Abbott	Clinical Investigation Plan Cover Page

NCT Number: NCT03884231
Infinity MRI PMCF
A Post-Market Study Evaluating the Safety of Infinity DBS System with MR Conditional Labeling
Study Document No: [redacted]
[redacted]
Date: 16 January 2019

Sponsor

Abbott (formerly St. Jude Medical)
The Corporate Village
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Clinical Investigation Plan

[redacted]

Infinity MRI PMCF

A Post-Market Study Evaluating the Safety of Infinity DBS System with MR Conditional Labeling

Version Number	[redacted]
Date	16 January 2019
Planned Number of Sites and Region(s)	Up to 25 centers in geographies where Infinity DBS systems with MR Conditional labeling are approved including the European Union and United States.
Clinical Investigation Type	Multicenter, observational, prospective, single-arm, post-market clinical follow-up (PMCF)
Abbott Medical Expert	[redacted]
Sponsor	Abbott (formerly St. Jude Medical) The Corporate Village Da Vincilaan 11 – Box F1 Belgium Tel: +32 2 774 69 47
CIP Author of Current Version	[redacted]

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SITE PRINCIPAL INVESTIGATOR SIGNATURE PAGE

I have read and agree to adhere to the clinical investigation plan and all regulatory requirements applicable in conducting this clinical investigation.

Site Principal Investigator

Printed name:
Signature:
Date:

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COMPLIANCE STATEMENT:

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki, applicable Good Clinical Practices (GCP) and regulations (e.g., US 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 812 and OUS ISO14155:2011) and the appropriate local legislation(s). The most stringent requirements, guidelines or regulations must always be followed. The conduct of the clinical investigation will be approved by the appropriate Institutional Review Board (IRB)/Ethics Committee (EC) of the respective investigational site and by the applicable regulatory authorities.

Clinical Investigation Plan

1.0 INTRODUCTION

This protocol outlines the multicenter, prospective, post-market clinical follow-up (PMCF) plan to support the safety of St Jude Medical Infinity™ deep brain stimulation (DBS) systems with MR Conditional labeling. The study will be conducted at up to 25 centers in geographies where Infinity DBS systems with MR Conditional labeling are approved including the European Union and the United States, results of which will be submitted to the European Union Notified Body.

The rate of magnetic resonance imaging (MRI) procedure-related adverse events will be used to support the safety of Infinity DBS systems with MR Conditional labeling when used in compliance with the approved requirements. All MRI procedures and the recommended MRI procedural workflow in this clinical investigation should be followed using the DBS MRI Procedure Information Clinican's Manual to ensure patient and device safety during and after the MRI procedure.

This clinical investigation will be conducted in accordance with this clinical investigation plan (CIP). All investigators involved in the conduct of the clinical investigation will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

1.1 Background and Rationale

1.1.1 Background

Deep brain stimulation has demonstrated long-term efficacy in the management of advanced Parkinson's disease (PD)[1-6] and other movement disorders such as tremor and dystonia.[7-10] This is accomplished by sending continuous electrical signals to specific target areas, which modulate the activity of the basal ganglia circuitry. DBS is reversible and can be tailored to a patient's clinical status (parameters are adjustable allowing for minimization of stimulation induced side effects and improvements in efficacy over time), and the system can provide continuous symptom control 24 hours a day with minimal patient and physician involvement.[5,11-14] The electrodes and electrical systems that provide stimulation are generally well tolerated with no significant changes in surrounding brain tissue.[10]

Magnetic resonance imaging is an imaging modality that allows visualization of two and three dimensional images of the body. MRI systems generate three electromagnetic fields that are used to produce an image. These include a static magnetic field, a time varying gradient magnetic field and a radiofrequency field. All three of these fields interact with implanted devices and could create hazards for the device, the patient or both. Due to these issues, currently marketed implantable pulse generators (IPGs), leads or accessories may be contraindicated for use in a MRI environment.

St Jude Medical has developed MR Conditional neurostimulation systems, designed to mitigate such interactions. The systems provide the option for conditionally safe scanning of patients requiring an MRI. Centers that are qualified will be approached to participate in the DBS MRI PMCF to support MR Conditional labeling of the Infinity DBS system.

According to Sharan et al[15] MRI is a necessary imaging modality in the management of DBS patients throughout the course of the therapy. For example, MRI is typically used as part of surgical planning, may be used post-operatively to verify lead location, and is required in rare circumstances in which clinical outcome is poor or results in significant side effects.[15-17] Furthermore, due to the progressive nature of neurological diseases such as Parkinson's disease, patients implanted with DBS may require multiple MRIs to monitor chronic symptoms or to evaluate other co-morbidities such as stroke, neoplasm,

or infectious diseases.[15] The increasing importance of MRI is expected to continue to rise and underscores the need for an MR Conditional neurostimulation system for DBS applications.

The Infinity DBS system used in this PMCF received CE mark on October 19, 2018. Patients can undergo MRI procedures using one of two device configurations: a leads-only configuration and a full system configuration. The leads-only configuration consists of at least one implanted lead connected to a lead protection boot, as well as an optional cranial burr hole cover. The full system configuration consists of at least one IPG, one lead, one extension, and an optional cranial burr hole cover. For subjects with the lead-only configuration, the lead(s) are completely implanted, have a lead protection boot on the proximal end of the lead, and the surgical incision is closed.

1.1.2 Rationale for Conducting this Clinical Investigation

MRI is an imaging modality used in treatment or diagnosis of many conditions, and could also be used for DBS lead location verification. DBS systems have been shown to be beneficial for patients with Parkinson's disease, tremor, and dystonia but may be contraindicated for MRI, requiring an imaging method that is less optimal. This study will support the claim that MRI procedures are safe when performed according to the approved guidance. MR Conditional safety improves patient care for other conditions and reduces patient burden.

2.0 CLINICAL INVESTIGATION OVERVIEW

2.1 Clinical Investigation Objective

2.1.1 Primary objective

The primary objective of the DBS MRI PMCF is to support the safety of the Infinity DBS system with MR Conditional labeling.

2.2 Device(s) To Be Used in the Clinical Investigation

2.2.1 Name of the Device(s) Under Investigation

The components of the Infinity DBS system with MR Conditional labeling under this investigation are listed in Table 1. The MR Conditional components of the system are shown in Figure 1 and non-MR Conditional components (external devices) are shown in Figure 2.

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Table 1. Device(s) Under Investigation					
Device name	**Model/ Type**	**Serial/Lot Controlled**	**Manufacturer**	**Region/ Country**	**Investigational or Market Released**
Infinity 5 IPG Infinity 7 IPG	6660 6662	Serial	St. Jude Medical	Global	Market Released
8CH Directional Lead, 30 cm, 0.5 8CH Directional Lead, 30 cm, 1.5 8CH Directional Lead, 40 cm, 0.5 8CH Directional Lead, 40 cm, 1.5	6170 6171 6172 6173	Serial	St. Jude Medical	Global	Market Released
8CH Flex Extn, 50 cm 8CH Flex Extn, 60 cm	6371 6372	Serial	St. Jude Medical	Global	Market Released
Guardian™ Cranial Burr Hole Cover System Screw, 5mm	6010 6015	Lot	St. Jude Medical	Global	Market Released
Lead Protection Boot, 8CH Infinity	N/A (Packaged with Infinity leads)	N/A	St. Jude Medical	Global	Market Released
External Devices (MR Unsafe): Artemis Clinician Programmer App Artemis Patient Controller App	 3874 3875	N/A	St. Jude Medical	Global	Market Released

Figure 1: Components of the Infinity DBS system with MR Conditional labeling. Left to right: Infinity DBS MR Conditional IPG, Infinity MR Conditional Lead and Extension, Guardian Burr Hole Cover System, and Lead Protection Boot.

