SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Implantable Peripheral Neurostimulator for Incontinence

Device Trade Name: Medtronic Altaviva™ System

Device Procode: QPT

Applicant's Name and Address: Medtronic Neuromodulation
7000 Central Ave., NE
MS RCE480
Minneapolis, MN 55432 USA

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P240011

Date of FDA Notice of Approval: September 18, 2025

II. INDICATIONS FOR USE

The Medtronic Altaviva System is indicated for treatment of urge urinary incontinence in patients who failed or could not tolerate more conservative treatments.

III. CONTRAINDICATIONS

The Altaviva™ system is contraindicated for the following patients:

- Poor surgical candidates, including:
    - Patients with skin lesions or compromised skin integrity
    - Patients with a current or recent history of venous insufficiency and/or venous stasis ulcers in the lower leg
    - Patients with anatomical defects or previous surgeries at the implant site which preclude use of the device
- Patients who are not able to operate or receive assistance in operating the system

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Medtronic Altaviva™ System labeling.

V. DEVICE DESCRIPTION

The Medtronic Altaviva™ System includes an Implantable Neurostimulator (INS) which is a rechargeable, leadless INS and is intended to treat urge urinary incontinence by stimulating the tibial nerve. The Altaviva™ INS is implanted, in a pocket created in the deep fascia, superior to the medial malleolus and anterior to the Achilles' tendon (Figure 1).

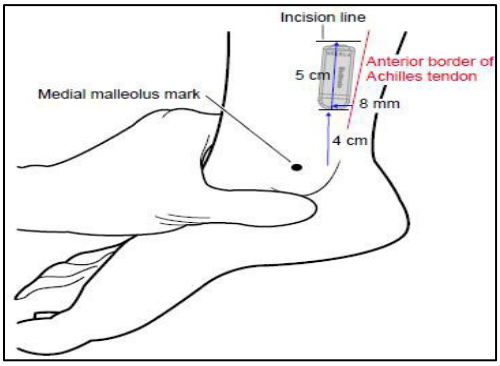


Figure 1: TNM INS Overview of Implant Location

The Medtronic Altaviva™ System includes a wireless recharger communicator (WRC) that is used to recharge and/or communicate with the INS. An optional ankle band component is provided to assist with holding the recharger in place over the INS during recharge and/or communication with the INS. The Clinician and Patient Therapy Applications are installed on the Clinician Tablet, and Patient Programmer/handset, respectively, and are used to program the implanted device. The different components of the Altaviva™ System are described below:

1. Altaviva™ Implantable Neurostimulator (Model P7850N)

   This INS (Figure 2) generates electrical pulses to provide stimulation therapy to the tibial nerve. The hardware of the INS is comprised of the connector assembly (active electrode) and the body, including the rechargeable battery. The physical characteristics of the INS is listed in Table 1 below:

Figure 2: Altaviva™ INS

Table 1: Physical Characteristics of Altaviva™ INS

Characteristic	Altaviva™ INS
Height	43.7 mm
Length	15.7 mm
Thickness	4.4 mm (Case) 4.5 mm (Connector)
Volume	2.6 cc
Weight	7.5 g

The stimulation parameters of the INS are listed in the Table 2 below:

Table 2: Stimulation Parameters of Altaviva™ INS

Parameters	Altaviva™ INS
Amplitude	Current-controlled Resolution 0.1mA steps Upper Limit 25.5 mA maximum Lower Limit 0.1 mA minimum
Rate	3 to 130 Hz
Rate Increments	3-30 Hz: 1 Hz, 30-130 Hz: 5 Hz
Pulse Width	Increments of 10 μs steps 450 μs maximum and 40 μs minimum

2. Wireless Recharger Communicator

The Model P720R1 Altaviva WRC (Figure 3) is used to recharge the patient's INS battery via inductive energy transfer. It also acts as the communication bridge between the Clinician Tablet/Patient Programmer and the INS. It has a self-contained user application to provide recharge information during recharge sessions, adjust recharger settings, and convey additional notifications and alerts to the user via LEDs and audible beeps. Additionally, it can be used along with the Clinician and Patient Therapy Apps to provide recharge information during recharge sessions, adjust recharger settings, and convey additional notifications and alerts to the user. The specification of the WRC is listed in the Table 3 below.

Table 3: Specification of the Wireless Recharger Communicator (WRC)

Item	Specification
Dimensions	142 mm x 117 mm x 23 mm (L x W x H)
Operating Temperature	5°C to 40°C (50°F to 104°F)
Bluetooth Low Energy 4.0	2.402 MHz – 2.480 MHz
Near Field Magnetic Communication (NFMC)	175 kHz
Wireless Power Transfer (Coil Frequency)	110 kHz
Weight (with Battery)	291.5 g
Power Supply	Internal Lithium-Ion Rechargeable Battery, 5.2 V d.c.

