulses to nerve/tissue in various combinations of amplitude, pulse width, and frequency. The electrical pulses travel from an implanted pulse generator (IPG), through the leads and extensions, to electrodes near selected brain targets in order to provide therapeutic stimulation. The IPG is powered by a hermetically sealed battery within a titanium case. It uses microelectronic circuitry to generate constant current electrical stimulation.

The Infinity DBS System includes the following device models approved under P140009/S001:

1. A 16-channel IPG (Infinity IPG, Models 6660, 6662, 6661, 6663);
2. An external pulse generator (Model 6599);
3. A 4 Channel lead kit (Models 6166, 6167, 6168, 6169);
4. A 8 Channel lead kit (Models 6170, 6171, 6172, 6173);
5. A 4 Channel extension kit (Models 6355, 6356, 6359);
6. A 8 Channel extension kit (Models 6371, 6372, 6373); and
7. Multilead trial cable (MLTC) (Model 3014).

The Infinity System is also compatible with the following devices that were approved under other FDA PMAs or PMA supplements:

1. An Abbott Medical Clinician Programmer App (Model 3874) (approved under P010032/S92)
2. An Abbott Medical Patient Controller App (Model 3875) (approved under P010032/S92)
3. DBS Leads (Models 6142, 6143, 6144, 6145, 6146, 6147, 6148, 6149) (approved under original PMA P140009);
4. DBS Extensions (Model 6345 and 6346) (approved under P140009);
5. 8 Channel Medtronic (MDT) Adapters (Model 2311 and 2316) (approved under P010032/S83)
6. Legacy MDT Adapter (Model 2303) (approved under P140009/S34)
7. Accessories (Models 1101, 1111, 1210) (approved under original PMA P010032);
8. Accessories (Model 1140) (approved under P140009); and
9. Accessories (Model 1803) (approved under P140009/S20).

A. **Implanted Components**

- Infinity IPG, Models 6660, 6662, 6661, 6663

  The Infinity IPG models are programmable, 16 channel devices that allow the connection of leads via an extension. It is powered by a hermetically sealed primary cell battery (5.3Ah or 7.5Ah capacity) within a titanium case and uses microelectronic circuitry (i.e. the hybrid) to generate constant current electrical stimulation. Clinicians are able to program and adjust the stimulation output through Bluetooth Low Energy (BLE) wireless communication. Patients are able to select programs created by clinicians using their patient controller through BLE. The Infinity IPG stores programmed information and delivers stimulation pulses to a selected combination of output electrodes on the connected lead. The stimulation output parameters are listed in Table 1 below:

Table 1: Stimulation Output Parameters

Number of Programs	15
Number of Channels	16
Waveform	Charge Balanced Biphasic
Pulse Shape	Rectangular
Current or Voltage Regulated	Current
Maximum Current Amplitude @ 500 Ω	12.75mA, 0.05 mA steps
Maximum Output Voltage @ 500 Ω	< 6.5V
Pulse Width	20-500µS , 10µS steps
Frequency	2-240Hz, 2Hz steps
Current Path Options	Unipolar or bipolar

- Leads: Model 6166, 6167, 6168, 6169, 6170, 6171, 6172

  The DBS leads deliver electrical pulses to specific targets within the human brain. A typical DBS lead is comprised of stimulating electrodes (proximal) with edge-to-edge spacing defined to stimulate specific targets in the brain. Stranded conductor wires carry the current from the terminal end contacts to the stimulating electrodes. The conductor wires are further insulated and housed within a flexible sheath known as the lead body. The distal end of the lead contains either 4 contacts or 8 contacts that connect into the 4-channel or 8 channel extension, respectively.

Table 2: Infinity Lead Specifications

	Infinity Leads
Lead Length (cm)	30, 40
Lead Diameter (inches)	.051 (1.30 mm)
Number of Electrodes	4 or 8
Electrode Material	MP35N
Electrode Spacing (edge-to-edge) (mm)	0.5 and 1.5
Array Length (mm)	7.5mm – 10.5mm
Electrode Surface Area (mm^2)	6.2
Impedance (Ω)	4 channel leads: 50.72 ohms (average) 8 channel leads: 52.55 ohms (average)

Leads with 8 contacts are configured in a 1-3-3-1 configuration, where electrodes 2 and 3 are segmented into three equal portions and electrodes 1 and 4 are traditional ring electrodes (i.e. non-segmented electrodes). The modifications provide expanded programming options based on orientation of the lead within the brain and allow for more precise targeting of brain structures. A diagram of the electrode segmentation (only being introduced for the middle two electrodes) can be seen below (0.5 mm spacing is found on the left, and 1.5 mm spacing is found on the right):

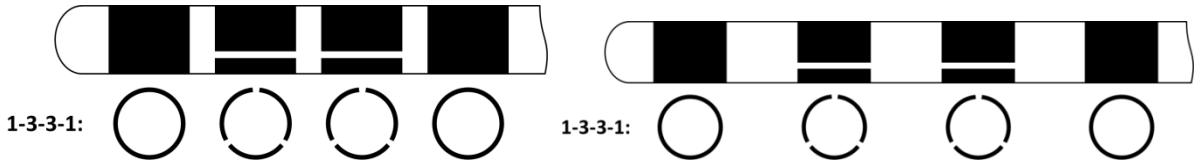

Figure 1: 8 Contact Lead Configurations

- Extensions:, Models 6355, 6356, 6359, 6371, 6372, 6373

  The Infinity extension physically and electrically connects the lead to the IPG and delivers electrical pulses from the IPG to the implanted lead. A typical Infinity extension is comprised of contact electrodes at one end (distal end) and a

connector assembly at the proximal end. The electrodes at the distal end are defined with edge-to-edge spacing to mate with electrical contacts of the DBS IPG header. Stranded conductor wires carry the current from the IPG to the lead. The conductor wires are further insulated and housed within a flexible biocompatible sheath known as the lead body, and a silicone header.

B. External Components

External components of the Infinity DBS System include the External Pulse Generator (EPG), the Multilead Trial Cable (MLTC), the Clinician Programmer (CP) App and the Patient Controller App (PC).

- External Pulse Generator, Model 6599

  The DBS EPG is a programmable, 16 channel device that is used intraoperatively to allow clinicians to deliver electrical pulses to specified areas of the brain to confirm proper placement and integrity of implanted leads prior to the implantation of an IPG. The stimulation parameters of the DBS EPG match those of the Infinity IPG. The DBS EPG is programmed over Bluetooth Low Energy (BLE) by the clinician programmer and stores the information to deliver pulses to the selected combination of output electrodes on the lead. The DBS EPG connects to the Multilead Trial Cable (MLTC), which then connects to the leads. The DBS EPG is powered by two CR2450 coin cell lithium batteries, which can be replaced as needed.