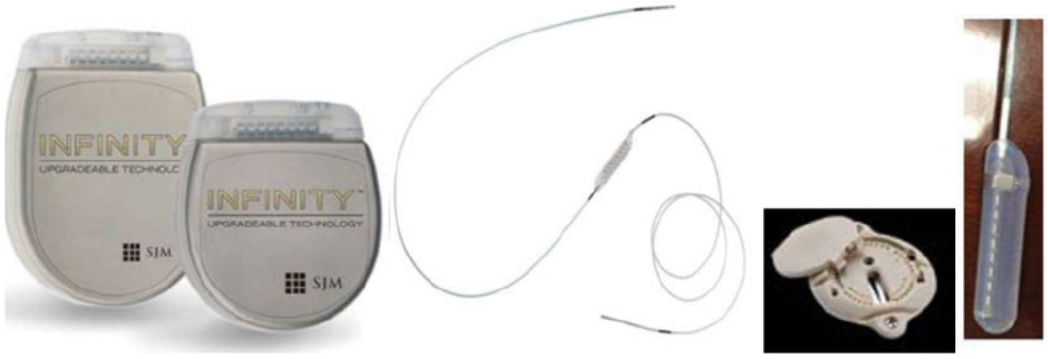

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Figure 2: External components of the Infinity DBS system that are MR Unsafe. Left to right: Artemis Clinician Programmer App, Artemis Patient Controller App.

2.2.2 Intended Indication for Use

The indications for use in the European Union for the Infinity DBS system with MR Conditional labeling are:

- Unilateral or bilateral stimulation of the thalamus, internal globus pallidus (GPi), or subthalamic nucleus (STN) in patients with levodopa-responsive Parkinson's disease.
- Unilateral or bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) for the management of intractable, chronic dystonia, including primary and secondary dystonia, for patients who are at least 7 years old.
- Unilateral or bilateral stimulation of the ventral intermediate nucleus (VIM) of the thalamus for the management of disabling tremor.

Please refer to the instructions for use (IFU) for locally approved indications for use.

2.2.3 Description of the Device(s) Under Investigation

The Infinity DBS system with MR Conditional labeling includes a primary cell implantable pulse generator designed to deliver low-intensity electrical pulses to targeted structures in the brain. A DBS 8-channel lead containing electrodes at the distal end is placed in the target brain structures, and is connected to the IPG via a DBS 8-channel extension. Up to 2 leads and extensions can be connected to the IPG. The electrical pulses travel from the IPG through the lead and extension, to electrodes placed near selected nerve fibers in order to provide therapeutic stimulation to patients suffering from movement disorders. The stimulation settings can be controlled wirelessly and are programmed over Bluetooth using the Artemis patient controller and Artemis clinician programmer. A DBS Lead Protection Boot is applied to

the terminal end of a DBS lead during staged implantation to protect the lead from damage and to allow for palpation of the terminal end of the lead through the scalp. Guardian Burr Hole cover is an accessory to the DBS system that is intended for use during cranial surgery as an implantable burr hole cover for the skull that can be used to secure the implanted lead. The product labeling describes the conditions for scanning patients requiring an MRI.

Please refer to the instructions for use (IFU) for additional information regarding the device used in this clinical investigation.

3.0 CLINICAL INVESTIGATION DESIGN

This study will be conducted as an international, multicenter, observational, prospective, single-arm, post-market clinical follow-up (PMCF). The study will evaluate the safety of the Infinity DBS system with MR Conditional labeling when an MRI procedure is performed according to the approved guidance. The results of this study will be submitted to the notified body.

The study will be conducted at centers that are qualified to participate and will enroll up to 74 subjects at up to 25 centers in geographies where Infinity DBS systems with MR Conditional labeling are approved including the European Union and the United States. A minimum of 10 centers will be included to ensure a range of MRI equipment brands, including a minimum of 6 in the European Union. Each site will have a maximum enrollment capped at 20% of total enrollment. Subjects who have a leads-only configuration or a full system configuration will participate in the study. Subjects may be enrolled when an MRI procedure is prescribed per standard of care.

Each subject will be limited to one MRI procedure during the course of the study. Selected sites will have this protocol approved to allow for data collection of the MRI parameters and any adverse events (AEs) that occur during the procedure and through 1-month following the procedure. An office visit will be added for all subjects for a 1-month (30 days ± 14 days) post-MRI follow-up visit after the initial MRI procedure is performed.

The clinical investigation has been designed to involve as little pain, discomfort, fear, and any other foreseeable risk as possible for subjects. Refer to the Risks Analysis section of this clinical investigation plan for details.

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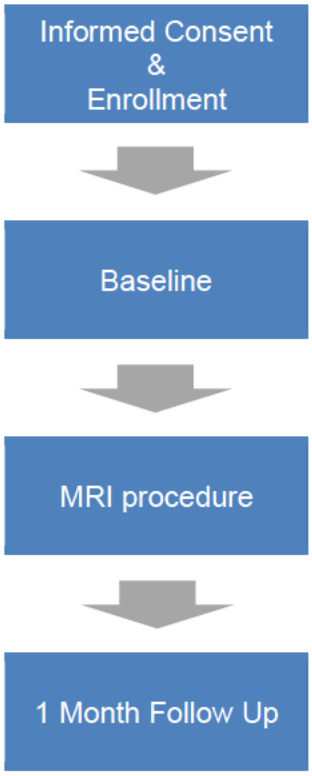
3.1 Clinical Investigation Procedures and Follow-up Schedule



Subjects will be screened to ensure they meet all inclusion criteria and none of the exclusion criteria, and will be considered enrolled in the study after providing written informed consent. Baseline data will be collected from the subject prior to the MRI procedure, and may be performed the same day as the MRI procedure. Device functionality will be checked immediately before and after the MRI procedure. Subjects will be followed for 1 month after the MRI procedure. Participation in the clinical study will end at the conclusion of the 1 month follow-up visit, and subjects will then be followed per standard of care.

3.2 Measures Taken to Avoid and Minimize Bias

All foreseeable factors that may compromise the outcome of the clinical study or the interpretation of the results have been considered by clinical study design and well defined subject selection criteria.

Subject recruitment and retention will be monitored throughout the study and includes, but is not limited to, the following activities:

- Evaluation of the site and investigators
- Training of site personnel
- Developing site support materials
- Providing subject visit calendars

An independent Clinical Events Committee (CEC) will review and adjudicate adverse events as defined in the CEC charter. The CEC will have final adjudication responsibilities for determining the relationship of adverse events to the MRI procedure. Use of an independent committee of medical experts will minimize bias in evaluation and reporting of adverse events that may be related to the MRI procedure.

3.3 Suspension or Early Termination of the Clinical Investigation

Because this study is used to support safety of the Infinity DBS system with MR Conditional labeling, no formal statistical rule for early termination of the clinical investigation for insufficient effectiveness of the device under investigation is defined.

The Sponsor reserves the right to discontinue the clinical investigation at any stage or reduce the follow-up period with suitable written notice to the investigator. Possible reason(s) may include, but are not limited to:

- Unanticipated adverse device effect (e.g., UADE) occurs and it presents an unreasonable risk to the participating subjects
- Any oversight committee (e.g., Steering/Executive Committee, Data Monitoring Committee) makes a recommendation to stop or terminate the clinical investigation (such as higher frequency of anticipated adverse device effects)
- Further product development is cancelled and MR Conditional labeled product will be removed from the market

Should the clinical investigation be discontinued by the Sponsor, subjects will be followed per routine clinical practice with device-related AEs reported to the Sponsor as per vigilance/commercial reporting requirements.

Should this occur, the investigator shall return all clinical investigation materials (including devices) to the Sponsor, and provide a written statement as to why the premature termination has taken place to the IRB/EC (if applicable). All applicable clinical investigation documents shall be subject to the same retention policy as detailed in Section 11.5 of the CIP.

A Principal Investigator, IRB/EC or regulatory authority may suspend or prematurely terminate participation in a clinical investigation at the investigational sites for which they are responsible. The investigators will follow the requirements specified in the Clinical Trial Agreement.