Figure 3: Wireless Recharger Communicator (WRC)

The recharger dock (CD9000A) (Figure 4) is used to recharge the battery of the WRC. When seated in the dock, pogo pins on the WRC contact electrical connection points on the charging dock, which allows the WRC to charge its internal battery.

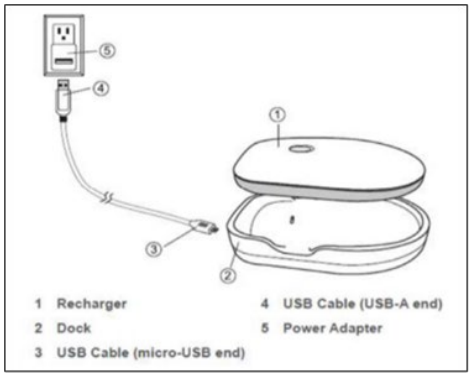


Figure 4: Configuration for charging the WRC

3. Ankle Band

The Altaviva Model P742A1 Ankle Band (Figure 5) is an optional positioning component, which will be provided in the Clinician Kit and the Patient Kit. The band will be provided with two (2) additional adjusters if needed for smaller or larger sized ankle dimensions. The ankle band and adjusters are being provided with the Medtronic Altaviva™ System to assist in positioning the WRC over the INS implant location. The band is universal and can be used with left or right ankle implants. Patients can also choose to place or hold the WRC over the INS implant location without the use of the ankle band.

Figure 5: Ankle Band

4. Clinician tablet (Clinician Programmer)

   The clinician tablet (Figure 6) is a commercial off-the-shelf tablet device. Its primary function is supporting implant functionality and therapy continuity. The clinician application allows the clinician and/or Medtronic representative to configure and manage therapy for the Altaviva™ INS and control recharge status.

Figure 6: Clinician tablet

5. Patient Programmer / Handset

   The Patient Programmer / Handset (Figure 7) is a commercial off-the-shelf smartphone device. The features of the smart phone are disabled so the patient programmer cannot be used as a phone and cannot make emergency calls. Its primary function is supporting implant functionality and therapy continuity. 'Altaviva My Therapy Application' is uploaded in the patient programmer which allows the patient to manage therapy for the Altaviva™ INS and control recharge status.

Figure 7: Patient Handset

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of urinary urge incontinence (UUI).

Non-invasive treatment options should be discussed with all patients, including incontinence management strategies, bladder training, behavioral therapies, pelvic floor exercises, maintaining a healthy weight, and fluid consumption management.

Medications for treatment of UUI may also be considered and include antimuscarinic medications or beta-3 agonists. These medications are taken daily and may have short- or long-term side effects that may affect a patient's ability to take or tolerate them.

For patients that fail to have improvement, cannot tolerate, or are not candidates for these treatment options, they may consider minimally invasive therapies. These include sacral neuromodulation, percutaneous tibial nerve stimulation, implantable tibial nerve stimulation and/or intradetrusor botulinum toxin injection. Percutaneous tibial nerve stimulation provides stimulation of the posterior tibial nerve to send signals to the bladder to reduce UUI episodes. It is an in-office procedure using a percutaneous needle; this technique requires multiple, on-going office visits. Implantable sacral nerve stimulation requires a hospital surgical procedure to place a stimulator in the vicinity of the sacral nerve to stimulate the nerve. Patients may also receive injections of Botox into the bladder wall. This treatment lasts typically 6-9 months. In some cases, it may lead to urinary retention requiring self-catheterization until the treatment begins to wear off. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Medtronic Altaviva™ System has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Implant site pain
- Implant site infection
- Clostridium Difficile Colitis infection
- Reaction to local anesthetic (such as redness, irritation at the injection site)
- Wound complications (such as swelling, hematoma, bruising, bleeding, seroma)
- Allergic or immune system reaction
- Lower leg pain or discomfort
- Neurostimulator movement or skin erosion at implant site
- Inappropriate shock delivery
- Adverse change in bowel or urinary function
- Worsening of underlying progressive diseases
- Nerve injury
- Discomfort during recharge (such as heating or uncomfortable stimulation sensations)
- Technical device problems
- Loss of therapeutic effect

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF NON-CLINICAL STUDIES

a. Laboratory Studies

1. Bench Testing

Bench testing described in this section were conducted to evaluate the safety and performance of the Medtronic Altaviva™ System. Key testing for the Medtronic Altaviva™ System components is summarized in the tables below. For every requirement, the acceptance criteria were met (i.e., device passed testing). The test results summarized below (Table 4, 5 and 6) demonstrate that all applicable requirements have been verified and that the design outputs meet the design input requirements.