- Multilead Trial Cable, Model 3014

  The Multilead Trial Cable (MLTC) is a universal trial cable that consists of a case, a cable, and a microHMDI connector. It is used to electromechanically connect an implanted lead to the DBS EPG. The MLTC case has two cavities in which implanted lead(s) can be inserted and locked into place via slider mechanism. The MLTC is provided sterile as it has direct patient contact.

- Clinician Programmer App, Model 3874

  The Clinician Programmer App is installed on an off-the-shelf iPad mini. It is used to enable and adjust stimulation parameters to test the proper position and integrity of an implanted lead. It is also used post-operatively to set up programs on the IPG. A clinician may use the CP at any point during the trial or implant phase. The clinician typically holds the iPad mini while standing close to or next to the patient and EPG/IPG when programming the device. The Clinician Programmer app communicates wirelessly with the EPG/IPG via a BLE connection.

- Patient Controller App, Model 3875

  The Patient Controller app is installed for use on an off-the-shelf Apple iPod touch and will provide the capability for the patient to turn stimulation on/off, select physician-provided programs, adjust stimulation amplitude within physician provided limits, and put the IPG into surgery mode or MRI mode as

required. The Patient Controller app communicates wirelessly with the Pulse Generator via a wireless BLE connection.

Additionally, the Infinity DBS System includes the following accessories:

- A pocket sizer (used to check the IPG implant pocket);
- A torque wrench (used to tighten the setscrew on the connector assemblies of the IPG and extension) (Model 1101);
- Port plugs (used with the IPG to occupy unused lead ports in the header) (Model 1111);
- Lead stop (used to attach to the lead at a desired distance from the tip of the lead and set the depth of the implant) (Model 1140;
- Lead protection boot (protects the terminal end of the lead until the extension is attached) (Model 1149);
- Lead Extension Insertion Tool (optional method to aid the physician in completing the connection between the IPG and lead or extension) (Model 1803);
- Lead Stylet;
- 8 Channel MDT Adapters (Models 2311 and 2316)
- Legacy MDT Adapter (Model 2303)
- Magnet (used turn on and off the EPG or IPG when the programming system is unavailable) (Model 1210).

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, these include: Medtronic Activa, Itrel, Soletra, and Kinetra DBS Systems which are approved for bilateral GPi and STN stimulation for PD and Boston Scientific's Vercise DBS system which is currently only approved for bilateral STN stimulation for PD.

VII. MARKETING HISTORY

The Medtronic Activa Parkinson's Control Therapy which is technologically equivalent to the Infinity DBS System has been commercially available in Europe since April 1998. Neither the Abbott Infinity DBS Stimulation System, which is approved for a different indications for use (P140009/S001), have been withdrawn from marketing in any country for any reason related to the safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The adverse events that may occur with the Infinity DBS System 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 Parkinson's Control Therapy which was approved under P960009/S007 and the data used to support approval of the Abbott Medical Brio Neurostimulation System for stimulation of the STN are directly applicable to the Infinity DBS System for bilateral GPi DBS as an alternative target for stimulation for advanced PD.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Nonclinical Safety Studies for Infinity DBS System

The Abbott Infinity™ DBS System (referred to in this summary as "the DBS system" or the "Infinity DBS system") is 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.

1. Infinity IPG

   The Infinity DBS IPG models are based on the Proclaim spinal cord stimulator (SCS) IPG models; therefore, testing in P140009/S001 was limited to the new hardware feature of the Medtronic header models and the firmware modifications for DBS. All other testing submitted for Proclaim SCS IPGs under

P010032/S096 is applicable to the Infinity IPGs. Testing was successfully completed as summarized in the table below.

Table 3: IPG Testing

Test	Test Purpose	Acceptance Criteria
Electrical/ Leakage Current Verification and Protection	Verifies the magnitude of leakage currents of the outputs of the IPG are within an acceptable range, and the device is not susceptible to external defibrillation or electromagnetic non-ionizing radiation per ISO 14708-3:2008.	The IPG outputs are electrically isolated to meet section 16.2 of ISO 14708-3; the device is not damaged after external defibrillation per clause 20.2 of ISO 14708-3; and the device operates as intended and its essential performance is not adversely affected by outside magnetic interferers per clause 27 of ISO 14708-3.
Electrical/ Stimulation Output and Lead Impedance	Verify proper output (amplitude, pulse width, frequency, etc.) and detection parameters of the IPG function are within specified tolerances and can be delivered across passive/active discharge modes or in a multi-stim program, and that impedance measurements are accurate.	The IPG stimulation output parameters: amplitude, pulse width, and frequency are within the specified tolerances across specified temperature and loading levels.
Mechanical/ Hardware Verification	Verifies the mechanical testing of the Infinity IPG. Testing included: • Weight • Operational Temperature/ Implantation Environment • Drop Test • Vibration Test • Transportation and Storage conditions • Operating Pressure • Surface Temperature During Use • Ultrasound • Radiopaque Identification • Connection Retention Force • Lead Insertion Test • Distribution Test	Testing demonstrated that all acceptance criteria was met.
Mechanical/ Hermeticity	Verifies neurostimulator hermetic seal and moisture levels.	Testing demonstrates that the hermetic seal has a leak rate no greater than 5×10^{-8} cc atm/sec during Helium Leak Testing and that the moisture within the hermetic barrier is below acceptable levels
Hybrid Verification	Verifies the proper functioning of the IPG hybrid. Hybrid Verification testing is intended to verify that requirements related to the Infinity IPG circuitry have been met.	Internal IPG circuits function within their specified limits.
Battery	Testing included:	The IPG can measure battery voltage accurately over the battery's usable range,

Test	Test Purpose	Acceptance Criteria
	• Battery Capacity Verification, Longevity, and Discharge Testing • Battery performance simulation under life test conditions	provides the specified time between the Electrive Replacement Indicator (ERI) voltage and End of Life (EOL) voltage, and the IPG battery meets the specified performance conditions.
Bluetooth & Magnet	Verifies the Bluetooth radio hardware receiver sensitivity and transmit power, and the magnet is detected within the specified field strength	The Bluetooth radio and magnet sensor met all performance specifications.
Firmware	Testing included firmware performance for: • Stimulation delivery in accordance with programmed settings • Programming of stimulation settings, magnet behavior, and MRI mode • Communication behavior upon activation of session • Telemetry requests used to get data, execute functions, and terminate functions • Measurement of program or system impedance • Measurement of battery voltage and current used, including ERI and End of Service (EOS) detection • Reset behavior and error handling	The firmware met the software system requirements as specified.

2. Clinician Programmer and Patient Controller Apps

Verification was performed to confirm that Clinician Programmer App and Patient Controller App software functionality conformed to its requirements specifications for the Infinity DBS system, submitted under P140009/S001 and summarized below.