If the Sponsor suspends or prematurely terminates the clinical investigation at an individual site in the interest of safety, the Sponsor will inform all other Principal Investigators.

If suspension or premature termination occurs, the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate, and return patients to their standard medical treatment.

4.0 ENDPOINTS

4.1 Primary Endpoint and Rationale

The primary endpoint is the rate of MRI-related adverse events. This endpoint was selected as the primary goal of the study is to support safety of Infinity DBS systems with MR Conditional labeling when undergoing a MRI procedure according to the approved guidelines defined in the MRI Procedure Information Clinician's Manual. A description of adverse events for inclusion in the primary endpoint is provided in section 8.2.1.

4.2 Secondary Endpoints

The following secondary endpoints are for subjects undergoing an MRI procedure with the full system configuration.

- Rate of successful MRI mode 'turn on/off' functionality of the MRI mode
- Rate of successful 'turn on/off' functionality for the stimulation
- Rate of successful adjustments to the stimulation amplitude
- Rate of successful interrogation and download of the IPG parameters
- Rate of successful ability to obtain lead impedance measurements

4.3 Additional Safety Endpoint

Characterization of all MRI-related adverse events.

5.0 SUBJECT SELECTION AND WITHDRAWAL

5.1 Subject Population

This clinical investigation will enroll male and female subjects with levodopa-responsive Parkinson's disease, primary or secondary dystonia, or disabling tremor, and have been, or will be, implanted with the Infinity DBS system with MR Conditional labeling. Subjects must meet all eligibility criteria and provide written informed consent prior to conducting any investigation-specific procedures.

5.2 Subject Screening and Informed Consent

5.2.1 Subject Screening

Potential patients presenting at the clinical sites will be fully informed about the clinical investigation, following the established Informed Consent process (described in Section 5.2.2).

The following assessments will be performed as part of the screening process:

- Ensure subject has, or is scheduled to have, an Infinity DBS system implanted, per locally approved indications for use
- Ensure subject is willing to undergo an MRI procedure without sedation (ensure subject is not claustrophobic). Note: Anti-anxiety agents may be used as long as the patient can communicate with the site personnel during the MRI procedure.
- Subject is able to come into the clinic or office for an MRI procedure, and can come back for follow-up visits as needed
- Other assessments, as needed. See Eligibility Criteria (Section 5.3) or the patient eligibility criteria in the MRI Procedure Information Clinician's Manual for more information.

Subjects must be screened for clinical investigation eligibility by a member of the site's clinical investigation team (physician and/or research coordinator) previously trained to the CIP.

In case the subject does not meet all inclusion criteria or meets any of the exclusion criteria, the subject is considered a screening failure. The Principal Investigator or the delegated clinical investigation personnel will record the screening failure in the hospital records and on a screening log as required.

Subjects who meet all inclusion criteria and no exclusion criteria will be asked to sign an Informed Consent form if they wish to participate in the clinical investigation. Once a duly dated and signed Informed Consent form is obtained, the clinical investigation-specific procedures may begin.

Subject data will be collected following enrollment into the clinical investigation.

5.2.2 Informed Consent

The Investigator or his/her authorized designee will conduct the Informed Consent process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate, such as details of clinical investigation procedures, anticipated benefits, and potential risks of clinical investigation participation. Subjects must be informed about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. Financial incentives will not be given to the subject. Subjects may be compensated for time and travel directly related to the participation in the clinical investigation. The subject shall be provided with the Informed Consent form written in a language that is understandable to the subject and has been approved by the center's IRB/EC. The subject shall have adequate time to review, ask questions and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the subject understands the information provided. If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and thereafter by the person obtaining the consent prior to any clinical investigation-specific procedures. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

Failure to obtain informed consent from a subject prior to clinical investigation enrollment should be reported to Sponsor within 5 working days and to the reviewing center's IRB/EC according to the IRB/EC's reporting requirements.

If, during the clinical investigation, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee will provide this information to the subject. If relevant, the subject will be asked to confirm their continuing informed consent in writing.

5.2.2.1 Special Circumstances for Informed Consent

Individuals under age of 18 or age of legal consent

Individuals who are minors (under the age of 18 or age of legal consent) may be enrolled in this clinical investigation. Informed consent must be obtained using the IRB/EC approved informed consent in accordance with IRB/EC requirements. The clinical investigation directly relates to a medical condition affecting the minor, or is such that it can only be carried out on minors. Additionally, the clinical investigation is expected to product a direct benefit to the individual, outweighing the risks and burdens involved.

If the subject is a minor, the legally acceptable representative will represent the individual during the Informed Consent process, which will be performed according to the requirements in section 5.2.2. The

minor will also be informed about the clinical investigation within his/her ability to understand. The explicit wish of the minor who can form an opinion and assess information to decline participation or withdraw from the clinical investigation at any time will be respected.

If the minor reaches 18 or the age of legal competence during the clinical investigation, informed consent will be obtained before the individual continues in the clinical investigation.

Individuals unable to read or write
Individuals unable to read or write may be enrolled in this clinical investigation.

Informed consent will be obtained through a supervised oral process. An independent witness will be present throughout the Informed Consent process. The written Informed Consent form and any other information will be read aloud and explained to the prospective subject or his/her legally acceptable representative and either will sign and personally date the Informed Consent form. The witness will also sign and personally date the Informed Consent form attesting that the information was accurately explained and that informed consent was freely given.

Incapacitated individuals, defined as mentally ill, mentally handicapped, or individuals without legal authority
Incapacitated individuals, defined as persons who are mentally ill, mentally handicapped, or individuals without legal authority, are excluded from the study population.

Pregnant or breastfeeding women
Pregnant or breastfeeding women are excluded from the study population.

5.3 Eligibility Criteria

5.3.1 General Eligibility Criteria

Assessment for general eligibility criteria is based on medical records of the site and interview with a candidate patient. If some of the clinical and laboratory tests are not included in site standard tests, they must be done but after written informed consent is obtained. Patients must meet ALL of the inclusion criteria to be considered for the clinical investigation. If ANY of the exclusion criteria are met, the patient is excluded from the clinical investigation and cannot be enrolled.

5.3.2 Inclusion Criteria

1. Subject or subject's legally acceptable representative must provide written informed consent prior to any clinical investigation related procedure.
2. Subject has been implanted, or is scheduled to be implanted, with a commercially available Infinity DBS system with MR Conditional labeling per locally approved indications for use.
3. Subject is scheduled to undergo a MRI procedure in compliance with the MRI Procedure Information Clinican's Manual. Anxiolytics and patient's regular medications may be administered, provided IFU criteria are met.
4. Subject is willing and able to comply with study requirements.

5.3.3 Exclusion Criteria

1. Subject has another implanted device (active or passive implanted device) that prohibits safe scanning.

2. Subject has previously experienced an MRI-related adverse event or cannot undergo MRI for any other reason.
3. Subject is pregnant or nursing, or plans to become pregnant during the clinical investigation follow-up period.
4. Subject has other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.
5. Subject is currently participating in another clinical investigation that may confound the results of this study.

5.4 Subject Enrollment

A patient is considered enrolled in the clinical investigation from the time the patient provides written informed consent.

5.5 Subject Withdrawal

Each enrolled subject shall remain in the clinical investigation until completion of the required follow-up period; however, a subject's participation in any clinical investigation is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but not be limited to, the following:

- Subject death (cause must be documented)
- Subject does not meet the inclusion/exclusion criteria and does not require additional follow-up
- Subject voluntary withdrawal
- Subject non-compliance
- Subject's participation is terminated by the PI or co-investigator
- Subject lost-to follow-up as described below
- Subject's follow-up is terminated according to Section 3.3.

The Sponsor must be notified of the reason(s) for subject discontinuation. The site will provide this information to the Sponsor. Investigators must also report this to their respective IRB/EC as defined by their institution's procedure(s).