Table 4. Summary of Key Bench Testing Performed on the Altaviva™ INS

Test	Test Purpose	Acceptance Criteria	Results
Stimulation Output	The following stimulation features were verified under this testing: • **Amplitude monotonicity (decreasing and increasing steps):** The testing verifies that the pulse amplitude can be decremented or incremented in 0.1 mA decrements or increments • **Pulse width monotonicity (decreasing and increasing steps):** The testing verifies that the pulse width can be decremented or incremented in 10 µsec decrements or increments. • **Amplitude and Pulse width accuracy:** This testing verifies that the Altaviva™ INS can output programmed pulse amplitudes /pulse width within the specified accuracy limits. • **Amplitude variation:** This testing verifies that the Altaviva™ INS can maintain the pulse amplitude output within the requirement limits over time.	All the stimulation parameters shall meet specifications.	Pass

Test	Test Purpose	Acceptance Criteria	Results
Stimulation Output	The following stimulation features were verified under this testing: • **Current drain:** This testing measures stimulation current drain to verify that a fully charged Altaviva™ INS at beginning of life, can deliver 6 months of "*Normal Therapy Use.*" • **Battery voltage accuracy:** This test was conducted to verify the Altaviva™ INS can measure internal battery voltage with appropriate accuracy. **Lead Z accuracy:** Testing verifies internal impedance measurement accuracy of Altaviva™ INS by using a programmable load to step through clinically relevant load impedances.	All the stimulation parameters shall meet specifications.	Pass
Altaviva™ INS Recharge Verification Testing	The following recharge related features were verified as part of these tests: • **Recharge current measurement:** When configured for recharge, the Altaviva™ INS shall provide an accurate primary recharge current measurement. • **Recharge battery voltage measurement:** The Altaviva™ INS shall accurately measure battery voltage during recharge. • **Over voltage:** Testing to detect and prevent over voltage of the Altaviva™ INS. • **Start dead battery:** This test simulates a battery being brought up from a fully discharged state to normal operation. • **Session Termination:** The Altaviva™ INS shall terminate a recharge session after pre-determined period of not receiving communication from the recharger.	All the parameters / functions shall meet specifications.	Pass
Labeled Shelf-life (18-months)	To verify Altaviva™ INS remains functional after exposure to the following conditions: • 3 cycles of ethylene oxide sterilization • Shipping/storage conditions	ISO 11135:2014 clause 7.2.1 and 7.2.2 EN 45502-1:2015 clause 26.2 and ISO 14708-1:2014 clause 26.2	Pass

Test	Test Purpose	Acceptance Criteria	Results
	• Distribution including manual handling, vehicle stacking, loose load vibration, vehicle vibration, manual handling (2nd series) • Current labeled shelf-life exposure • Hermeticity testing and Altaviva™ INS functional testing including the stimulation output and recharge verification testing.	ASTM D4169 Distribution Cycle (DC) 2 EN 45502-1: 2015, Clause 26.2 ISO 14708-1: 2014, Clause 26.2	
Altaviva™ INS heating during recharge / Thermal Safety	To verify the temperature of the implanted Altaviva™ INS does not exceed limits per CEM43. The sponsor conducted an in-Vivo GLP Animal Study to verify the Altaviva™ INS heating during recharge.	EN 45502-1:2015 clause 17.1 & 19.3 ISO 14708-3:2017 clause 17.1 & 19.3	Pass
Mechanical Shock	To verify the Altaviva™ INS remains functional and hermetic following exposure to mechanical shock.	EN 45502-1:2015 ISO 14708-1:2014 clause 23.7	Pass
Random Vibration	To verify the Altaviva™ INS remains functional and hermetic following exposure to random vibration.	EN 45502-1:2015 ISO 14708-1:2014 clause 23.2	Pass
Atmospheric Pressure Changes	To verify the Altaviva™ INS remains functional and hermetic following exposure to atmospheric pressure changes.	EN 45502-1:2015 ISO 14708-1:2014 clause 25.1	Pass
Shipping Conditions of Temperature Exposure & Thermal Shock	To verify the Altaviva™ INS passes functional testing, and the Altaviva™ INS packaging maintains integrity after exposure to temperature cycling which includes extreme temperatures and thermal shock exposure per the standards.	EN 45502-1 clause 10.2 ISO 14708-1:2014 Clause 10.2 ISO 14708-1:2014 Clause 26.2 EN 45502-1 Clause 26.2	Pass
Particulate Testing	To verify the Altaviva™ INS does not release unacceptable particulate matter at the time of implantation.	EN 45502-1:2015 ISO 14708-1: 2014 Clause 14.2.	Pass
Current Leakage	To verify that the Altaviva™ INS limits direct current output on any electrode conducting surface in contact with the body to less than or equal to 0.75 $\mu A/mm^2$.	ISO 14708-1 Clause 16.2	Pass
Diagnostic Ultrasound	To verify if the Altaviva™ INS can withstand diagnostic ultrasound.	ISO 14708-1:2014 Clause 22.1	Pass

