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Example - Early Feasibility Investigational Device Exemption

IDE Section:

Device Evaluation

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6. Device Evaluation

This section contains:

6.1. Risk Analysis High-Level Overview

Please refer to *Appendix C – Risk Analysis* for a detailed presentation of the Risk Analysis.

To summarize briefly, we followed a three-step risk analysis process that allowed us to conclude the following:

- The **highest *severity* risks** tended to be **lowest *likelihood*** and are fully mitigated through skilled surgical technique (for surgical risks) and engineering design (for risks associated with the technology).
- One event in the Failure Modes and Effects Analysis (FMEA) scored a Risk Priority Number (RPN) in the Intolerable region, therefore requiring mitigation: excessive heating during recharging. Multiple mitigations are used in this EFS IDE in order to minimize both the likelihood and severity of this event.
- Eleven (11) events in the FMEA scored in the ALARP region, and appropriate mitigations were identified for each.

6.2. Device Evaluation Strategy

The Device Evaluation Strategy is a construct developed for the Early Feasibility IDE Program to "facilitate the FDA's understanding of the value of leveraged information, and why the information included in the Report of Prior Investigations is adequate to support IDE approval" (Final Guidance – IDE's for Early Feasibility Medical Device Clinical Studies, 2013).

Our Device Evaluation Strategy Table is presented below, and characterizes the risk-based development of our system in three broad categories, as noted in Column 1:

- Performance Related Functions
- Safety Related Features
- Implant Procedure and Clinical Care Related Functions

The **Potential Failure Modes** (Column 2) and **Potential Effects of Failure** (Columns 3 and 4) trace back to an internal Failure Modes and Effects Analysis (FMEA) document, a synopsis of which is presented above, and which appears in more detail in *Appendix C – Risk Analysis*.

Our primary risk mitigation is the fact that the system is designed to minimize risks, and maximize performance. Formal risk-based engineering design principles were used throughout the development of the NNP System. These design principles are outlined in **Device Design Information** (Column 5), and also appear in Section 2.3 of this IDE.

The **Supportive Information** section (Columns 6 and 7) establishes the connection from our past experience with our earlier systems to our current NNP system. Our past experience with previous neuromodulation systems provides ample evidence of patient functional outcomes, long-term stability and reliability of the implant, and overall safety of the components in both animals and humans. Many aspects of the NNP system are identical to our previous generation systems, allowing direct use of earlier testing in support of this application; other aspects are functionally equivalent and permit extensive leveraging of earlier evidence. This long history of use substantially reduces the knowledge gap for the development of the current NNP system, and provides confidence in our ability to design,

manufacture, and clinically deploy implantable neuromodulation systems that safely and effectively restore function.

We identified very few places where our existing design principles, leveraged pre-clinical and clinical evidence, and bench and animal testing resulted in an **Evidence Gap** (Column 8). Those gaps relate to areas of risk that are considered low in both severity and likelihood, and include the following:

- Full biocompatibility characterization,
- MR compatibility characterization, and
- Sterilization validation.

These issues were raised in our pre-IDE discussions with FDA (I111144), and we have received ample guidance from the agency on how to stage our remaining testing over the next phases of product development.

We conclude from our Device Evaluation Strategy that the remaining evidence gaps are appropriate for a limited Early Feasibility clinical trial. In other words, based on our Risk Analysis, and our Device Evaluation Strategy, we believe:

1) All risks of significance have been either addressed through formal engineering design, or characterized fully or partially through prior clinical, animal, and bench testing; and
2) All remaining gaps in evidence have been identified, discussed with FDA, and we believe there is agreement as to the level of characterization and mitigation that will be performed *at this stage*, versus what will be performed later. Please refer to our discussions documented in I111144, as well as our responses to FDA's issues in Section 1.0 of this IDE.
3) This Early Feasibility IDE is designed so that lessons learned from a small number of real-world clinical cases will allow us to further develop the technology and refine the investigational plan prior to conducting a pivotal clinical trial.