Table 4: Clinician Programmer App and Patient Controller App Testing

Test	Test Purpose	Acceptance Criteria
Clinician Programmer	Testing included software performance for: • Application Initialization and Background functions • Device Programming • CP and IPG Diagnostics Logs • Customized Lead Configuration • IPG Authorization and Wireless Communication	The App met the software system requirements as specified.

Test	Test Purpose	Acceptance Criteria
	• IPG Battery and Information Display • Globalization/Localization (Region Date and Time formatting) • Impedance Measurement (Program and Full System measurements) • Multiple Programs • Patient Management • Program Mode (Sleep/Cycle/Continuous Modes) • Reports & Programming History • Usage Metrics • Wireless Communication	
Patient Controller	Testing included software performance for: • IPG Authorization and Wireless Communication • Program Selection and Display • Stimulation Status Adjustment and Display • Amplitude Adjustment and Display • Application Initialization and Backgrounding • IPG Battery and Information Display • Patient Controller Information and Logging	The App met the software system requirements as specified.

3. External Pulse Generator (EPG)

The DBS EPG models are identical to the SCS EPG models, with minor modifications to the firmware; therefore, testing was limited to the firmware and system functionality related to the modifications. Testing of the hardware submitted in file P010032/S092 for the SCS EPG is applicable to the DBS EPG. The complete summary of testing is shown in the table below.

Table 5: EPG Testing

Test	Test Purpose	Acceptance Criteria
System / Firmware (EPG and BLE Telemetry) Functionality	Verifies system functionality including testing of: • Stimulation Therapy • System Integrity Assessment • Diagnostic Data • Firmware Operation, Performance, Usability, Upgrade and Installation • System Communication • Commercial Off the Shelf Components • Maximum Delivered Charge • BLE Telemetry Performance	All verification testing of the system and firmware showed that the system met its acceptance criteria.

Test	Test Purpose	Acceptance Criteria
	• Wireless Telemetry Communication with Clinician Programmer and Patient Controller • Usability	
Mechanical Hardware	Verifies mechanical functionality including testing of: • Connection and wipe down fatigue • Header, Header/MLTC and lead interfaces • Ability to withstand temperature, vibration, drop, and battery insertions • Distribution and Storage Environment • Indelibility of ink used on packaging labels • Mechanical Safety	All verification testing for mechanical functionality complied with the specified requirements including applicable clauses of IEC 60601-1, IEC 60601-1-11, EN 45502-1, ISO 14708-1, and 14708-3. All acceptance criteria were met.
Electrical Hardware	Verifies electrical functionality including testing of: • Electrical Functionality • Output Stimulation Parameters • Lead Impedance Measurement • Magnet Response • EMC/EMI and Radio Compliance • Hardware Reliability • Electrical Safety	All verification testing for electrical functionality complied with the specified requirements including applicable clauses of IEC 60601-1, IEC 60601-1-11, EN 45502-1, ISO 14708-1, 14708-3 and 60601-1-2. All acceptance criteria were met.

4. Infinity Leads and Extensions

Verification testing performed on the Infinity Leads and Extensions was identical to the DBS Leads and Extensions approved under original PMA P140009 (and its PMA supplements) aside from a new test developed for the coiled extension and a modification to the tensile load acceptance criteria (5 N instead of 7.5 N) due to the elongation design property. The complete summary of testing is provided in the table below.

Table 6: Lead and Extension Testing

Test	Test Purpose	Acceptance Criteria
Lead and Extension Mechanical Verification	Verifies the following: • Use with surgical accessories • Stylet Extraction • Lead Stop • Cannula Insertion • Lead trajectory • Electrical testing	All tests successfully met acceptance criteria per requirements, including: • Lead does not deviate from intended target. • Stylet removal below specification • No damage to lead after five insertion and removal cycles of the stylet. • Lead stop supports weight of lead

Test	Test Purpose	Acceptance Criteria
		• No damage to lead after five actuations of lead stop • Lead shall pass through insertion cannula without buckling • No damage to lead after 5 pass-through cycles of the cannula. • Lead remains within electrical specifications during intended use
Lead and Extension Visibility Testing	Verifies the visibility of the DBS leads and Extensions under x-ray/fluoroscopy	All tests successfully met acceptance criteria per requirements, including: • Visible when using x-ray fluoroscopy equipment. • When placed on a standard blue surgical drape and viewed at 18" under normal lighting conditions
Lead and Extension Insertion/Extraction Testing	Verifies the insertion/extraction of the lead into boot or extension and the extension into the IPG does not damage lead or extension.	All tests successfully met acceptance criteria per requirements, including: • Lead inserts into boot without buckling. • No damage to lead after five insertion and removal cycles into the lead boot. • Lead inserts into extension without buckling. • Extension inserts into the IPG without buckling. • No damage to lead or extension after five insertion and removal cycles.
Lead and Extension Tensile Load	Verifies the lead and extension can withstand normal acute body stresses after implantation.	All tests successfully met acceptance criteria per requirements, including: • Lead supports a 7.5N load without mechanical or electrical damage to the lead. • Extension supports 7.5N load for extensions without extensibility or a 5N load for extensions with extensibility (due to elongation design property) without mechanical or electrical damage to the extension.
Lead and Extension Axial Fatigue	Verifies the lead and extension can withstand normal cyclic body stresses after implantation.	All tests successfully met acceptance criteria per requirements, including: • No mechanical or electrical damage to the lead after 100,000 flex cycles. • No mechanical or electrical damage to the extension after 1,400,000 flex cycles.

5. Biocompatibility Testing

Biocompatibility of all patient-contacting components of the Infinity DBS system was evaluated in consideration of ISO 10993-1 and ISO 14708-3. The Infinity DBS IPG, DBS Leads and Extensions are considered permanent (> 30 days) implants with tissue/bone contact. Biocompatibility of the Infinity DBS IPG was demonstrated by leveraging testing previously conducted on the Proclaim SCS IPG (P010032/S096). Leveraging this testing information was appropriate because the Infinity DBS IPG is identical to the Proclaim SCS IPG in terms of the patient-contacting materials, manufacturing and sterilization processes. Biocompatibility testing was conducted on the Infinity DBS leads and extensions (P140009/S1) as summarized in the table below.

The DBS EPG is classified as a surface contacting device with limited skin contact per ISO 10993-1. Biocompatibility of the DBS EPG was demonstrated by leveraging testing previously conducted on the SCS EPG (P010032/S092). Leveraging this testing information was appropriate because the DBS EPG is identical to the SCS EPG in terms of the patient-contacting materials and manufacturing processes.

The table below summarizes the applicable testing performed on the IPG, EPG, Lead and Extension components of the Infinity DBS system. All biocompatibility studies were conducted on the finished, sterilized devices in compliance with Good Laboratory Practices (GLP), 21 CFR Part 58. All pre-specified test acceptance criteria were met and all tests passed. The Infinity DBS system also contains other implantable accessories with prolonged (24 hours – 30 days) tissue/bone contact and accessories with limited (≤ 24 hours) skin contact. These components are either the identical components used for the Proclaim SCS system or use the same materials used for the permanently implantable components of the Brio DBS system approved under P140009.