No additional follow-up will be required or data recorded from subjects once withdrawn from the clinical investigation, except for the status (deceased/alive) at the time of withdrawal, if not previously collected.

However, if a subject withdraws from the investigation due to problems related to the safety or performance of the device under investigation, the investigator shall ask for the subject's permission to follow his/her status/condition outside of the clinical investigation as appropriate.

<u>Lost-to-Follow-up</u>

A subject is considered lost-to-follow-up if the subject does not adhere to the scheduled follow-up visit but has not explicitly requested to be withdrawn from the clinically study. Site personnel shall make all

reasonable efforts to locate and communicate with the subject (and document these efforts in the source documents), including the following, at each contact time point:

- A minimum of two telephone calls on different days over the specified follow-up windows to contact the subject should be recorded in the source documentation, including date, time and initials of site personnel trying to make contact.
- If these attempts are unsuccessful, a letter (certified if applicable) should be sent to the subject.
- If a subject misses the follow-up contact time point, it will be considered a missed visit. If the subject misses their 1-month follow-up visit and the above-mentioned attempts at communicating with the subject are unsuccessful, the subject will be considered lost-to-follow-up.

Note: Telephone contact with General Practitioner, non-clinical investigation neurologist or relative without the presence of the subject or indirect documentation obtained via discharge letters will not be considered as subject contact.

5.6 Total Expected Duration of the Clinical Investigation

[redacted]

5.7 Expected Duration of Each Subject's Participation

Each subject will be followed for approximately 1 month after the MRI procedure. Participation will end after the 1 month follow-up visit.

5.8 Number of Subjects

To support the safety of the Infinity DBS system with MR Conditional labeling, up to 74 subjects will be enrolled in this study. Approximately 35 subjects will be included in each device configuration group (Leads Only and Full System). The total number of enrolled subjects assumes a 5% attrition rate following enrollment (e.g., due to subject unwilling to undergo DBS implant procedure, or for any other reason). Data from only one MRI procedure for each subject will be collected.

6.0 TREATMENT AND EVALUATION OF ENDPOINTS

6.1 Enrollment

Enrollment and baseline may take place in the same visit. The enrollment visit will take place in the clinic prior to the MRI procedure. The following activities are performed after the subject has been screened and must occur before any procedure/visit.

- The principal or delegated investigator is responsible for screening all potential patients to determine subject eligibility for the study.
- If a patient meets all inclusion criteria and does not meet any of the exclusion criteria, he/she is eligible for the study.
- The patient is enrolled in the study after signing the IRB/EC approved consent form.

Record enrollment information (date of consent and inclusion/exclusion information) in the hospital records and complete the enrollment form, preferably within 5 days of enrollment.

As soon as the patient signs the Subject Informed Consent Form, adverse events need to be reported according to the guidelines mentioned in this CIP [section 7.0].

In case the subject was consented to participate in the study, but is later found to not meet inclusion/exclusion criteria, and did not undergo an MRI procedure, the subject should be withdrawn and a withdrawal form must be completed. The subject will resume his/her regular standard of care with his/her physician.

In case the subject was consented to participate in the study and did undergo an MRI procedure, but does not meet inclusion/exclusion criteria, it is considered a protocol deviation. A protocol deviation form needs to be completed and the sponsor must be informed. The subject will be followed through the 1 month visit.

6.2 Baseline Data Collection

There is no minimum required time between implantation of the device and the MRI procedure. This will be determined by the physician based on the subject's standard of care. The following data will be collected at baseline:

- Subject demographics
- Medical condition for performing an MRI procedure
- Medical indication for having received/receiving DBS
- Adverse events
- Protocol deviations (if applicable)
- Withdrawal (if applicable)
- Device deficiency (if applicable)
- Product out of service data (if applicable)

6.3 MRI Procedure

The MRI procedure will take place at an appropriate facility. The MRI procedure must be performed according to the guidelines outlined in the MRI Procedure Information Clinician's Manual.

6.3.1 Pre-MRI/MRI Procedure Data Collection/Clinical Assessments (In clinic)

Subjects will be screened to ensure that they are eligible to undergo an MRI procedure. The following data will be collected before the MRI procedure:

- Subject eligibility for MRI procedure
- DBS lead(s) information
- Adverse events
- Protocol deviations (if applicable)
- Withdrawal (if applicable)
- Device deficiency (if applicable)
- Product out of service data (if applicable)

For subjects in the full system configuration group, the following additional data will be collected:

- DBS extension and DBS IPG information
- Success or failure of 'turn on' functionality of MRI mode
- Success or failure to 'turn on/off' functionality of the stimulation
- Success or failure to make adjustments to the stimulation amplitude
- Success or failure of device interrogation and download of IPG parameters
- Success or failure to obtain lead impedance measurements (only if the Clinician Programmer is being used to interrogate the IPG)

6.3.2 Immediate Post-MRI Procedure (In clinic, after the MRI procedure has been performed)

The following data will be collected after the MRI procedure:

- MRI scanner manufacturer/model
- Scan region (anatomic location)
- Subject position during MRI procedure
- Static field strength
- RF coil type
- RF power
    - B1+RMS, head SAR, and/or whole body SAR, if applicable
    - Duration of each scan
- Total active scan time
- DICOM image files (de-identified), if available
- Adverse events
- Protocol deviations (if applicable)
- Withdrawal (if applicable)
- Device deficiency (if applicable)
- Product out of service (if applicable)

For subjects in the full system configuration group, the following additional data will be collected immediately after the MRI procedure:

- Success or failure of 'turn off' functionality of MRI mode
- Success or failure to 'turn on/off' functionality of the stimulation
- Success or failure to make adjustments to the stimulation amplitude
- Success or failure of device interrogation and download of IPG parameters
  Success or failure to obtain lead impedance measurements (only if the Clinician Programmer is being used to interrogate the IPG)

6.4 Follow-up Assessments

6.4.1 1 Month Post-MRI Procedure Follow-up (In clinic)

The only follow-up visit for all subjects in this study will be scheduled for 30 days ± 14 days after the MRI procedure. The follow-up visit will be conducted in the clinic and data collection will include:

- For subjects with a full DBS system implanted (includes subjects in the full system configuration group and subjects in the leads-only group who had an IPG implanted and connected to at least one lead after the MRI procedure):
    - Success or failure to 'turn on/off' functionality of the stimulation

[redacted]

- Success or failure to make adjustments to the stimulation amplitude
- Success or failure of device interrogation and download of IPG parameters
- Success or failure to obtain lead impedance measurements (only if the Clinician Programmer is being used to interrogate the IPG)

- Adverse events
- Protocol deviations (if applicable)
- Withdrawal (if applicable)
- Device deficiency (if applicable)
- Product out of service data (if applicable)

6.4.2 Unscheduled visit

Subjects may be asked or need to return to the clinic before the 1 month visit to assess various program parameters or undergo additional surgery to replace, reposition/revise or explant the DBS component(s) or system. This is considered an unscheduled visit. An IPG implant procedure for the Leads-Only group occurring after the MRI procedure is acceptable and will also be considered an additional surgery. If an unscheduled visit occurs, the following information will be recorded:

- Reason for visit
- Action taken
- Adverse events
- Session records, if (re)programmed
- Additional surgery information (if applicable)
- Protocol deviation (if applicable)
- Withdrawal (if applicable)
- Device deficiency (if applicable)
- Product out of service data (if applicable)

6.4.3 Non-Study MRI Procedures

In some cases, a non-study MRI procedure may be medically necessary. A non-study MRI procedure is defined as an MRI scan occurring after the study MRI procedure but prior to the 1 month follow-up visit. Non-study MRI procedures should be performed according to the center's standard of care.

For non-study MRI procedures, the same safety precautions outlined in the MRI Procedure Information Clinican's Manual should be followed. However, data for the non-study MRI procedures will not be collected within the study setting.