Test	Test Purpose	Acceptance Criteria	Results
External Defibrillation	To verify if the Altaviva™ INS can withstand the use of external defibrillator (monophasic and biphasic).	ISO 14708-1:2014 clause 20.2	Pass
X-Ray/CT scan	To verify if the Altaviva™ INS can withstand the use of X-ray and CT scan.	ISO 14708-3:2017 clause 22	Pass
Electrosurgery	To verify that the Altaviva™ INS does not experience irreversible changes to its function caused by electrosurgery which is not performed directly above the Altaviva™ INS.	ISO 14708-1:2014 clause 21.1	Pass
Battery External Short	To verify the Altaviva™ INS generates no more than a 2°C temperature rise at the device surface when implanted subcutaneously, in the event of a single fault battery short as well as during normal use in the absence of external influence.	EN 45502-1: 2015 Clause 17.1 ISO 14708-3:2017 Clause 17.1 EN 45502-1: 2015 Clause 19.3 ISO14708-1:2014 Clause 19.3	Pass
Altaviva™ INS Mechanical-Electrical 15 Year Use Life	To demonstrate that successful therapy output, mechanical integrity, and battery performance is maintained in device-level testing representing 15 years of use life with clinically relevant stimulation duration and stimulation parameters.	Testing demonstrates Altaviva™ INS durability supporting 15 years of use life with clinically relevant stimulation duration.	Pass
Altaviva™ INS Rechargeable Battery 15 Year Use Life	To demonstrate implantable rechargeable battery function and performance throughout Altaviva™ INS use life by acceleration of beyond worst-case degradation factors.	Testing demonstrates rechargeable battery functionality supporting 15 years of use life	Pass

Table 5. Summary of Key Bench Testing Performed on the WRC & Recharger Dock

Test	Test Purpose	Acceptance Criteria	Results
WRC Communication	To verify successful communication between the WRC and the Clinician Tablet and Patient Programmer/handset Mobile Devices.	Communication consistently achieved at relevant distances between the two elements.	Pass
WRC Battery Safety	To verify the safety of the WRC battery including battery protection circuitry for over-charging, over-discharging, and over-heating as well as battery short-circuit protection.	IEC 62133-2:2017 Secondary Cells and Batteries Containing Alkaline or Other Non-Acid Electrolytes, UL 2054, Second Edition, Revision 2011 UL Standard for Safety for Household and Commercial Batteries, and UL 1642 Fifth Edition 2012 UL Standard for Safety for Lithium Batteries.	Pass
Recharge Dock Functional test	This test confirms the basic functionality of the recharge dock	• Power on via micro-USB connector • Recharge WRC LED functionality: The WRC was placed on the dock, and it was confirmed that the WRC battery LED was illuminated, indicating the WRC was recharging.	Pass

Table 6. Summary of Key Bench Testing Performed on the Ankle Band

Test	Test Purpose	Acceptance Criteria	Results
Velcro Cycling	To verify the Ankle Band with recharger maintains fixation after an appropriate number of attaching/separating cycles.	The ankle band shall maintain fixation after an appropriate number of attaching/separating cycles.	Pass
Size	To verify the Ankle Band with recharger shall fit ankles of the patient population while maintaining the wireless recharger.	The Ankle Band with recharger shall be able to wrap around and attach onto cylinders representative of patient ankles.	Pass
WRC Insertion	To verify the Ankle Band prevents the wireless recharger from falling out after an appropriate number of insertion/removal cycles with the WRC in the sleeve.	The wireless recharger shall not fall out of the Ankle Band after an appropriate number of insertion and removal cycles.	Pass
Cleaning for multi-use	To provide cleaning instructions for the non-sterile ankle band and extensions testing was performed to determine handwashing and air-drying cycles.	Ankle Band and extensions shall maintain functionality after an appropriate number of handwashing cycles in accordance with IEC 60601-1 sub-clause 11.6.6.	Pass

2. Biocompatibility

Biocompatibility testing was performed for all the patient-contacting materials of the Medtronic Altaviva™ System in accordance with the FDA Guidance Document, *Use of International Standard ISO 10993-1,"Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process*". All biocompatibility studies were conducted in compliance with Good Laboratory Practices (GLP), 21 CFR Part 58.