Table 7: BiocompatibilityTesting

Biological Effect (Applicable Standard)	Test Method	Acceptance Criteria	Results
DBS IPG, EPG, Lead & Extension			
Cytotoxicity (ISO 10993-5)	ISO MEM Elution Assay	Reactivity grade is not greater than mild reactivity (Grade 2)	PASS
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

Biological Effect (Applicable Standard)	Test Method	Acceptance Criteria	Results
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
DBS IPG			
Systemic Toxicity (ISO 10993-11)	ISO Acute Systemic Toxicity Test – Mouse Systemic Injection	None of the test animals show a significantly greater biological reaction than the animals treated with vehicle control.	PASS
Genotoxicity (ISO 10993-3)	Bacterial Mutagenicity 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 TA98, TA100, and WP2uvrA and/or less than 3-fold increase in the number of revertants when compared to the solvent control in strains TA1535 and TA1537.	PASS
DBS IPG, Leads & Extension			
Particulate (ISO 14708-3)	Extract condition in Normal Saline (NS) per ISO 10993-3	<100 particles/mL for >5.0 µm and <5 particles/mL for >25 µm	PASS
Chemical Characterization (ISO 10993-18)	GC / MS Direct Inject	Acceptable toxicological profile	PASS
	Inductively Coupled Plasma (ICP)	Acceptable toxicological profile	PASS
	Exhaustive extraction	Acceptable toxicological profile	PASS
	Ion Chromatography	Acceptable toxicological profile	PASS
	IR	Acceptable toxicological profile	PASS
	UPLC-MS	Acceptable toxicological profile	PASS

6. Sterilization

The Infinity Neurostimulation System 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 10993-7: 2008. Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals.

7. Packaging and Shelf Life
   Distribution Testing was completed for the IPG, EPG, leads, extensions, and accessories in accordance with ASTM D4169:2009. All acceptance criteria were met. The testing confirmed that the device packaging adequately protects the product during conditions that may be encountered during storage, shipping, and handling. The packaging design and testing of the packaging for the IPG, DBS Leads, and DBS Extensions complies with the requirements of BS EN ISO 11607-1:2009.

   Shelf Life for the Infinity IPG, Infinity Leads and Extensions has been established as two (2) years from the date of manufacturing.

B. Technological Comparison

In lieu of providing a clinical data set for GPi stimulation with the Infinity DBS System, the sponsor provided a technological comparison (including a comparison of the technology, surgical procudures, and instructions for use) of the Infinity DBS System to the Medtronic Activa Parkinson's Control Therapy which was approved under P960009/S007 for the requested indications for use. The purpose of the technological comparison was to establish sufficient similarity of the two 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 Infinity DBS.

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/GuidanceDocu ments/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 Infinity DBS System and the Medtronic Activa Parkinson's Control Therapy, the sponsor provided a technical comparison of the two 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

Infinity™ DBS System to the Medtronic Activa Parkinson's Control Therapy it was determined that the Infinity DBS System stimulates, and thus activates, neurons in the same area of the brain that was shown to be safe and effective for the Medtronic Activa Parkinson's Control Therapy approved in P960009/S007.

VTA modeling has been used to estimate the degree of neuronal activation and by extension the degree of stimulation efficacy (Butson & McIntyre, 2005). Thus, the sponsor provided comparative modeling of the VTA between the stimulation produced by Infinity™ DBS System IPG and the associated non-segmented and segmented leads and the Medtronic Activa Parkinson's Control Therapy using the Soletra Neurostimulator and the Medtronic leads (Models 3387 and 3389) that were approved in P960009/S007. Note that although two spaces and array length options are available, the leads used in the modeling are spaced at 1.5mm and have a 10.5mm array length. The 1.5mm spaced/10.5mm array length leads were used because the wider spaced leads are more typically used in the GPi since it is a larger target compared to the STN (5 and 6).

The electric fields generated during stimulation by the DBS electrodes were calculated from the Poisson equation with a Fourier finite element model (FEM) solver to determine time- and space-dependent voltage within the tissue medium (1). Finite element models were constructed to calculate the electric fields and current densities produced by DBS leads using COMSOL version 4.0 (COMSOL Inc, Burlington, MA). The models were made using a previously published and described methodology (1, 2, 3). There are no differences in assumptions and boundary conditions between the previous modeling papers and the modeling data presented by the sponsor.

The tissue model was based on the MIDA model published by the FDA. The MIDA model is a multimodal imaging-based detailed anatomical computer model of the human head and neck. The model offers detailed representations of brain surfaces, meninges, cerebrospinal fluid distribution, eyes, ears, and several deep brain structures, as well as several distinct muscles, bones and skull layers, blood vessels, cranial nerves, dental structures, and glands. The MIDA model can be used for computational modeling studies and electromagnetic modeling studies on many structures including deep brain structures (4).

The Abbott Infinity IPG waveform is passively charged balanced which differs from the Medtronic Soletra IPG waveform which is actively charged balanced. The waveform was accounted for in this modeling. Both waveforms were measured from their respective IPGs and the components of the waveform were fed into the model: electrode 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). Since the maximum clinically relevant output stimulation parameter range used to support approval of P960009/S007 do not appear to be publicly available the sponsor used

the values put forth by the Limousin-Dowsey and Tisch (2009) book chapter as typically used parameters for GPi stimulation in Parkinson's disease (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 Abbott 4 channel and 8 channel non-segmented and segmented leads with current was titrated to achieve a comparable VTA.:

Table 8: Parameters Used in Model of the Medtronic Soletra VTA

Lead	Configuration	Voltage	Pulse Width[§]	Frequency
Medtronic 4 channel	Monopolar	1.5 V	60 µs	130 Hz
Medtronic 4 channel	Monopolar	5 V	120 µs	185 Hz
Medtronic 4 channel	Bipolar	1.5 V	60 µs	130 Hz
Medtronic 4 channel	Bipolar	5 V	120 µs	185 Hz

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

A total of 12 modeling scenarios were modeled for the Medtronic and Abbott leads. These scenarios represented relevant output parameters, configurations, and lead types (non-segmented and segmented). The scenarios were created to demonstrate the capability of both the Abbott Infinity 4 channel non-segmented lead and the Abbott Infinity 8 channel segmented lead to produce a VTA comparable to that produced by the Medtronic 4 channel lead. Then for each Medtronic VTA, various parameters were used with the Abbott 4 channel non-segmented lead and the Abbott 8 channel segmented lead to achieve a VTA comparable to that achieved by the Medtronic lead.