6.2.1. Device Evaluation Strategy Table

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8	Column 9
		Potential Effects of Failure			Supportive Information			
Device-Related Attibute	Potential Failure Modes	Potential Device Effects of Failure	Potential Clinical Effects of Failure **(Reference FMEA Risk Analysis)**	Device Design Information **(Reference Section 2.2 - Design Principles)**	Leveraged nonclinical (bench/animal) information	Supportive clinical information **(Reference Section 4.0 Prior Clinical Studies)**	Nonclinical Device Testing and **Evidence Gap (Reference Section 6.3 and Appendices)**	Clinical Study Mitigation Strategies
PERFORMANCE RELATED FUNCTIONS								
Safe and reliable electrical activation of targeted neural structures	Unsafe current delivered to tissue	None	Tissue necrosis	Stimulation Levels: Only well-understood, safe stimulation parameters are used. Pulse generator is hardware limited to safe max cathodic stim pulse amplitude level.	Section 5 - Summary of *In Vivo* Safety Studies of Electrical Stimulation - fully establishes the safe stimulation parameters used by NNP.	Tissue damage from unsafe current: No cases in 28 years clinical experience based on direct observation of tissue during revision surgeries.	**Evidence gap: None.** No further testing or characterization of safe stimulation levels is needed.	Section 8 - Investigational Plan: Long-term follow-up of study subjects.
	Inadvertent sensory stimulation	None	FMEA:3-autonomic dysreflexia	Programmable: System designed to be easily reprogrammed to provide appropriate stimulation levels.		N/A	**Evidence gap: None**	Section 8 - Investigational Plan: Undesirable sensory stimulation will be captured as adverse event in clinical study; protocol permits modification to stimulation levels to mitigate inadvertent sensory stimulation.
Safe and reliable software operation	Erratic function	Intermittent system failure	FMEA:15,26,17-Unreliable performance	Critical and safety-related functions are not controlled by software	Appendix H - Software V&V.	N/A	**Evidence gap: None**	Section 8 - Investigational Plan: Long-term follow-up of study subjects.
	Loss of function	System failure	Loss of functional gains	Critical and safety-related functions are not controlled by software				

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8	Column 9
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Safe and reliable internal powering	Overheating of power module	Excessive heating during charging	FMEA:11,12,13-tissue burns	Recharge limited to safe transcutaneous heating standards.	Appendix I - Battery Testing. Results showed adequate useable cycle-life; and maximum temp increases below safe limits.	Prior Clinical Studies - Summary of Published Info on Li-Ion Batteries: No adverse events related to Li-ion rechargeable batteries have been reported in literature, or in FDA MAUDE database.	**Evidence gap: EFS IDE will be used to understand subjects' usage levels, power consumption, and recharge patterns to finalize the recharging protocol.**	Section 8 - Investigational Plan: First recharge sessions will be done in clinic under supervision. Patient Manual includes instructions in proper recharging; precautions about heating. User training will be provided.
	Overheating of power module	Runaway heating resulting in battery rupture	FMEA:7,14-tissue burns	Battery cells have self-extinguishing feature.				
	Power module failure	Premature battery depletion	FMEA:15,16,17-power module replacement surgery	Lifetime of at least 2 years before recharge capacity or shelf-life is exhausted				
Safe and reliable implantable electronics (sensing and stimulating modules)	Erosion of hardware	None	FMEA:20-Tissue necrosis	Physical Design: Small form factor to allow placement in average adult forearm.	Appendix E - Design Verification Testing; Appendix J - Mechanical Testing	Erosion: 3 cases of precautionary revision surgery; no erosion was present at the time. MR imaging: no prior cases of MR exposure. Header fracture: Three known cases of header separation in lower extremity (standing) systems used under extreme conditions (earlier design).	**Evidence gap: MR compatibility has not been characterized. Device is assumed to be incompatible with MR imaging.**	Section 13 - Draft Labeling: MR Compatibility: Device is contraindicated for use with MR imaging; labeling and training for users and clinicians. Section 8 - Investigational Plan: Long-term follow-up of study subjects.
	Erosion of hardware	None	FMEA: 21-Skin breach causing systemic infection	Physical Design: Small form factor to allow placement in average adult forearm.				
	MR incompatible	Heating of components due to MR field	FMEA:14-tissue burns	MR compatibility has not been characterized. Device is assumed to be incompatible with MR imaging.				
	Header fracture	Header fracture	FMEA:15,16-replacement surgery	Adhesives chosen with long history of reliability in similar medical applications.				