The following biocompatibility endpoints were assessed:

- The Altaviva™ INS is an implant device, contacting tissue/bone for permanent duration (>30 days)
    - Cytotoxicity
    - Sensitization
    - Intracutaneous and In-vitro Irritation
    - Acute systemic toxicity
    - Material Mediated Pyrogenicity
    - Implantation and Sub-chronic toxicity
    - Genotoxicity
    - Chemical characterization followed by Toxicological Risk Assessment of compounds extracted from the device to evaluate chronic systemic toxicity, and carcinogenicity

- WRC is a surface device contacting intact skin for permanent duration (>30 days)
    - Cytotoxicity
    - Intracutaneous Irritation
    - Sensitization

- Ankle Band is an optional component of the Medtronic Altaviva™ System. If used by a patient, the Ankle Band will be a surface device contacting intact skin for permanent duration (>30 days). The sponsor cited Attachment G of the FDA biocompatibility guidance to address the biocompatibility of the Ankle Band which is acceptable.

The results of biocompatibility testing demonstrated that all components of the Medtronic Altaviva™ System are biocompatible.

3. Sterility/Shelf-life/Reprocessing

The Altaviva™ INS is the only component of Medtronic Altaviva™ System which is provided sterile. The implant is sterilized by ethylene oxide (EO) gas to an assurance level (SAL) of 10^{-6} per ISO 11135:2014, *Sterilization of health care*

products – Ethylene oxide – Requirements for development, validation and routine control of a sterilization process for medical devices. The sponsor tested the INS for EO residuals in conformance with ISO 10993-7:2008 to ensure that the maximum residual levels of EO and ethylene chlorohydrin (ECH) remaining on the INS after sterilization do not exceed the recommended limits for medical devices with permanent patient contact.

The shelf-life for the Altaviva™ INS is established at 18 months based on an accelerated aging study and real time aging conducted a on similar previously approved INS. To support the 18 months shelf life, package integrity testing and functional testing were conducted. Package integrity testing was conducted per EN 45502-1:2015/ ISO 14708-1:2014 clause 26.2. The functional testing conducted after accelerated aging is described in Table 4 above. The results demonstrated that Altaviva™ INS has acceptable package integrity and functional performance over the duration of its 18 months shelf life and after simulated shipping distribution.

The Ankle Band needs reprocessing (cleaning) during its use life. The reprocessing validation testing provided for the Ankle Band demonstrated that the reprocessing instructions are adequate.

4. Electromagnetic Compatibility & Electrical Safety

The sponsor conducted electromagnetic compatibility and electrical safety testing on the Medtronic Altaviva™ System in accordance with the following standards:

- ISO 14708-1:2014: *Implants for surgery – Active implantable medical devices – Part 1: General requirements for safety, marking and for information to be provided by the manufacturer.*
- ISO 14708-3:2017 *Implants for surgery – Active implantable medical devices – Part 3: Implantable neurostimulators.*
- IEC 60601-1-2: 2020, *General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests*
- IEC 60601-1:2005 (Third Edition) + CORR. 1:2006 + CORR. 2:2007 + A1:2012, *Medical electrical equipment — Part 1: General requirements for basic safety and essential performance*
- IEC 60601-1-11:2015 (Second Edition), *Medical electrical equipment – Part 1-11: General requirements for basic safety and essential performance – Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment.*
- UN Transportation Testing for Lithium Batteries (UN 38.3)

The Medtronic Altaviva™ System passed electrical safety and electromagnetic compatibility testing consistent with the acceptance criteria outlined in these standards. The sponsor provided adequate labeling instructions related to electrical safety and electromagnetic compatibility of the Medtronic Altaviva™ System.

The Medtronic Altaviva™ System uses wireless technology. The sponsor conducted testing on the wireless technology per the FDA guidance document, *Radio Frequency Wireless Technology in Medical Devices* published in 2013. The sponsor also conducted wireless coexistence testing per ANSI C63.27-2017: *American National Standard for Evaluation of Wireless Coexistence.* The Medtronic Altaviva™ System passed all the wireless technology testing, i.e., wireless coexistence, quality of service and wireless security testing. The sponsor provided adequate labeling instructions related to the wireless technology of the Medtronic Altaviva™ System.

5. Magnetic Resonance (MR) Compatibility

The sponsor conducted MRI compatibility testing on the Altaviva™ INS to verify that it can be used in MRI environments (of 1.5 Tesla and 3 Tesla) per ISO/TS 10974:2018, *Assessment of the safety of magnetic resonance imaging for patients with an active implantable medical device*. The results demonstrated that the Altaviva™ INS is MR compatible under the conditions specified on the labeling.