Results:
The modeled Abbott 8 channel segmented and 4 channel non-segmented leads were able to achieve a comparable VTA shape when compared the Medtronic lead.

In all the scenarios above the percent deviation of the VTAs of the Abbott leads from the VTA of the Medtronic lead was between 7.41% (meaning greater coverage for Abbott leads) and -4.26%.

Conclusions:
The results show that parameters of the Infinity™ DBS System can be varied to achieve a VTA comparable to that achieved by the Medtronic Activa Parkinson's Control Therapy approved in P960009/S007; 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 three lead models (Abbott 4 channel non-segmented, Abbott 8 channel segmented, Medtronic lead models 3387 and 3389).

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. 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 Parkinson's Control Therapy Soletra IPG to InfinityTM DBS System IPG

	Infinity™	**Soletra™**	**Safety**	**Efficacy**
Amplitude (settings)	0 - 12.75 mA	1 – 10.5V	1. Both confined by charge density limit (30 μC/cm^2) 2. Abbott Parkinson's Study to be safe for use in the STN which is also relevant to the GPi	Can be programmed within clinically relevant parameter ranges, wider ranges that are available through Infinity provide additional programming flexibility.
Frequency (settings)	2 - 240 Hz	2 – 185 Hz	Parameters verified through the Abbott Parkinson's Study to be safe for use in the STN which is also relevant to the GPi	Can be programmed within clinically relevant parameter ranges, wider ranges that are available through Infinity provide additional programming flexibility.
Pulse width (settings)	20 – 500 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 Infinity provide additional programming flexibility.
Number of Programs	15	1	All programs created must be within the available safe parameters	Can be programmed within clinically relevant parameters, additional parameters provide programming flexibility
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	2 seconds – 24 hours	0.1 seconds – 24 hours	Programming capabilities limit programs that cause a charge imbalance condition	Can be programmed within clinically relevant parameters, additional parameters provide programming flexibility.
Charge balance	Passive discharge	Active discharge	System requirements have been incorporated into the Infinity 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 and Cycle	System requirements have been incorporated into the Infinity 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

The table above demonstrates that the Infinity DBS System has the capability to replicate at least the same output as the Medtronic Activa Parkinson's Control Therapy system indicating it can provide at least a comparable level of efficacy. Though the waveforms of Infinity and Soletra differ in their method of charge

balancing they both 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 Infinity DBS System ensures safety by providing a charge density limit (30 μC/cm^2) and preventing charge imbalance conditions. The Abbott Medical Parkinson's study of STN stimulation provides further assurance of the safety of the additional parameters provided by the Infinity device. . 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 GPi 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 Infinity™ DBS System leads and Medtronic Activa Parkinson's Control Therapy leads

	ABBOTT Leads			**DBS leads cited in the literature**	**Clinically Equivalent Discussion**
	Conventional 4-channel legacy ABBOTT DBS lead	**Conventional 4-channel Infinity DBS leads**	**Segmented 8-channel Infinity DBS lead**	**Medtronic DBS leads Models 3387 and 3389**	
Electrode configuration	1-1-1-1  4 electrode configuration with an active tip	1-1-1-1  4 electrode configuration , no active tip	1-3-3-1  8 electrode configuration (1-3-3-1), no active tip	1-1-1-1  4 electrode configuration, no active tip	See VTA analysis in Section IX(B)(1). Additionally, segmented lead has the same stimulation output capabilities with additional programming options. 1st and 4th electrodes provide omnidirectional stimulation 2nd and 3rd electrodes bands can use all 3 segments to provide omnidirectional stimulation that is clinically equivalent or use segmented electrodes
Active tip	Yes	No	No	No	The presence of Active Tip at the tip electrode (contact 1) as in the case of legacy DBS leads, results in one contact (tip) with a larger surface area than the other three contacts. The differences in electrode surface area do not impact clinical safety since a common charge density limit

	ABBOTT Leads			DBS leads cited in the literature	Clinically Equivalent Discussion
	Conventional 4-channel legacy ABBOTT DBS lead	**Conventional 4-channel Infinity DBS leads**	**Segmented 8-channel Infinity DBS lead**	**Medtronic DBS leads Models 3387 and 3389**	
					applies to all leads. 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	Platinum/Iridium	Same
Conductor Wire	Platinum/Iridium	Platinum/Iridium	Platinum/Iridium	Platinum/Iridium	Same
Lead Body	90A Bionate Thermoplastic Polycarbonate Urethane	55D Bionate Thermoplastic Polycarbonate Urethane	55D Bionate Thermoplastic Polycarbonate Urethane	80A Urethrane	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	12.7 mm^2 (electrode 1) 6.42 mm^2 (electrodes 2-4)	6.20 mm^2 (electrodes 1-4)	Electrodes 1 & 4: 6.20 mm^2 Electrodes 2 & 3: Combined surface area of 3 segments is 5.38 mm^2 (1.79 mm^2 per each segment x3)	5.98 mm^2	See VTA analysis in Section IX(B)(1).
Number of electrodes	4	4	8	4	See VTA analysis in Section IX(B)(1).
Contact length (mm)	1.5	1.5	1.5	1.5	Same
Contact spacing (mm)	0.5, 1.5	0.5, 1.5	0.5, 1.5	0.5, 1.5	Same
Array length (mm)	9, 12	7.5, 10.5	7.5, 10.5	7.5, 10.5	See VTA analysis in Section IX(B)(1).
Leads length (cm)	25, 30, 35, 40	30, 40	30, 40	28, 40	The shorter lead can prevent excessive coiling of the lead under the scalp in smaller patients. Leads of shorter lengths allow for smaller patients to be appropriately implanted, so the

	ABBOTT Leads			DBS leads cited in the literature	Clinically Equivalent Discussion
	Conventional 4-channel legacy ABBOTT DBS lead	**Conventional 4-channel Infinity DBS leads**	**Segmented 8-channel Infinity DBS lead**	**Medtronic DBS leads Models 3387 and 3389**	
					lead will end in the intended anatomical location, to be fitted with a lead protection boot temporarily or an extension for connection to the IPG.
Lead diameter (mm)	1.397	1.295	1.295	1.27	See VTA analysis in Section IX(B)(1).

[1]

As outlined in Table 10 above, the Abbott Infinity DBS System and the Medtronic Activa Parkinson's Control Therapy 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. Externsions

The table below shows a comparison between attributes of the Infinity extension and the Soletra extension.