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Hermeticity	Loss of hermeticity	System failure	FMEA:15,16-replacement surgery	100% unit testing for hermeticity for all capsules.	Appendix J - Mechanical Testing	N/A	**Evidence gap: None.**	Section 8 - Investigational Plan: Long-term follow-up of study subjects.
Safe and reliable implantable leads and connectors	Disconnection of lead from header or connector	System failure or intermittent operation	FMEA:18-surgical revision or removal required	Adequate connection from leads to the header are assured by the use of Pt-Ir spring contacts (BalSeal) isolated by silicone ring.	Section 5 - *In Vivo* Safety Study of Epimysial and IM Electrodes. Appendix J - Mechanical Testing. Leads passed endurance tests (stretch, crush, flex, twist).	Lead and electrode failure: 4 confirmed cases of electrode failure out of 472 electrodes implanted in 24 years; Kaplan-Meier survival of 98.9% at 20 years. Electrode migration: no clinical evidence to date. Lead abrasion: No clinical evidence to date.	**Evidence gap: None.** No further testing necessary to characterize performance of leads and connectors.	Section 8 - Investigational Plan: Long-term follow-up of study subjects.
	Lead fracture	Loss of power or communication	FMEA:18-lead fracture requiring removal or replacement	Designed to withstand 1.2E6 stretching cycles, 1.2E5 crushing cycles, 1.2E6 bending cycles, 6.0E5 twisting cycles.				
	Abrasion of lead or complete fracture causing foreign body embolization	Intermittent operation	FMEA:18-surgical revision or removal required	Materials chosen with long history of long-term reliability.				
	Abrasion of lead causing insulation failure	Intermittent operation	FMEA:18-surgical revision or removal required	Materials chosen with long history of long-term reliability.				
	MR incompatible	None	FMEA:14-heating of tissue due to MR field	N/A	N/A	No reported cases of MR exposure.	**Evidence gap: MR compatibility has not been characterized. Device is assumed to be incompatible with MR imaging.**	Section 13 - Draft Labeling: Contraindicated for use in MR imaging; labeling and training for users and clinicians