6.4.4 Schedule of Events

Table 2. Schedule of Events						
CIP Activity	Enrollment	Baseline	MRI visit		1 Month post-MRI Follow-up (30 days ± 14 days after MRI procedure)	Unscheduled
			Pre-MRI/ MRI Procedure	Immediate Post-MRI Procedure		
Informed Consent Process	X					
Inclusion/Exclusion Criteria Check	X					
Demographics		X				
Medical condition indicated for MRI procedure		X				
Subject eligibility for MRI procedure			X			
Medical indication for DBS		X				
DBS Lead information			X			(X)
IPG and extension information			X*			(X)
MRI procedure			X			
DICOM image files				(X)		
MRI parameters				X		
Turn "on" of MRI mode			X*			
Turn "off" of MRI mode				X*		
"On/off" of stimulation			X*	X*	X**	
Adjustments to the stimulation amplitude			X*	X*	X**	
Interrogation and download of IPG parameters			X*	X*	X**	
Impedance testing			(X*)	(X*)	(X**)	
Session records			(X*)	(X*)	(X**)	(X**)
Adverse Events	(X)	(X)	(X)	(X)	(X)	(X)
Protocol Deviation	(X)	(X)	(X)	(X)	(X)	(X)
Withdrawal	(X)	(X)	(X)	(X)	(X)	(X)
Product Out of Service Data	(X)	(X)	(X)	(X)	(X)	(X)
Device Deficiency Information	(X)	(X)	(X)	(X)	(X)	(X)

(X) = if applicable
X* = for subjects in the full system configuration group
X** = for subjects with a full DBS system implant (includes subjects in the full system configuration group and subjects in the leads-only group who had an IPG implanted and connected to at least one lead after the MRI procedure)

7.0 ADVERSE EVENTS

To comply with worldwide standards and guidelines on clinical investigation adverse event reporting, the Sponsor has adopted uniform and worldwide applicable standard definitions and reporting timelines to be used and adhered to by the investigators.

7.1 Definition

7.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device under investigation.

Note 1: This definition includes events related to the medical device under investigation or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to medical devices under investigation.

7.1.2 Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE).

a) Led to a death,

b) Led to a serious deterioration in health of the subject, that either resulted in

   1. a life-threatening illness or injury, or
   2. a permanent impairment of a body structure or a body function, or
   3. in-patient hospitalization or prolongation of existing hospitalization, or
   4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function, or
   5. chronic disease

c) Led to fetal distress, fetal death or a congenital abnormality or birth defect.

Note: A planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered to be an SAE.

7.2 Device and Procedure Relationship

Determination of whether there is a reasonable possibility that the device under investigation or the DBS procedure (if applicable) caused or contributed to an AE is to be determined by the Investigator and recorded on the appropriate case report form (CRF). Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition).

7.3 MRI Relationship

Determination of whether there is a reasonable possibility that the MRI procedure caused or contributed to an AE is to be determined by the Investigator and recorded on the appropriate CRF. The CEC will provide final adjudication of MRI related AEs. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition). Adverse events will be classified as MRI-related if no other cause can reasonably be attributed to the event. Examples of possible adverse events that may occur in the MRI environment include, but are not limited to the following:

- Intracranial hemorrhage, which can lead to stroke, paralysis, or death (that may result from lead electrode heating)
- Persistent pain, tightness, or discomfort around the implanted parts (that may result from IPG heating)
- Stimulation-related complications such as sensory or motor disturbance or cognitive impairment (that may result from induced currents on leads)
- Loss of therapeutic benefit or undesirable changes in stimulation (that may result from damage to the system components). This would only occur after the MRI since stimulation is off during the MRI scan.
- Failure to deliver stimulation due to damage to the IPG (that may result from damage to the system components).
- Migration or dislodgement of one or more of the system components (that may result from induced forces).
- Sensation of warmth at the IPG (that may result from device heating).

Refer to the specific device manuals [redacted] for the adverse events that are associated with implanting or using the neurostimulation system for DBS and for MRI related adverse events.

In addition, it is possible that subjects may experience unavoidable events related to the MRI procedure. An unavoidable event is an event related to the MRI procedure that is expected to occur within a finite duration (See Table 3). Unavoidable events may occur with any MRI procedure and are not reportable unless the condition worsens or continues beyond the time frame listed below. Unavoidable events do not need to be reported on an adverse event form if they are resolved within the time frame specified.

Table 3: Unavoidable Events Related to the MRI Procedure	
Event	Timeframe
Claustrophobia	During MRI scan
Mild diaphoresis	During and < 1 hour post MRI scan
Sensation of bodily warmth	During and < 1 hour post MRI scan
Hearing impairment	< 24 hours post MRI scan
Body stiffness related to immobility	< 48 hours post MRI scan

7.4 Adverse Event

7.4.1 Adverse Event Reporting

General AE Reporting

Safety surveillance and reporting starts as soon as the patient is enrolled in the clinical investigation. Safety surveillance and reporting will continue until the one month follow-up visit has been performed, the subject is deceased, the subject concludes participation in the clinical investigation or the subject withdraws from the clinical investigation, whichever comes first. All adverse event data will be collected throughout the time period defined above and will be reported to the Sponsor on a CRF. Additional information with regard to an adverse event should be updated within the appropriate CRF.

Unchanged, chronic, non-worsening or pre-existing conditions are not AEs and should not be reported.

An offline form will be made available to allow the investigator to report SAEs in the event the entry cannot be made in the electronic data capture (EDC) system. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

SAE Reporting

The investigator should report all SAEs to the Sponsor as soon as possible but no later than outlined below.

Clinical Site	Reporting timelines
All Sites	SAEs must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the site's local requirements, if more stringent than 3 calendar datys.

The date the site staff became aware the event met the criteria of an SAE must be recorded in the source document. The Investigator will further report the SAE to the local IRB/EC according to the local IRB/EC reporting requirements.

Reportable events to the sponsor are considered:

- All serious adverse events regardless of relatedness to the device and/or implant procedure
- All device- or implant procedure-related adverse events
- All MRI-related adverse events

Refer to the specific device manuals for the adverse events that are associated with implanting or using the neurostimulation system for DBS and for MRI related adverse events.

7.4.2 Device Deficiency/Malfunction Reporting

All device deficiencies/malfunctions should be reported on the appropriate CRF. The investigator should report all device deficiencies/malfunctions to the Sponsor as soon as possible but no later than 3 calendar days from the day the site personnel became aware of the event or as per the site's local requirements, if more stringent than 3 calendar days.

Device deficiencies/ malfunctions should be reported to the IRB/EC per the site's local requirements.

An offline form will be made available to allow the investigator to report device deficiencies/malfunctions in the event that the entry cannot be made in the EDC system. This does not replace the EDC reporting system. All information must still be entered in the EDC system as soon as feasible.

7.4.3 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

The Sponsor will report SAEs to the country regulatory authority, per local requirements.

7.4.4 Procedure for Recording and Reporting Subject Death

Should death occur, the investigator is requested to record death information in the hospital records and immediately document the information on the AE case report form and submit to Sponsor. The investigator should report the death as soon as possible and per the reporting timeline for SAEs in section 7.4.1.

- All efforts to obtain the details about the circumstances surrounding the patient death should be made by the Investigator.

The subject's death is an outcome of an AE and an early conclusion of the subject's participation in the clinical investigation. Therefore, the Investigator is required to complete the Withdrawal form.

8.0 STATISTICAL CONSIDERATIONS

The following section describes the statistical methods for the clinical investigation. Additional details on statistical analyses, including justification of clinical investigation design, and analysis of additional endpoints, may be maintained in a separate Statistical Analysis Plan (SAP).

8.1 Analysis Populations

All subjects who have signed a Subject Informed Consent Form will be considered enrolled in the clinical investigation. However, it is anticipated that there will be subjects who are enrolled in the study, but will not be included in the primary endpoint analysis, such as:

- Subjects who are enrolled, but do not meet inclusion criteria or meet exclusion criteria and do not undergo and MRI procedure; these subjects will be withdrawn from the study.
- Subjects who are enrolled, but do not undergo an MRI procedure; these subjects will be withdrawn from the study.