6. Software and Cybersecurity

Software development was based on IEC 62304:2006+A1:2015, *Medical device software – Software life cycle processes* and is controlled in a lifecycle consistent with this standard. The software documentation was provided in accordance with the FDA Guidance Document entitled, "*Content of Premarket Submissions for Device Software Functions*," issued in 2023.

Software and firmware were tested to ensure that the functional requirements as defined in the product software, and firmware requirements were met.

Cybersecurity assessment and evaluation of the Medtronic Altaviva™ System was conducted in accordance with the FDA Guidance Document entitled, "*Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions,*" issued in 2023.

b. Animal Studies

Animal studies were conducted to determine the safety and recharge performance of the INS prior to its clinical use. Testing demonstrated that the device met the study endpoints. Key information from the animal studies is summarized in Table 7 below:

Table 7. Summary of Animal Studies Performed

Study	Objective	Result and conclusion
A non-GLP, 28 Days Chronic Study in Ovine (N=2)	To evaluate and troubleshoot the tibial neuromodulation technology in a chronic in vivo setting	Overall, the neurostimulation results, tissue findings (i.e., no damage) and in vivo tolerance level of the animals were found to be consistent with prior knowledge of similar device type.
A GLP, acute Study in Ovine (N=3)	To collect temperature data from the surface of INS during the recharge sessions for the INS using the WRC	The sponsor evaluated worst case recharging scenario (i.e., each animal was implanted with two INS and 6 recharge data set were obtained). The maximum time for recharging was around 70 mins and the maximum tissue temperature was less than 42 ° C, which was acceptable.

c. Additional Studies

Human Factor Testing

Human Factors (HF) testing was conducted per FDA Guidance Document entitled, "Applying Human Factors and Usability Engineering to Medical Devices," issued in 2018. The HF study involved multiple user groups with 67 total participants: 15 implanting physicians, 15 clinicians (7 physicians, 6 nurse practitioners, and 2 physician assistants), 20 patients, and 17 caregivers. The protocol included both performance and knowledge tasks, with testing conducted in simulated use environments that represented real-world conditions. Performance tasks involved realistic use scenarios tailored to each user group, including implant and explant procedures for physicians, device programming tasks for clinicians, and patient operation and troubleshooting scenarios for patients and caregivers. Knowledge tasks assessed participants' understanding of critical safety information, proper device operation procedures, troubleshooting protocols, and warning and precaution comprehension. The study incorporated comprehensive training programs that mirrored real-world training expectations.

The HF validation testing demonstrated that the device was safe and effective for intended users, uses, and use environments. Performance results documented task performance, use errors, close calls, and use problems across all user groups through detailed tables covering various scenarios. Comprehensive participant interviews provided feedback analysis regarding device use, critical tasks, and encountered difficulties. The study concluded that the user interface effectively mitigated potential use errors, with close calls and use difficulties appropriately managed through design features. The residual use-related risks were identified and addressed through appropriate risk control measures.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

Feasibility Study (TITAN 1)

The Evaluation of Implantable Tibial Neuromodulation (TITAN 1) feasibility study (under IDE #G210001) was a prospective, multicenter investigation designed to evaluate the implantation procedure and initial safety profile of the Medtronic Altaviva™ System in patients with overactive bladder. After the 14-day follow-up visit, subjects continued follow-up through 12 months to collect data on additional measures. There were no pass/fail criteria and statistical analysis plan for the study. The study enrolled 24 subjects across 8 US sites, with 20 subjects ultimately receiving device implantation. Four subjects exited prior to implantation due to various reasons including unsuitable candidacy, withdrawal, and pregnancy. The study population had a mean age of 63.1 years and was predominantly female (90%).

Of the 20 implanted subjects, 40 total AEs were reported in 90.0% (18/20) of implanted subjects, three of which were serious AEs; of these 40 AEs, 17 device-, procedure-, and/or therapy-related AEs were reported in 60.0% (12/20) of subjects. The safety profile of the subject device was generally acceptable, with three serious adverse events reported during the 12-month period. One serious adverse event (wound infection requiring device explant) was procedure-related, while the other two (pneumonia and pubic rami fracture) were unrelated to the device or procedure. Common procedure-related adverse events included pain, swelling, infection, and local site reactions, with two adverse events leading to study discontinuation. Based on results from the TITAN 1 study, the sponsor implemented procedural modifications to the INS implantation technique for the pivotal TITAN 2 trial. Based on exploratory analysis, after 12 months of follow-up, subjects experienced 29% mean reduction in daily urinary leaks (from 3.8 to 2.7 per day) and in daily voids (from 13.5 to 9.6 per day) compared to baseline. Quality of life measures also improved, with mean Overactive Bladder Symptom Quality of Life Questionnaire (OAB-q) scores increasing by 24 points.