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Device-Related Attibute	Potential Failure Modes	Potential Device Effects of Failure	Potential Clinical Effects of Failure **(Reference FMEA Risk Analysis)**	Device Design Information **(Reference Section 2.2 - Design Principles)**	Leveraged nonclinical (bench/animal) information	Supportive clinical information **(Reference Section 4.0 Prior Clinical Studies)**	Nonclinical Device Testing and **Evidence Gap (Reference Section 6.3 and Appendices)**	Clinical Study Mitigation Strategies
Safe and reliable implantable electrodes	Corrosion	Electrode failure	FMEA:18,20-surgical revision or removal required	Materials: 316LVM stainless steel electrical contact.	Section 5 - *In Vivo* Safety Study of Epimysial and IM Electrodes.	Corrosion: 0 cases. Erosion: 1 case of a superficial lead repositioned to reduce risk of erosion; no erosion was present at the time.	**Evidence gap: None.** No further testing necessary to characterize performance of electrodes.	Section 8 - Investigational Plan: Long-term follow-up of study subjects.
	Erosion - leading to infection	System failure or intermittent operation	FMEA:18-erosion causing skin break, leading to infection resulting in sepsis	Physical Design: form factor chosen to minimize erosion				
	Migration of lead	System failure or intermittent operation	FMEA:18-surgical revision or removal required	Physical Design: Presence of anchoring barbs or suture skirts				
	Erosion - other	System failure or intermittent operation	FMEA:18-surgical revision or removal required	Physical Design: form factor chosen to minimize erosion				
Reliable functioning of the system in the presence of electromagnetic sources	Susceptibility to external sources of EM	Intermittent or erratic system performance	Temporary, intermittent loss of functional gains	Communication methods and protocols chosen to permit coexistence with other emitters in the same band; wireless communication not used for safety-related or time-critical functions.	Appendix F - EMC Testing. Tesults for ESD testing, immunity / susceptibility testing, emissions testing, and wireless co-existence showed continuous safe operation of the system.	No cases of erratic system function in the presence of common EM sources. Subjects with other active implantable medical devices required adjustments to the coil frequency to avoid interference. No patient-to-patient interference has been observed.	**Evidence gap: None**	Section 8 - Investigational Plan: training to avoid sources of EM; Section 13 - Draft Labeling: warnings and precautions.
	Susceptibility to external sources of EM	Damage to implanted electronics	FMEA:15,16-surgical revision or removal required					
Safe and reliable external components	Unsafe current delivered to tissue	Damage to external control unit	FMEA:8-electrical shock due to leakage currents from external accessories	Specifications defined based on safe stimulation parameters established in published studies and prior bench and animal data.	Appendix E - Design Verification Testing	No reported cases of unsafe current levels or excessive heat from external components.	**Evidence gap: None**	None needed.

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		Potential Effects of Failure			Supportive Information			
Device-Related Attibute	Potential Failure Modes	Potential Device Effects of Failure	Potential Clinical Effects of Failure **(Reference FMEA Risk Analysis)**	Device Design Information **(Reference Section 2.2 - Design Principles)**	Leveraged nonclinical (bench/animal) information	Supportive clinical information **(Reference Section 4.0 Prior Clinical Studies)**	Nonclinical Device Testing and **Evidence Gap** **(Reference Section 6.3 and Appendices)**	Clinical Study Mitigation Strategies
	Excessive heat delivered to tissue	Recharge coil failure	FMEA:23-skin burn from recharge coil during recharging.	Recharge limited to safe transcutaneous heating standards.				
OTHER SAFETY RELATED FEATURES								
Biocompatible materials	Non-biocompati-bility	None	FMEA:20-Adverse biological reaction, including allergic reaction potentially leading to anaphylactic shock.	Materials: Chosen for known biocompatibility	*In Vivo* Safety Study of Epimysial and IM Electrodes; Appendix D - Biocompatibility	No reported cases of device rejection due to components or materials in 28-year experience. Observations during revision surgeries indicate good encapsulation of all implanted components with ~1mm thick connective tissue, no signs of adverse reaction. Removed components show no signs of corrosion or degradation.	**Evidence gap: A subset of biocompatibility testing (cytotoxicity testing) was agreed-upon for the purposes of this Early Feasibility IDE. Whereever possible, identical materials have been chosen from earlier generation devices.**	Section 8 - Investigational Plan: Long-term follow-up of study subjects.
Biocompatible physical configuration	Erosion	None	FMEA:20-skin integrity broken requiring surgical intervention	Physical Design: form factor chosen to minimize erosion	*In Vivo* Safety Study of Epimysial and IM Electrodes	Erosion: 1 case of a superficial lead repositioned to reduce risk of erosion; no erosion was present at the time. Migration: no clinical evidence to date.	**Evidence gap: None**	Section 8 - Investigational Plan: Long-term follow-up of study subjects.
	Erosion	None	FMEA:10-skin integrity broken causing infection resulting in sepsis	Physical Design: form factor chosen to minimize erosion				