Table 11: Comparison between Abbott Infinity™ DBS System extensions and Medtronic Activa Parkinson's Control Therapy extensions

	Infinity 8-Ch DBS Extension Models 6371, 6372, 6373[1]	**Medtronic DBS Extension Model 7482**	**Clinically Equivalence Discussion**
Body diameter (mm)	1.4	2.8	The diameter does not impact the delivery of electrical stimulation to the target location through the lead contacts.
Connector thickness (mm)	4.57	3.8 plus boot (total diameter 5.0)	The connector thickness does not impact the delivery of electrical stimulation to the target location through the lead contacts. Physically the connectors are almost identical in size with the inclusion of the boot for the Medtronic extension.
Body construction	Continuous	Continuous	The body construction for both extensions is continuous and therefore they are clinically equivalent.
Lengths (cm)	50, 60, 90	51	The 50cm Infinity lead extension length and the 51cm Soletra lead extension length are substantially equivalent and therefore considered clinically equivalent. The additional lengths offered for the Infinity system are available for physicians to use as

	Infinity 8-Ch DBS Extension Models 6371, 6372, 6373[1]	Medtronic DBS Extension Model 7482	Clinically Equivalence Discussion
			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.
# 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 (Infinity segmented lead) would require 8 distal contacts in order to adequately connect to the extension and deliver therapy from the IPG to the target location. If only 4 contacts existed for the extension, then the 8-contact lead would not adequately fit into the extension and 4 of the 8 contacts would not provide stimulation output because they have no connection to the stimulation source (IPG). 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	Coiled	Coiled	The wiring for both extensions is coiled therefore 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 Infinity System has fewer setscrews, testing establishes that a single setscrew provides sufficient retention force of 5 N or greater for its safe and efficacious use which is a force greater than what would occur clinically.
Extensible	Yes	No	The ability of the lead to stretch under a mechanical stimulus does not impact the delivery of electrical stimulation to the target location through the lead contacts. Physically, the extensibility of the Infinity does not impact safety and effectiveness since testing shows that the lead body does not incur mechanical or electrical damage after 1,400,000 flex cycles.
Patient Contacting Materials -- Abbott and Medtronic Extensions			
Extension Header	Nusil MED 4870 Nusil MED 1524	Siloxane coated silicone rubber (2)	All headers are silicone rubber polymers; silicone rubbers are robust, biocompatible and flexible materials. In both devices the backbone of the polymer chain of silicone elastomers consists of a silicone-oxygen (Si-O) repeat unit. This repeat unit is known to have good stability against known biodegradation mechanisms in the body (4). Another key chemical similarity for all implanted silicones, except fluids, is they are highly cross-linked using reactive groups in the polymer side chains and catalysts. Cure

	Infinity 8-Ch DBS Extension Models 6371, 6372, 6373[1]	Medtronic DBS Extension Model 7482	Clinically Equivalence Discussion
			chemistries differ considerably in the types of reactive groups and catalysts used, but all cure chemistries result in the same biostable crosslinks. Lastly, virtually all silicone polymers, except fluids, are reinforced with fillers or resins, most commonly fumed silica, in order to improve their mechanical properties. Due to these key chemical similarities, all types of medical implant grade silicones are generally recognized as being biostable. Since the materials of both headers have similar characteristics and all materials are biostable, this helps to ensure that the stimulation from the IPG to the target site is transmitted effectively, and there should be no impact on the safety or efficacy of the device based on these material differences.
Extension Body	Carbosil 20 80A, Silicone Rubber 40076	Silicone Rubber and polyurethane (2)	The Infinity extension body is composed of Carbosil 80A which thermoplastic silicone polycarbonate polyurethane and Silicone Rubber 40076. The Medtronic extension body material is also composed of Silicone rubber and Polyurethane. Both silicone rubber and polyurethane robust, biocompatible and flexible materials (3). The characteristics of silicone rubber are discussed above. Since the materials of extension bodies have similar characteristics and all materials are biostable, this helps to ensure that the stimulation from the IPG to the target site is transmitted effectively, and there should be no impact on the safety or efficacy of the device based on these material differences.

[1] Extensions were approved in P140009/S1 for stimulation of the STN.

As outlined in Table 11 above, the the Abbott Infinity™ DBS System and the Medtronic Activa Parkinson's Control Therapy 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 GPi target location.

Table 12: Comparison between Abbott Infinity™ DBS System extensions and Medtronic Activa Parkinson's Control Therapy extensions

Accessories Name	Infinity	Soletra	Function	Clinical Equivalence Justification
IPG Implant Accessories				
Torque Wrench	Yes	Yes	Secure the leads 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)
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	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 pocket adapters are considered biocompatible for their intended use per ISO 10993.
Patient Magnet	Yes	Yes	Used to perform magnet enabled functions on the IPG	The magnetic properties and dimensions are compatible with the IPG magnet sensor to safely ensure system performance.
Pocket Sizer	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 sizers are considered biocompatible for their intended use per ISO 10993.
EPG Accessories				
Trial Cable	Yes	Yes	Evaluate lead placement location and integrity during the procedure	The dimensions and mechanical properties are compatible with the EPG/extensions to safely ensure system performance (e.g. via electrical connection). From a material perspective the trial cables are considered biocompatible for their intended use per ISO 10993.
Lead Surgical Accessories				

Accessories Name	Infinity	Soletra	Function	Clinical Equivalence Justification
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 Protection 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.
Lead and Extension Insertion Tool	Yes	No	To help guide the lead into the IPG header	The dimension of the tool is compatible with the IPG and lead as an optional method to aid the physician in completing the system connection. System connection can be performed with or without the tool.

6. Labeling
   The instructions for use are equivalent regarding implant procedures, device programming 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 Parkinson's Control Therapy approved (P960009/S7)

Because of the technological similarity of the Abbott Infinity™ DBS System to the Medtronic Activa Parkinson's Control Therapy approved under P960009/S7, 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 Parkinson's Control Therapy under P960009/S7 apply equally well to Abbott Infinity™ DBS System. A prospective open label study was used to establish reasonable assurance of the safety and effectiveness of the Medtronic Activa Parkinson's Control Therapy and is summarized as follows. Additional details of these studies are provided in the SSED for P960009/S7 that is available on the CDRH website.

The study enrolled subjects with advanced, levodopa-responsive Parkinson's disease that are not adequately controlled with medication. Patients were to have a disability level due to Parkinson's disease based on the following criteria:

- Hoehn and Yahr staging 3 or worse when the patient is in the "off" state;

- Unified Parkinson's Disease Rating Scale (UPDRS) motor exam score of 30 or more in the "off" state; and
- Complications of levodopa therapy motor responses including motor fluctuations and dyskinesias.

Subjects were either implanted in the STN or the GPi. Patients participated in the studies for 12 months; there were 2 pre-implant visits and 4 follow-up visits (1, 3, 6, and 12 months). Each patient's dosage of antiparkinsonian medication was held constant for 1 month prior to surgery. Following surgery, physicians monitored antiparkinsonian medication status throughout the remainder of the study. Data collected at each pre-implant and follow-up visit included the Unified Parkinson's Disease Rating Scale (UPDRS) and 2-day patient diaries recorded prior to the visit. At each visit, patients were evaluated without medication (OFF medication) and with medication (ON medication). At follow-up visits, patients were also assessed without stimulation (stimulation OFF) and with stimulation (stimulation ON).