8.2 Statistical Analyses

8.2.1 Primary Endpoint Analysis

The primary endpoint is the event rate of MRI-related adverse events through 1 month post-MRI procedure. The clinical acceptance criterion for the rate of MRI-related adverse events is 7%, drawn from historical rates of significant adverse events in DBS studies. The endpoint will be evaluated for each group and will be reported as the percentage of subjects experiencing the events. The clinical acceptance criterion must be satisfied in both groups (leads-only and full system).

The primary analysis will be conducted on subjects who meet all of the following criteria:

- Signed informed consent

- Met the MRI procedure eligibility requirements at the time of the MRI procedure (as per the MRI Procedure Clinician's manual)
- Had a study MRI procedure

Any adverse event will be included in the primary endpoint analysis if it:

1. Is classified as being MRI-related (as determined by the CEC), occurs during or after the MRI procedure, and cannot be attributed to any other cause; **and**
2. Is classified as being related to the device (implanted or external component) (as determined by the Investigator); **and**
3. Meets the criteria for serious adverse event **or** is a non-serious adverse event that is the result of irrecoverable failure of therapy delivery or device communication.

Examples of MRI-related adverse events that will be included in the primary endpoint analysis are:

- Symptomatic intracranial hemorrhage that cannot be attributed to the implant procedure.
- New and permanent neurological symptoms that cannot be attributed to a cause other than the MRI procedure.
- Lack of therapeutic benefit due to damage to the IPG requiring device replacement (e.g., stimulation cannot be turned on following the MRI procedure, stimulation cannot be adjusted following the MRI procedure).

Examples of adverse events that may be reported but will not be included in the primary analysis are:

- Transient, non-serious complications such as sensory or motor disturbance during the MRI procedure that may result from induced currents on leads.
- Sensation of warmth at the IPG that resolves following the MRI procedure.
- Pain around the implanted IPG site that could be related to the implant procedure.

8.2.2 Secondary Endpoint Analysis

The following secondary endpoints will be analyzed for subjects who undergo an MRI procedure with a full system configuration. The endpoint "Rate of successful ability to obtain lead impedance measurements" will include only those subjects who had their IPG interrogated using the Clinician Programmer. Data (success or failure) for these endpoints will be collected immediately after the MRI procedure.

- Rate of successful MRI mode 'turn on/off' functionality of the MRI mode
- Rate of successful 'turn on/off' functionality for the stimulation
- Rate of successful adjustments to the stimulation amplitude
- Rate of successful interrogation and download of the IPG parameters
- Rate of successful ability to obtain lead impedance measurements

Rates will be reported as the percentage of subjects in which the device functionality could be successfully completed.

8.2.3 Additional Safety Endpoint

The frequency of all MRI-related adverse events will be reported as the number of occurrences of each event and the percentage of subjects experiencing each event, and will be summarized in table format.

8.3 Sample Size Calculation and Assumptions

[redacted]

8.4 Timing of Analysis

Analysis of the primary endpoint and additional endpoints will occur once all subjects have either completed the 1-month follow-up or withdrawn from the study.

8.5 Subgroup Analysis

No subgroup analyses are planned for this clinical investigation.

8.6 Procedures for Accounting for Missing Data

No imputation techniques will be used in this study.

8.7 Planned Interim Analysis

Interim analysis will not be conducted; however the CEC will review and adjudicate events periodically until the study is completed.

8.8 Statistical Criteria for Termination

There are no statistical criteria for termination of this clinical investigation.

8.9 Success Criteria

The clinical investigation is successful if the primary endpoint is met for both the lead-only configuration group and the full DBS system group.

8.10 Labeling Claim

This Post-Market Clinical Follow up (PMCF) supports the safety of the Infinity DBS system with MR Conditional Labeling.

8.11 Deviations from Statistical Plan

Any major changes to the statistical plan will be documented in an amendment to the statistical plan. Less significant changes to the planned analyses will be documented in the final report.

9.0 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The investigator/institution will permit direct access to source data/documents for the purpose of performing clinical investigation-related monitoring, audits, IRB/EC review and regulatory inspections.

Subjects providing informed consent are agreeing to allow clinical investigation monitors or regulatory authorities to review, in confidence, any records identifying the subjects in this clinical investigation. This information may be shared with regulatory agencies; however, Sponsor undertakes not to otherwise release the subject's personal and private information.

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Selection of Clinical Sites and Investigators

The Sponsor will select investigators qualified by training and experience to participate in the clinical investigation. Sites will be selected based upon review of a recent site assessment, if applicable, and the qualifications of the investigators who will participate in the clinical investigation.

10.2 Clinical Investigation Finances and Agreements

The clinical investigation is fully financed by the Sponsor. The Sponsor will establish written agreements with the sites before patient enrollment.

10.3 CIP Amendments

Approved CIP amendments will be provided to the Investigators by the Sponsor prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB/EC or equivalent committee of the CIP amendment (administrative changes) or obtaining IRB/EC's approval of the CIP amendment (changes in subject care or safety), according to the instructions provided by the Sponsor with the CIP amendment.

Acknowledgement/approval by the IRB/EC of the CIP amendment must be documented in writing prior to implementation of the CIP amendment. Copies of this documentation must also be provided to the Sponsor.

10.4 Training

10.4.1 Site Training

All Investigators and clinical investigation personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit or other appropriate training sessions. Over-the-phone or self-training may take place as required. Training of Investigators and clinical investigation personnel will include, but is not limited to, the CIP requirements, MR Conditional labeling for the Infinity DBS system, electronic case report form completion and clinical investigation personnel responsibilities. All Investigators and clinical investigation personnel that are trained must sign a training log (or an equivalent) upon completion of the training. Prior to signing the training log, Investigators and clinical investigation personnel must not perform any CIP-related activities that are not considered standard of care at the site.

10.5 Monitoring

Sponsor and/or designee will monitor the clinical investigation over its duration according to the CIP-specific monitoring plan which will include the planned extent of source data verification.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The investigator understands and accepts the obligation to conduct the clinical investigation according to the CIP and applicable regulations, and has signed the Clinical Trial Agreement.
- The Investigator and his/her staff should have sufficient time and facilities to conduct the clinical investigation and should have access to an adequate number of appropriate subjects to conduct the clinical investigation.
- Source documentation (including original medical records) must be available to substantiate proper informed consent procedures, adherence to CIP procedures, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- The Investigator/site will permit access to such records. A monitoring visit sign-in log will be maintained at the site. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the monitor with a suitable working environment for review of clinical investigation-related documents.

10.6 Deviations from CIP

The Investigator should not deviate from the CIP for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety and well-being of the subject or eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify Sponsor immediately by phone or in writing.

No waivers for CIP deviations will be granted by the Sponsor. All deviations must be reported to the Sponsor using the Deviation CRF. The occurrence of CIP deviations will be monitored by the Sponsor for evaluation of investigator compliance to the CIP and regulatory requirements and dealt with according to written procedures. Investigators will inform their IRB/EC or equivalent committee of all CIP deviations in accordance with their specific IRB/EC or equivalent committee reporting policies and procedures.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the CIP or any other conditions of the clinical investigation may result in further escalation in accordance with the Sponsor's written procedures, including securing compliance or, at its sole discretion, Sponsor may terminate the investigator's participation in the clinical investigation.

10.7 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical investigation records, including source documentation, for inspection during a Quality Assurance audit.

In the event that an investigator is contacted by a Regulatory Agency in relation to this clinical investigation, the Investigator will notify Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide Sponsor with copies of all correspondence that may affect the review of the current clinical investigation (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). Sponsor may provide any needed assistance in responding to regulatory audits.