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8	Column 9
		Potential Effects of Failure			Supportive Information			
Device-Related Attibute	Potential Failure Modes	Potential Device Effects of Failure	Potential Clinical Effects of Failure **(Reference FMEA Risk Analysis)**	Device Design Information **(Reference Section 2.2 - Design Principles)**	Leveraged nonclinical (bench/animal) information	Supportive clinical information **(Reference Section 4.0 Prior Clinical Studies)**	Nonclinical Device Testing and **Evidence Gap (Reference Section 6.3 and Appendices)**	Clinical Study Mitigation Strategies
	Migration	None	FMEA:18-migration causing nerve damage	Physical Design: Presence of anchoring barbs or suture skirts to prevent migration.				
IMPLANT PROCEDURE AND CLINICAL CARE RELATED FUNCTIONS								
Ability to be surgically implanted	Inability to be surgically implanted within reasonable procedure time.	None	FMEA:1-Catastrophic surgical complication	Modularity: Device is designed for ease of implantation; shorter procedure time.	N/A	Long history of skilled surgical methods; surgical complications fully characterized and understood. 0 cases of serious procedure-related adverse events in 28 years clinical experience.	**Evidence gap: The EFS IDE will be used to confirm surgical implantation technique, and document subject outcomes including adverse events.**	Section 8 - Investigational Plan: Acute surgical follow-up of study subjects.
	Surgical complication - inappropriate lead placement	current flow across heart	FMEA:4,5,6,9-cardiac arrhythmia	Implant procedure calls for prior testing to assure appropriate placement.				
	Surgical complication - severed nerve	None	FMEA:9-permanent nerve damage	Modularity: Device is designed for ease of implantation.				
Sterility	Surgical complication - compromised sterility	Non-sterile components or tools	FMEA:2-Post-op infection	Devices are provided sterile	Appendix G - Sterilization.	Post-Op Infections: 0 cases of post-operative infections in 28 years clinical experience.	**Evidence gap: None. Full validation will be performed prior to expansion of the EFS study.**	Section 8 - Investigational Plan: Acute surgical follow-up of study subjects.
	Surgical complication - compromised sterility	Poor sterile technique	FMEA:2-Post-op infection	N/A				
Ability to remain implanted chronically	Biofilm formation	Biofilm forms on implanted components	FMEA:21-late infection	Materials: Chosen for known biocompatibility	*In Vivo* Safety Study of Epimysial and IM Electrodes	Late Infection: N=3 subjects with late infections, resulting in implant removal	**Evidence gap: None**	Section 8 - Investigational Plan: Long-term follow-up of study

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		Potential Effects of Failure			Supportive Information			
Device-Related Attibute	Potential Failure Modes	Potential Device Effects of Failure	Potential Clinical Effects of Failure **(Reference FMEA Risk Analysis)**	Device Design Information **(Reference Section 2.2 - Design Principles)**	Leveraged nonclinical (bench/animal) information	Supportive clinical information **(Reference Section 4.0 Prior Clinical Studies)**	Nonclinical Device Testing and **Evidence Gap (Reference Section 6.3 and Appendices)**	Clinical Study Mitigation Strategies
	Late infection due to illness or skin wound	None	FMEA:10,24-systemic infection	Modularity: Components can be easily replaced if necessary		in implant removal (N=2) or electrode removal (N=1). Cellulitis: 1 subject, resulting in implant removal.		follow up of study subjects.

6.3. High-Level Summary of Testing and Evaluation

A high-level overview of testing is provided below, with references to the appropriate appendices for detailed reports.

6.3.1. Biocompatibility

Please see *Appendix D - Biocompatibility* for details.

For every direct-contact implantable material, we have supported our assertion of material biocompatibility in one or more of the following ways: 1) by characterizing biocompatibility through cytotoxicity testing; 2) by establishing the material's prior use in our own previously approved IDEs; and/or 3) by providing right-of-reference letters to materials Master Files. **Based on our Risk Analysis and Device Evaluation Strategy, and following previous discussions with FDA, we conclude that for the purposes of conducting an Early Feasibility study on a limited number of subjects, no additional biocompatibility testing is necessary *at this stage*. Full biocompatibility testing will be completed after refining the manufacturing processes for the technology, prior to expanding to a multi-center trial.**

6.3.2. Control Tower System Testing

Please see *Appendix E – Control Tower System Testing* for detailed reports. The following is a direct excerpt.