B. Results Used to Establish Reasonable Assurance of Safety of Infinity™ DBS System for GPi Stimulation

1. Safety Results for P140009

The sponsor performed a prospective, multi-center, randomized, controlled clinical study, which compared patients randomized to receive immediate as compared to delayed stimulation with DBS implanted in the STN which was used to support approval of the Brio Neurostimulation System under P140009. Additional details of these studies are provided in the SSED for P140009 that is available on the CDRH website. The Infinity DBS System was approved under P140009/S1 based on a similarity of technological characteristics to the Brio Neurostimulation 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 GPi since the STN and GPi are both grey matter nuclei 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 safety endpoint compared the adverse event incidence rates between the Active Stimulation Group and the Control Group throughout the duration of the study. The analysis of safety was based on the 136 patients implanted in the trial. The safety profile was based on a comparison of adverse events that occurred during the randomized phase as well as a comparison of all adverse events that occurred through the last follow-up visit. Patients were randomized in a 3:1 ratio to the stimulation or control groups. 58.4% (59/101) of the subjects in the stimulation group had a total of 144 adverse events and 45.7% (16/35) of the subjects in the control group had a total of 25 adverse events.). There were no significant differences between the occurrence of adverse events in the Stimulation Group compared to the Control Group between implant and 90 days. A total of 18 patients, 13.9% (14/101) in the stimulation group and 11.4% (4/35) in the control group experienced a serious adverse event during the first 90 days. There were a total of 18 SAEs in the stimulation group and 7 in the control group.

107 patients (78.7%) experienced a total of 409 adverse events during the first year of the study. A total of 5 intracranial hemorrhages occurred during this study. Three out of five hemorrhages occurred during microelectrode recording and only one out of five patients experienced long term effects due to the event. There were also three deaths. The causes of these deaths were unrelated to the device and include sepsis secondary to urinary tract infection (UTI), cancer and multiple infections which started with osteomyelitis of the big toe. There were no unanticipated adverse device effects.

2. Safety Results for P960009/S7

For the safety analysis data from both the STN and GPi were combined in the SSED. As stated above, due to the similarity of the technological characteristics, adverse effects are expected to be similar between the STN and GPi, except for some stimulation related adverse effects that may be particular to the location of stimulation. Stimulation related adverse effects typically can be resolved by adjusting the output stimulation.

Of the 160 enrolled patients, 106 patients (106/160, 66.3%) underwent procedures that targeted the STN (bilateral: 96, unilateral: 6, not implanted: 4) and 54 (54/160, 33.8%) underwent procedures that targeted the GPi (bilateral: 38, unilateral: 15, not implanted: 1). All 160 enrolled patients were evaluated for the occurrence of adverse events. One hundred and fifty-four (154/160, 96.3%) of the enrolled patients experienced one or more adverse events. The SSED lists adverse events for all patients reported during the clinical investigation by major category and subcategories.

Over the entire study duration, 12/160 patients (7.5%) had intracranial hemorrhage; 17/160 patients (10.6%) had device-related infection; 16 patients (10.0%) had paresis/asthenia; and 13/160 patients (8.1%) had hemiplegia/hemiparesis. The rate of stimulation-related adverse events was 51.9% (83/160 patients) and the rate of ongoing stimulation-related events was 22.5% (36/160 patients). The rate of serious stimulation-related adverse events was 9.4% (15/160) and the rate of ongoing serious stimulation related adverse events was 3.1% (5/160) patients. Ongoing serious stimulation-related adverse events included: worsening of motor impairment/PD symptoms (dyskinesia), sensory impairment (pain); and speech/language (dysarthria, hypophonia, and speech disorder). Other stimulation related adverse events included: worsening of motor impairment/PD symptoms (worse motor fluctuations, incoordination, abnormal gait, akinesia/bradykinesia, tremor, rigidity, myoclonus and dysphagia); sensory impairment (paresthesia, sensory disturbance, hypesthesia, hearing [tinnitus] and headache); speech/language (voice alteration); eye (visual disturbances [diplopia, abnormal vision and visual field defect] and eye disorders [twitching]); cognitive (thinking abnormal, confusion, alteration of mentation [dizziness]); general (respiratory [laryngismus], musculo-skeletal [abnormal posture], gastrointestinal [vomiting], urogenital [urinary incontinence], metabolic/nutritional [weight loss], skin and appendages [sweating] and systemic [accidental injury]; sleep [somnolence and insomnia]; neuropsychological (psychiatric disturbances [manic reaction and neurosis]); general paresis/asthenia; internal system events (shock/jolt, positioning difficulties); cardiovascular

(cerebrovascular accident); hemiplegia/hemiparesis (asthenia) and depression.

C. Results Used to Establish Reasonable Assurance of Effectiveness of Abbott Infinity™ DBS System for GPi Stimulation

1. Effectiveness Results for P960009/S7

   For effectiveness purposes only the data from subjects implanted in the GPi were used from P960009/S7. Additional details are provided in the SSED for P960009/S7 that is available on the CDRH website. A summary of results follows:

   Patient Diary Results

   "On" time improved between pre-implant and 12 months for GPi and STN subjects. "On" time with dyskinesia decreased between pre-implant and 12 months for GPi and STN subjects. For the subset of subjects whose data were verified against medical records:

   - The duration of "on" time increased by an average of 6.7 hours in GPi patients and 6.1 hours in STN patients; and
   - The duration of "on" time with dyskinesias decreased by an average of 4.2 hours in GPi patients and 2.8 hours in STN patients.

   UPDRS Total Motor Examination (TME) Scores

   Data from the STN and GPi were combined in the SSED report of UPDRS TME scores. UPDRS TME scores improved between pre-implant and 12 months for both GPi and STN patients when assessed while ON medication with stimulation ON and when assessed while OFF medication with stimulation ON. For the subset of patients whose data were verified against medical records:

   - Symptoms of Parkinson's disease (UPDRS TME scores) improved for 56/117 patients while ON medication;
   - Symptoms of Parkinson's disease (UPDRS TME scores) improved for 102/117 patients while OFF medication.

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

D. 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 Abbott Infinity™ DBS System approved under P140009 included 15 investigators. The pivotal clinical study included 15 investigators of which none were full-time or part-time employees of the sponsor and 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: 1 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. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

The pivotal clinical studies for Medtronic Activa Parkinson's Control Therapy under P960009/S007 included 18 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 Abbott Infinity™ DBS System was approved for stimulation of the STN in P140009/S001. The pre-clinical studies provided to support approval in P140009/S001 are directly applicable to this PMA because the only requested change is to the indications for use to include stimulation of the GPi, and this change would not affect the non-clinical testing.