10.8 Sponsor Auditing

1. The Sponsor shall prepare an audit plan as well as the operating procedures for the related duties, and conduct audits in accordance with the audit plan and the operating procedures.
2. Individual engaged in auditing (hereinafter referred to as "auditor") shall be different than those in charge of medical device development or monitoring.
3. The auditor shall prepare an audit report documenting the matters confirmed in the audit to certify and verify that the audit has been conducted, and submit them to the Sponsor.

10.9 Committees

10.9.1 Clinical Events Committee (CEC)

The Clinical Events Committee (CEC) is an independent adjudication body comprised of qualified physicians who are not participants in the clinical investigation. The CEC will review and adjudicate pre-specified events reported by investigators or identified by Safety personnel for the clinical investigation

as defined in the CEC charter and according to definitions provided in this CIP. For this study, the CEC will review events periodically regarding their relationship to the MRI procedure.

11.0 DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection for the duration of the clinical investigation.

CRF data collection will be performed through a secure web portal and only authorized personnel will access the Electronic Data Capture (EDC) system using a unique username and password to enter, review or correct data. Passwords and electronic signatures will be strictly confidential.

The data will be subjected to consistency and validation checks within the EDC system and supplemental review by the Sponsor. The de-identified MRI images may be transferred to the Sponsor using the EDC system or through a secure file transfer method.

At the conclusion of the clinical investigation, completed CRF images with the date-and-time stamped electronic audit trail indicating the user, the data entered, and any reason for change (if applicable) will be provided to the investigational sites, if requested.

For the duration of the clinical investigation, the Investigator will maintain complete and accurate documentation including, but not limited to, medical records, clinical investigation progress records, laboratory reports, CRFs, signed ICFs, device accountability records (if applicable), correspondence with the IRB/EC and clinical investigation monitor/Sponsor, adverse event reports, and information regarding subject discontinuation or completion of the clinical investigation.

11.1 Protection of Personally Identifiable Information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical investigation.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a ‘need to know’ basis, including periodic review of access rights, and revocation of access when an individual’s employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the investigational sites to transfer into Sponsor’s data management systems only pseudonymous Personal Information (key-coded) necessary to conduct the Clinical Investigation, such as the patient’s medical condition, treatment, dates of treatment, etc. The Sponsor discloses as part of the clinical investigation informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring and quality control purposes. Confidentiality of Personal Information will be observed by all parties involved at all times throughout the clinical investigation. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any

Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical Investigation data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

11.2 Data Management Plan

A Data Management Plan (DMP) will describe procedures used for data review, data cleaning, and issuing and resolving data discrepancies. If appropriate, the DMP may be updated throughout the duration of the clinical investigation. All revisions will be tracked and document controlled.

11.3 Source Documentation

Regulations and GCP require the Investigator to maintain information in the subject's original medical records that corroborates data collected on the CRFs. In order to comply with these regulatory requirements/GCP, the following information should be included in the subject record at a minimum and if applicable to the clinical investigation:

- Medical history/physical condition of the subject before involvement in the clinical investigation sufficient to verify CIP entry criteria
- Dated and signed notes on the day of entry into the clinical investigation referencing the Sponsor, CIP number, subject ID number and a statement that informed consent was obtained
- Dated and signed notes from each subject visit (for specific results of procedures and exams)
- Adverse events reported and their resolution, including supporting documents, such as discharge summaries, office notes and any other pertinent patient's records, including documentation of site awareness of SAEs and of investigator assessment of device relationship for SAEs
- Subject's condition upon completion of or withdrawal from the clinical investigation
- Any other data required to substantiate data entered into the CRF

11.4 Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the CIP and CRF completion. The investigator will ensure accuracy, completeness, legibility and timeliness of the data reported to the Sponsor on the CRFs and in all required reports.

Data on CRFs will be collected for all subjects that are enrolled into the clinical investigation.

Only authorized site personnel will be permitted to enter the CRF data through the EDC system deployed by the Sponsor. An electronic audit trail will be used to track any subsequent changes of the entered data.

11.5 Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical investigation as per the applicable regulatory record retention requirements. The Investigator must obtain

permission from Sponsor in writing before destroying or transferring control of any clinical investigation records.

12.0 ETHICAL CONSIDERATION

12.1 Institutional Review Board/Medical Ethics Committee Review and Approval

Institutional Review Board (IRB) or Ethics Committee (EC) approval for the CIP and ICF/other written information provided to the patient will be obtained by the Principal Investigator at each investigational site prior to consenting and enrolling patients in this clinical investigation. The approval letter must be received prior to the start of this clinical investigation and a copy must be provided to the Sponsor.

Any amendments to the CIP as well as associated ICF changes will be submitted to the IRB/EC and written approval obtained prior to implementation, according to each institution's IRB/EC requirements.

No changes will be made to the CIP or ICF or other written information provided to the patient without appropriate approvals, including IRB/EC, the Sponsor, and the regulatory agencies (if applicable).

Until the clinical investigation is completed, the Investigator will advise his/her IRB/EC of the progress of this clinical investigation, per IRB/EC requirements. Written approval must be obtained from the IRB/EC yearly to continue the clinical investigation, or according to each institution's IRB/EC requirements.

No investigative procedures other than those defined in this CIP will be undertaken on the enrolled subjects without the written agreement of the IRB/EC and the Sponsor.

13.0 CLINICAL INVESTIGATION CONCLUSION

The clinical investigation will be concluded when:

- All sites are closed AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of clinical investigation closure.

14.0 PUBLICATION POLICY

The data and results from the clinical investigation are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during the clinical investigation. The Investigators will not use this clinical investigation-related data without the written consent of the Sponsor for any purpose other than for clinical investigation completion or for generation of publication materials, as referenced in the Clinical Trial Agreement. Single-center results are not allowed to be published or presented before the multi-center results. Any proposals for publications or presentations by the investigators must be reviewed and approved by the Sponsor in a timely manner to enable Sponsor review in compliance with the Sponsor's publication policy set forth in the Clinical Trial Agreement.

The Sponsor will be responsible for determining whether to register the clinical investigation on www.clinicaltrials.gov or any other clinical trial registries, in accordance with the International Committee of Medical Journal Editors guidelines, or any other applicable guidelines. In the event Sponsor determines that the clinical investigation should be registered, Sponsor shall be responsible for any such

registration and results posting as required by the ClinicalTrials.gov website. Institution and/or Principal Investigator(s) shall not take any action to register the clinical investigation.

15.0 RISK ANALYSIS

15.1 Anticipated Clinical Benefits

The primary benefit of the MR conditional neurostimulation system is that it provides subjects with the option to undergo an MRI procedure when clinically necessary, while defining the conditions for use that maximize subject safety.

If subjects take part in this study, there may or may not be direct medical benefits to individual subjects. The scientific use of the data collected in this study is intended to support the CE label of the Infinity DBS system with MR Conditional labeling by supporting the safety of MRI procedures when performed per manufacturer's requirements.

15.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Risks associated with the specified device and procedure, together with their likely incidence, are described in the device IFU and the MRI Procedure Information Clinician's Manual. There may be risks related to the device under investigation that are unknown at present. Likewise, the exact frequency of the risk may be unknown.

15.3 Residual Risks Associated with the Device Under Investigation, as Identified in the Risk Analysis Report

The clinical risks associated with neurostimulation systems for DBS applications are well known. Many of the clinical risks may develop as a consequence of not following the manufacturer recommended guidelines at the time of performing the MRI procedures.

Any potential residual risks are considered to be outweighed by the benefits, and the overall residual risk was determined to be acceptable. Clinical evidence demonstrates acceptable safety and performance of the device under investigation.

15.4 Risks Associated with Participation in this Clinical Investigation

The risks involved with this study are comparable to those associated with the implant of any other commercially available MR Conditional neurostimulation system.

15.5 Steps Taken to Control or Mitigate Risks

The devices in use for this study are CE marked with MR Conditional labeling. In-depth recommendations, special precautions and instructions regarding MR Conditional procedures are included in the MRI Procedure Information Clinician's Manual. Physician users are expected to be aware of the known and foreseeable safety risks associated with the use of the devices in an MRI environment.