The purpose of the Control Tower System Testing is to characterize the electrical safety of the external components of the NNP System. The Control Tower System under test included the Control Tower, recharge coil, external AC adapter, remote display, and USB isolator.

Test Name	Components Tested	Test Purpose / Pass-Fail Criteria	Results
Dielectric Strength	Control Tower System	Establish dielectric strength using criteria described in UL 60601-1:2003, 20.	Pass
Recharge Coil Dielectric Strength	Recharge Coil	Characterize leakage current levels as a function of test voltage, to highest value achieved without arcing.	Characterization curves generated
Leakage Current Test	Control Tower System	Followed methods and pass-fail criteria described in IEC 60601-1, Section 19.4g.	Pass

CONCLUSIONS

- Insulation of the Control Tower System provides sufficient protection to users.
- The Control Tower System demonstrates safe levels of leakage currents.

6.3.3. Electromagnetic Compatibility (EMC) Testing

Please see *Appendix F – Electromagnetic Compatibility Testing* for detailed reports. The following is a direct excerpt.

SUMMARY OF RESULTS FROM IMMUNITY TESTING

NORMAL MODE	CHARGING MODE	NAME	IEC 60601-1-2 REQUIREMENT	80 MHZ TO 1 GHZ	1 – 2.5 GHZ
Implantable components only	Implantable components communicating with external components	Electric fields, alternating	ESSENTIAL PERFORMANCE is maintained.	3 V/m (4 positions, horizontal and vertical antenna) **PASSED**	3 V/m (2 positions, horizontal and vertical antenna) **PASSED**
				18 V/m (1 position: horizontal and vertical antenna) **PASSED**	

EVALUATION OF ESSENTIAL PERFORMANCE, PER IEC 60601-1-2

DEGRADATIONS: *Under the test conditions specified in 36.202, the EQUIPMENT or SYSTEM shall be able to provide the ESSENTIAL PERFORMANCE and remain safe. The following DEGRADATIONS associated with ESSENTIAL PERFORMANCE and safety shall **not** be allowed:*	
COMPLIANCE CRITERIA	**DEGRADATIONS OBSERVED**
Component failures	None
Reset to factory defaults	None
Change in operating mode	None
False alarms	None
Cessation / interruption of any intended operation, even if accompanied by an alarm	None
Error of a displayed numerical value sufficiently large to affect diagnosis or treatment	None
Noise on a waveform in which the noise is indistinguishable from physiologically-produced signals or the noise interferes with interpretation of physiologically-produced signals.	None
Artifact or distortion in an image in which the artifact is indistinguishable from physiologically-produced	None
Signals or the distortion interferes with interpretation of physiologically-produced signals	None
Failure of automatic diagnosis or treatment EQUIPMENT and SYSTEMS to diagnose or treat, even if accompanied by an alarm	None

OBSERVATIONS: *The equipment or system may exhibit degradation of performance (e.g., deviation from manufacturer's specifications) that does not affect essential performance or safety.*	
OBSERVED PERFORMANCE	**RATIONALE**
Radio disruption: Some radio telemetry packets were dropped.	Dropped radio packets do not affect the safety of the system, or cause a change in the mode of operation of the NNPS. The system can be left running in any mode and will either shut itself down after its batteries drop below a critical level or can be shut down via the Failsafe Function at any time. The observed effects were transient and did not result in permanent alteration in performance requiring revision or replacement of the implanted components of the system.