Pivotal Clinical Study (TITAN 2)

The applicant performed a pivotal clinical study to demonstrate safety and effectiveness of the Medtronic Altaviva™ System for the treatment of urinary urge incontinence (UUI) in the US under IDE # G210001/S006. Data through twelve months post-implantation from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were implanted with the Medtronic implantable TNM system between March 10, 2022, and April 27, 2023. The last 12-month visit occurred on May 10, 2023, and the database for this PMA submission reflects data collected through October 18, 2024 (data cutoff date). In total, 26 sites enrolled subjects and 126 subjects were implanted.

The TITAN 2 study was a single arm prospective, multicenter, pivotal study to assess safety and effectiveness for the subject device in subjects with OAB symptoms. Enrolled subjects completed baseline procedures, including a baseline 3-day voiding diary and assessment of medical history. Subjects who were consented and met all inclusion and no exclusion criteria were implanted with the INS.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the TITAN 2 study was limited to patients who met the following inclusion criteria:

   1) Subjects 18 years of age or older
   2) A 3-day voiding diary demonstrating a minimum of 3 episodes of urinary urge incontinence in 72 hours
   3) Have a diagnosis of UUI for at least 6 months
   4) No OAB pharmacotherapy for 2 weeks prior to completion of the baseline voiding diary and Overactive Bladder Quality of Life (OAB-q) questionnaire
   5) Failed, or are not a candidate for, conservative non- pharmacologic treatment (e.g., pelvic floor training, biofeedback, behavioral modification)
   6) Failed and/or are intolerant to at least 2 overactive bladder medications (antimuscarinics or beta-3 agonist) or contraindicated to all pharmacological therapies for the treatment of overactive bladder
   7) Willing and able to accurately complete study diaries, questionnaires, attend visits, operate the system, and comply with the study protocol
   8) Willing and able to provide signed and dated informed consent

   Patients were not permitted to enroll in the TITAN 2 study if they met any of the following exclusion criteria:

   1) Have neurological conditions such as multiple sclerosis, clinically significant peripheral neuropathy, or spinal cord injury (e.g., paraplegia)
   2) Severe uncontrolled diabetes
   3) History of urinary retention within the previous 6 months
   4) Current symptomatic urinary tract infection
   5) Have primary stress incontinence or mixed incontinence where the stress component overrides the urge component
   6) Diagnosis of bladder pain syndrome, pelvic pain, or interstitial cystitis
   7) Current urinary tract mechanical obstruction (e.g., benign prostatic enlargement or urethral stricture)
   8) History of a prior implantable tibial neuromodulation system
   9) Knowledge of planned diathermy procedures
   10) Have had treatment of urinary symptoms with sacral neuromodulation in the past 6 months, botulinum toxin therapy in the past 9 months or percutaneous tibial nerve stimulation (PTNS)/percutaneous tibial neuromodulation (PTNM) in the past 3 months

11) Skin lesions or compromised skin integrity (e.g., skin atrophy, thinning, fragility, etc.) which may affect incision healing at the implant site
12) Current or a recent history (within the past 6 months) of a medical condition such as venous insufficiency and/or venous stasis ulcers, clinically significant malnutrition, immunocompromised state, or other relevant chronic disease which may indicate a higher risk for delayed or poor wound healing.
13) Anatomical defects, clinically significant edema or previous surgeries which precludes use of the device (including any metal implant that is within 20 cm of the intended neurostimulator location)
14) Previous pelvic floor surgery in the last 6 months
15) Women who are pregnant or planning to become pregnant during the course of the study
16) Any subject who is considered to be part of a vulnerable patient population.
17) Characteristics indicating a poor understanding of the study or characteristics that indicate the subject may have poor compliance with the study protocol requirements.
18) Concurrent participation in another clinical study that may add additional safety risks and/or confound study results.

2. Follow-up Schedule

All subjects were scheduled to return for follow-up examinations at 7 days, 1, 2, 3, 6, 12 and 24-months post-implant. Though the study includes a 24-month follow-up, clinical data up to 12-month follow-up were submitted to support this PMA.

Preoperatively, a 3-day urinary voiding diary, OAB-q, and Urgency Perception Scale (UPS) were completed for each study subject.