B. Effectiveness Conclusions

In this PMA the sponsor provided adequate evidence of the sufficient similarity of

the Abbott Infinity™ DBS 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 Parkinson's Control Therapy approved under P960009/S007 in support of the reasonable assurance of its effectiveness is directly applicable towards establishing reasonable assurance of the effectiveness of the Infinity™ DBS System for GPi stimulation. As detailed in the SSED for the Medtronic Activa Parkinson's Control Therapy prospective open label studies of the Medtronic Activa Parkinson's Control Therapy demonstrated that "On" time improved between pre-implant and 12 months by an average of 6.7 hours for the subset of GPi patients whose data were verified against medical records. Additionally, for the subset of patients whose data were verified against medical records, for the GPi and STN, symptoms of Parkinson's disease (UPDRS TME scores) improved for 56/117 patients while ON medication and symptoms of Parkinson's disease (UPDRS TME scores) improved for 102/117 patients while OFF medication.

C. Safety Conclusions

The sponsor performed a prospective, multi-center, randomized, controlled clinical study, which compared patients randomized to receive immediate as compared to delayed stimulation with DBS implanted in the STN which was used to support approval of the Brio Neurostimulation System under P140009. Additional details of these studies are provided in the SSED for P140009 that is available on the CDRH website. The Infinity DBS System was approved under P140009/S001 based on a similarity of technological characteristics to the Brio Neurostimulation 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 GPi 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 tostimulation parameters.

In P140009, the risks of the device for Parkinson's disease were based on a comparison of the adverse events during the randomized phase and longterm follow-up. There were no significant differences between the occurrence of adverse events in the Stimulation Group compared to the Control Group between implant and 90 days. Thirty six patients (36, 28.3%) experienced a total of 50 serious adverse events during the one year study, and one hundred and seven patients (107, 78.7%) experienced at least one adverse event. A total of five intracranial hemorrhages occurred during this study. Three out of five hemorrhages occurred during microelectrode recording and only one out of five patients experienced long term effects due to the event. There were also three deaths. The cause of these deaths were unrelated to the device and included sepsis secondary to UTI, cancer and multiple infections which started with osteomyelitis of the big toe. There were no unanticipated adverse device effects.

In this PMA the sponsor also provided adequate evidence of the sufficient similarity of the Infinity DBS 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 Parkinson's Control Therapy approved under P960009/S007 is directly applicable towards establishing reasonable assurance of the safety of the Infinity™ DBS System for GPi stimulation.

As detailed in the SSED for the Medtronic Activa Parkinson's Control Therapy all 160 enrolled patients (both the STN and GPi) were evaluated for the occurrence of adverse events. One or more adverse events occurred in one hundred and fifty-four enrolled patients (154/160, 96.3%). Table 3 of the SSED lists adverse events for all patients reported during the clinical investigation by major category and subcategories. Over the entire study duration, 12/160 patients (7.5%) had intracranial hemorrhage; 17/160 patients (10.6%) had device-related infection; 16 patients (10.0%) had paresis/asthenia; and 13/160 patients (8.1%) had hemiplegia/hemiparesis. In addition to the adverse events collected through the 12 months of study follow-up, the sponsor has provided adverse event information for 100 patients at 2 years (60 STN and 40 GPi), 82 patients at 3 years (47 STN and 35 GPi), 38 patients at 4 years (17 STN and 21 GPi), and 16 patients at 5 years (4 STN and 12 GPi). FDA review of the safety data concluded that the probable benefits to health outweigh the probable risks.

D. Benefit-Risk Determination

The probable benefits of the Infinity DBS System are based on data collected in the clinical study conducted to support PMA approval of the Medtronic Activa Parkinson's Control Therapy. As described above, the sponsor also provided adequate evidence of the sufficient similarity of the Infinity DBS System 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 Parkinson's Control Therapy in support of a determination of reasonable assurance of the effectiveness of the Infinity DBS System for GPi stimulation. As documented in the SSED for the Medtronic Activa Parkinson's Control Therapy, evaluation of the primary effectiveness showed that "On" time improved between pre-implant and 12 months by an average of 6.7 hours for the subset of GPi patients and for the GPi and STN subjects combined, symptoms of Parkinson's disease (UPDRS TME scores) improved for 56/117 patients while ON medication and symptoms of Parkinson's disease (UPDRS TME scores) improved for 102/117 patients while OFF medication.

The probable risks and safety profile of the Abbott Infinity DBS System are similar to those of the Abbott Brio Neurostimulation System and the same as for the Medtronic Activa Parkinson's Control Therapy due to to similarity of the technological characteristics.

As documented in the SSED for the Abbott Brio Neurostimulation System "The adverse events that were reported were consistent with the safety profile of a legally marketed DBS system."

As documented in the SSED for the Medtronic Activa Parkinson's Control Therapy, "although there were a number of serious adverse events experienced by patients in this study, Parkinson's disease can be very disabling, both because of the "off" periods and also the dyskinesias patients can experience, related to medication treatment. Both of these components of the disease may worsen over time. The patients treated in this study had a Hoehn and Yahr stage 3 or worse in the "off" state; Unified Parkinson's Disease Rating Scale (UPDRS) motor exam score of 30 or more in the "off" state; and complications of levodopa therapy motor responses including motor fluctuations and dyskinesias. These patients have symptoms of advanced, levodoparesponsive Parkinson's disease that are not adequately controlled with medication. For this group of patients, FDA believes that the benefits outweigh the risks."

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 Infinity DBS System, the data support that for the requested indications for use the probable benefits for the Infinity DBS System outweigh its probable risks.

E. Overall Conclusions

The data in this application and its applicability to the Infinity DBS System for GPi stimulation 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 the effectiveness of the Infinity DBS System, the sponsor provided adequate evidence of the sufficient similarity of the Infinity DBS System and the Medtronic Activa Parkinson's Control Therapy 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 Parkinson's Control Therapy is directly applicable towards establishing reasonable assurance of the effectiveness of the Infinity DBS System.

With regard to reasonable assurance of the safety of the Infinity DBS System, the sponsor also provided adequate evidence of the sufficient similarity Abbott Medical Brio Neurostimulation System approved under P140009. Although the data were used to support the safety of DBS at the STN, the findings have applicability to the safety of stimulation at the GPi because of the similarity of the technological characteristics. The only difference is the location of the stimulation. The sponsor also provided adequate evidence of the sufficient similarity of the Infinity DBS System and the Medtronic

Activa Parkinson's Control Therapy with regard to technological characteristics. Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Parkinson's Control is directly applicable towards establishing reasonable assurance of the safety of the Infinity DBS System.

In conclusion, given the available information identified above and its applicability to the Infinity DBS System, the data support that for the requested indications for use the probable benefits for the Infinity DBS System outweigh its probable risks.

XIII. CDRH DECISION

CDRH issued an approval order on 1/02/2020.

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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