SUMMARY OF RESULTS FROM EMISSIONS TESTING

NORMAL MODE	CHARGING MODE	NAME	47 CFR 15.109 REQUIREMENT	CLASS A (RESIDENTIAL) LIMIT	CLASS B (INDUSTRIAL) LIMIT
Implantable components only	Implantable components communicating with external components	Radiated fields	Per 47CFR15.109 (g), the simple IEC CISPR 22 section 6.1 emissions limits can be used by Class B (residential) unintentional radiators at 10 meters.	**EXCEEDS LIMIT** Exceeds limits in both modes. Control Tower exceeded limit between 150-400 MHz. Implant exceeds limit between 30-50 MHz.	**PASSED**

CONCLUSIONS

Based on our prior discussions with FDA, it is understood that we do not intend to make modifications to our system to address EMC-related issues *prior* to embarking on the Early Feasibility study. Based on our Risk Analysis, Device Evaluation Strategy and results of EMC characterization conducted to date, we conclude the following:

- The external and internal components demonstrate adequate defense against electrostatic discharge and are safe to begin use in an Early Feasibility IDE study.
- The NNP System can be safely used in the presence of a wide variety of emitters without degradation of performance.
- The NNP System complies with Class B (Industrial) limits on emissions, but is a very weak emitter in a narrow range of Class A (Residential) frequencies.
- The NNP System can be safely used with cell phones, Wifi, and cordless phones without interference.

6.3.4. Sterilization

Please see *Appendix G – Sterilization* for further details of our validation plan. The following is a direct excerpt.

At the time of submission of this EFS-IDE, we are providing a promissory note for a future device-specific final report for a worst case sterilization validation study for Ethylene Oxide sterilization of the NNP System implanted components.

The single-lot batch release protocol will not result in a fully validated sterilization process required for routine sterilization. However, following exposure performed under the CWRU single-lot batch release protocol, the NNP system components will be considered sterile in accordance with ISO 11135-1:2007, and appropriate for human implant use if:

- **An SAL of 10-6 is achieved, *and***
- **The EO residual levels are below the allowable limits per ISO 10993-7:2008(R)2012.**

No devices will be implanted that do not meet these two criteria.

As noted in our Device Evaluation Strategy Table, our prior experience with providing sterile devices for implant have resulted in 0 cases of post-operative infection over the course of several decades and hundreds of patients, which serves as clinical validation of our past sterilization, packaging, and handling practices.

6.3.5. Software Verification and Validation

Please see *Appendix H – Software Description and V&V* for detailed reports. A Traceability Matrix is provided which lists the software testing conducted for each software component, as well as general functional, interface, and performance requirements. Each test in the Traceability Matrix may be tied to several requirements. The pass/fail criteria are specified within the requirement. Much of the software testing is actually system testing, relying on multiple software and hardware components.

For the purposes of the Early Feasibility IDE, it is recognized that ongoing improvement of the software will be necessary. Prior to the start of the IDE, all requirements with Priority Levels marked "Critical" and "Major" will be met. No subjects will be entered into the study until these requirements are met.

6.3.6. Battery Testing and Heating Characterization

Please see *Appendix I – Battery Testing and Heating Characterization* for detailed reports.

Test Name	Components Tested	Test Purpose / Pass-Fail Criteria	Results
Cell characterization testing	Battery cells	Mechanical, Electrochemical, Environmental, Safety and Storage tests were performed according to MIL-STD-202F, prEN 45502-2-1 (Sections 23.2 and 23.7), and UL 1642.	Pass

Charge-discharge testing	Batteries	Cycle life testing at charge-discharge cycles at 10, 1000, 2000, and 4000 cycles.	Life cycle characterization curves generated
Recharge Heating Characterization in Saline Phantom	Power Module and External Coil	Outer surface of implant (Power Module) must demonstrate < 2 deg.C rise under aggressive recharging conditions.	Pass
Recharge Heating Characterization in Air	Power Module and External Coil	Outer surface of implant (Power Module) must demonstrate < 2deg.C rise under aggressive recharging conditions.	Pass

6.3.7. Mechanical Testing

Please see *Appendix J – Mechanical Testing* for detailed reports. The following is a direct excerpt.