Risks associated with the use of the device under investigation are minimized through device design, investigator selection and training, pre-specified patient eligibility requirements, study monitoring to ensure adherence to the protocol. All adverse events will be reported to the Sponsor and will be monitored internally for safety surveillance purposes.

15.6 Risk to Benefit Rationale

Since no design changes exist between the MR Conditional DBS system and the predicate DBS system, except for implementation of the MRI mode, the non-MR performance of these products is already well established.

In addition, the clinical evidence demonstrates that the safety and performance of the device under investigation, when used under the conditions and for the purposes intended, as specified by the manufacturer, are in compliance with the Requirements of the AIMD Directive 90/385/EEC, including the Essential Requirements.

Any undesirable side effects, under normal conditions of use, are considered to be acceptable risks when weighted against the performance of the device and benefits to the subject.

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APPENDIX I: ABBREVIATIONS AND ACRONYMS

ABBREVIATION	TERM
ADE	Adverse Device Event
AE	Adverse Event
ASADE	Anticipated Serious Adverse Device Event
CA	Competent Authority
CIP	Clinical Investigational Plan
CRF	Case Report Form
DBS	Deep Brain Stimulation
DD	Device Deficiency
DMP	Data Management Plan
EC	Ethics Committee
ET	Essential Tremor
GCP	Good Clinical Practice
GP	General Practitioner
GPi	Internal Globus Pallidus
IB	Investigator Brochure
ICMJE	International Committee of Medical Journal Editors
ICF	Informed Consent Form
IFU	Instructions For Use
IPG	Implantable Pulse Generator
ISB	Investigator Site Binder
ISO	International Organization for Standardization
MP	Monitoring Plan
MRI	Magnetic Resonance Imaging
NA	Not Applicable
OPC	Objective Performance Criteria
PD	Parkinson's disease
PG	Performance Goal
PI	Principal Investigator
PMCF	Post Market Clinical Follow UP
RDC	Remote Data Capture
SADE	Serious Adverse Device Event
SAE	Serious Adverse Event
SJM	St. Jude Medical
STN	Subthalamic nucleus
SOC	Standard-of-care
UCB	Upper Confidence Bound
USADE	Unanticipated Serious Adverse Device Event
WMA	World Medical Association

Clinical Investigation Plan

APPENDIX II: DEFINITIONS

Medical Device

Any instrument, apparatus, machine, appliance, implant, software, material, or other similar or related article:

- Intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of
  - Diagnosis, prevention, monitoring, treatments or alleviation of disease
  - Diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury
  - Investigation, replacement, modification, or support of the anatomy of a physiological process
  - Supporting or sustaining life
  - Control of conception
  - Disinfection of medical devices and
- Which does not achieve its primary intended action in or on the human body by pharmacological, immunological, or metabolic means, but which may be assisted in its intended function by such means

Device Deficiency/Device Malfunction

Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: Performance specifications include all claims made in the labeling of the device.

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the instructions for use or CIP.

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APPENDIX III: SITE CONTACT INFORMATION

Contact information for each participating clinical site is available under separate cover by contacting the Sponsor at:

Abbott
The Corporate Village
Da Vincilaan 11, Box F1
1935 Zaventem Belgium
Email: monique.vanbree@abbott.com
Phone: +32 2 774 69 47

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APPENDIX IV: REFERENCES

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APPENDIX V: CASE REPORT FORMS

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APPENDIX VI: INFORMED CONSENT FORM

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APPENDIX VII: MONITORING PLAN

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APPENDIX IX: LABELING

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APPENDIX X: CIP SUMMARY

Clinical Investigation Name and Number	CRD_950 Infinity MRI PMCF
Title	A Post-Market Study Evaluating the Safety of Infinity DBS System with MR Conditional Labeling
Objective(s)	The primary objective of the Infinity MRI PMCF is to support the safety of the Infinity DBS System with MR Conditional labeling.
Device Under Investigation	The following devices will be used in the study: Infinity DBS System • Infinity IPGs used with 8 channel leads (Models 6660, 6662) • Infinity Clinician Programmer App and Patient Controller App (Models 3874, 3875) The following components may be implanted in subjects with "lead-only" configuration: Leads: • 6170 St. Jude Medical Infinity DBS System Directional lead, 30 cm, 0.5 mm spacing • 6171 St. Jude Medical Infinity DBS System Directional lead, 30 cm, 1.5 mm spacing • 6172 St. Jude Medical Infinity DBS System Directional lead, 40 cm, 0.5 mm spacing • 6173 St. Jude Medical Infinity DBS System Directional lead, 40 cm, 1.5 mm spacing Lead protection boot (included in lead kit) 6010 Guardian cranial burr hole cover system (optional) 6015 Screw, 5mm (optional) The following components may be implanted in subjects with "full-system" configuration: IPG (implanted in pectoral or abdominal area): • 6660 St. Jude Medical Infinity DBS IPG 5.3 Ah • 6662 St. Jude Medical Infinity DBS IPG 7.5 Ah Leads: • 6170 St. Jude Medical Infinity DBS System Directional lead, 30 cm, 0.5 mm spacing • 6171 St. Jude Medical Infinity DBS System Directional lead, 30 cm, 1.5 mm spacing • 6172 St. Jude Medical Infinity DBS System Directional lead, 40 cm, 0.5 mm spacing • 6173 St. Jude Medical Infinity DBS System Directional lead, 40 cm, 1.5 mm spacing

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	Extensions: • 6371 St. Jude Medical Infinity DBS System 8CH Flex Extn, 50 cm • 6372 St. Jude Medical Infinity DBS System 8CH Flex Extn, 60 cm 6010 Guardian cranial burr hole cover system (optional) 6015 Screw, 5mm (optional)
Number of Subjects Required for Inclusion in Clinical Investigation	The study will be conducted at centers that are qualified to participate and will enroll up to 74 subjects at up to 25 centers in geographies where Infinity DBS systems with MR Conditional labeling are approved including the European Union and the United States.
Clinical Investigation Design	This study will be conducted as an international, multicenter, observational, prospective, single-arm, post-market clinical follow-up (PMCF). The study will evaluate the MRI safety of the Infinity DBS system with MR Conditional labeling when used according to the approved guidance.
Primary Endpoint	The primary endpoint is the rate of MRI-related adverse events.
Secondary Endpoints	The following secondary endpoints are for subjects undergoing an MRI procedure with the full system configuration. • Rate of successful MRI mode 'turn on/off' functionality of the MRI mode • Rate of successful 'turn on/off' functionality for the stimulation • Rate of successful adjustments to the stimulation amplitude • Rate of successful interrogation and download of the IPG parameters • Rate of successful ability to obtain lead impedance measurements
Additional Safety Endpoint	Characterization of all MRI-related adverse events.
Subject Follow-up	• Enrollment/Baseline (in clinic) • MRI Procedure Visit (in clinic) • 1 month post-MRI procedure (in clinic)
Inclusion Criteria	• Subject or subject's legally acceptable representative must provide written informed consent prior to any clinical investigation related procedure. • Subject has been implanted, or is scheduled to be implanted, with a commercially available Infinity DBS system with MR Conditional labeling per locally approved indications for use. • Subject is scheduled to undergo a MRI procedure in compliance with the MRI Procedure Information Clinician's manual. Anxiolytics and patient's regular medications may be administered, provided IFU criteria are met. • Subject is willing and able to comply with study requirements.

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Exclusion Criteria	• Subject has another implanted device (active or passive implanted device) that prohibits safe scanning. • Subject has previously experienced an MRI-related adverse event or cannot undergo MRI for any other reason. • Subject is pregnant or nursing, or plans to become pregnant during the clinical investigation follow-up period. • Subject has other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results. • Subject is currently participating in another clinical investigation that may confound the results of this study.