Test Name	**Components Tested**	**Test Purpose / Pass-Fail Criteria**	**Results**
Feedthrough Test	Power Module and Remote Modules	Assure durability of feedthrough assembly. Leak testing is performed according to MIL-STD-883. Standard leak rate is to be $2.7x10^{-9}$ atm-cc/sec helium.	Pass
Hermeticity Test	Power Module and Remote Modules	Leak testing is performed according to MIL-STD-883. Standard leak rate is to be less than $2.7x10^{-9}$ atm-cc/sec helium.	100% unit testing (units will not be used if they do not meet the acceptance criteria)
Network Cable Durability Test	Network Cable	<u>10-year simulated use</u>: • 1.2×10^6 cycles of stretching to 120% • 1.2×10^5 cycles of crushing by a force of 1.2N • 1.2×10^6 cycles of bending • 6×10^5 cycles of twisting	Pass
Stainless Steel Electrode Lead Durability	Stainless Steel Electrode Lead		Pass

CONCLUSION
Damage to feedthrough pins does not cause leaking through the lidthroughs. The Network Cable and stainless steel electrode leads demonstrate long-term mechanical durability and electrical performance following simulated 10-year conditioning.

6.3.8. NNP Simulated Use Testing

Please see *Appendix K – NNP Simulated Use Testing* for detailed reports. The following is a direct excerpt.

The purpose of the NNP Simulated Use Test is to demonstrate end-to-end function of the entire NNP System.

Test Name	**Components Tested**	**Test Purpose / Pass-Fail Criteria**	**Results**
Power Up Operation	NNP System	Verify that powering up does not cause unwanted stimulation.	Pass
Wireless Communication	NNP System	Verify proper module ID and charge state.	Pass
Proportional Control	NNP System	Verify appropriate output levels based on input signals.	Pass
Failsafe Shutdown and Restart	NNP System	Verify performance of inductive forcing function and recovery.	Pass

6.4. Anticipated Changes to the IDE

We anticipate making modifications to the technology over the course of our Early Feasibility IDE. Modifications to the NNP will be submitted as IDE/Supplements (either 5-Day Notices or supplements requiring contingent approval) as noted in our pre-IDE I114444. The following table lists the kinds of modifications to the technology we anticipate making over the course of the Early Feasibility IDE.

6.4.1. Anticipated Design Changes to the Technology

TYPE OF SUBMISSION	DESCRIPTION OF CHANGE	COMMENTS / RATIONALE
IDE Annual Report	Expand the environments in which a subject is approved to use the system for function, e.g., use at home or workplace.	Testing will be performed in the environments in which functional use is to be approved.
	Modifications to the Programming Computer and Clinical Interface Software. These will typically be modifications to improve usability by the programming technician, such as displayed information and intuitive interfaces.	Software changes only; does not alter the function of the implanted system. V&V procedures will be followed.
5-Day Notice	Change in myoelectric signal processing algorithm.	Software change only; not a safety-related change. V&V procedures will be followed.
	Addition of accelerometer or thermistor sensor data to control algorithm.	Software change only; not a safety-related change; does not alter maximum stimulation output. V&V procedures will be followed.
	Modifications to the NNP network communication commands, error checking, or data formats that are maintained within the CAN protocol.	Low-level software commands do not control areas of system risk. V&V procedures will be followed.
	Modifications of system software to improve power management, or to improve communication.	Low-level software commands do not control areas of system risk. V&V procedures will be followed.
	Modifications to the shape of *connectors* without a change in materials.	Changes will be qualified using Pull-Out Test.
	Modifications to the configuration of an external recharge coil *spacer*.	The need for a spacer will be determined as part of the EFS IDE. The spacer materials will be chosen based on limited skin-contact.

Contingent Approval (IDE/S)	Changes in external recharge coil design, possibly to include 3D printing, enhanced drive circuitry, closed-loop control, redesign of remote display, and/or addition of Bluetooth Low Energy interface to Control Tower for user control from a tablet.	Modified coil must pass Charge/Recharge Test and heating profile must be fully re-characterized and within previously-approved limits.
	Increase allowable temperature rise for the implanted Power Module during closed-loop recharge.	Testing TBD, following consultation with FDA.
	Install a separate network power line for modules requiring increased power consumption.	Full-system test must be performed demonstrating outputs within specifications.