Postoperatively, subjects were instructed to initiate their therapy within 24 hours of implant and to complete voiding diaries at all follow-up visits following the 7-day visit. 3-day urinary voiding diary, OAB-q, UPS, Patient Global Impression of Improvement (PGI-I), patient questionnaires, and device data were collected at various time points, as described in Figure 8. Adverse events were recorded at all visits.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

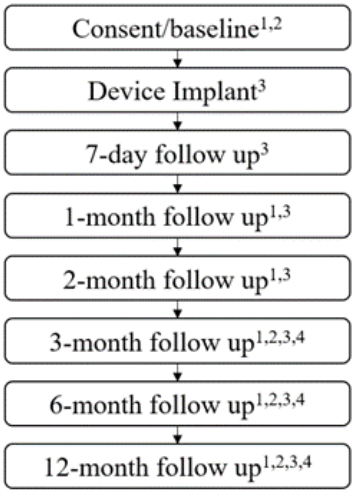


Figure 8: Subject Follow Up Schedule Through 12 months

3. Clinical Endpoints

With regards to safety, the adverse device effects (ADEs) from device implantation to 12 months after device implant were evaluated. ADEs are all events related to the subject device (including WRC related AEs), procedure, therapy, or study aids. Safety was evaluated by review of all adverse events that occurred during the study.

With regards to effectiveness, the primary effectiveness endpoint was defined as the proportion of subjects experiencing a reduction of 50% or more in daily UUI episodes (UUI responder rate) at 6 months after device implant. This endpoint was also evaluated at 12-months post-implant.

The following secondary effectiveness endpoints were evaluated at 6 and 12 months:

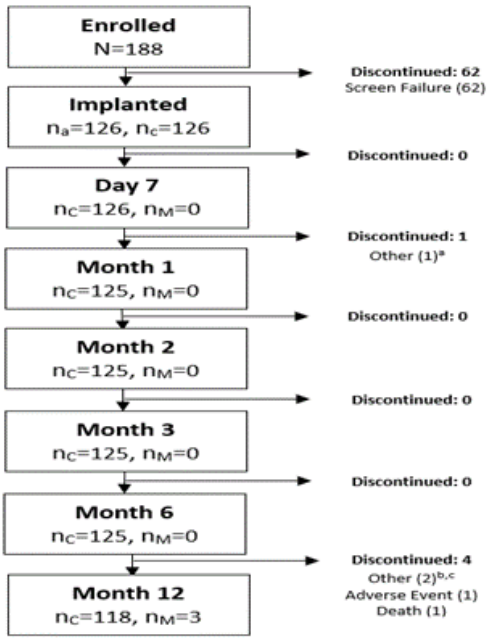
- Change in UUI episodes compared to baseline in subjects with UUI at baseline.
- Change in daily UF episodes compared to baseline in subjects with UF at baseline.
- Change in urinary urgency assessed through the UPS compared to baseline.
- Change in OAB-q health related quality of life (HRQL) total score compared to baseline.

The sponsor defined the study success criteria as greater than 40% of subjects with an attempted implant achieving a greater than 50% reduction in UUI episodes (UUI responder) at 6 and 12 months compared to baseline. However, the FDA evaluated study success based on a threshold of 50% of subjects being UUI

responders at 6 and 12 months, as this responder rate is consistent with success criteria used in clinical studies of similar devices.

B. Accountability of PMA Cohort

At the time of database lock, 188 subjects were enrolled in the clinical study; patients were considered enrolled after signing the informed consent. Of the 188 enrolled subjects, 62 discontinued prior to implant (screen failures). Of the 126 subjects implanted, 1 (1%) discontinued prior to Month 6 and 4 (3%) discontinued prior to Month 12, as shown in Figure 9.



Note: n_a: number of attempted implants. n_C: number of subjects who completed the visit. n_M: number of subjects who missed the visit.

"Other" discontinuation reasons are:

a. "device explant with no planned replacement" (discontinuation prior to the 1-month visit). The explant reason for this subject was due to an ADE of wound infection.

b. "Subject is planning to have surgery with an implanted metal material within 20 cm of the INS."

c. "Transitioned to urethral catheter/suprapubic tube in goals of care discussions with the patient and family."

Figure 9: Disposition of Subjects

The analysis sets were pre-specified in the protocol as follows:

- All Enrolled analysis set (ITT): Includes subjects who completed the informed consent process.
- Full Analysis Set (FAS): Includes subjects with an attempted implant. Because all subjects had successful implant procedures, the FAS is equivalent

to the All Implanted Analysis Set, and the name "All Implanted Analysis set" is used in this document.

- All Implanted analysis set: Includes subjects who are implanted.
- Complete Case analysis set: Includes subjects who are implanted and provide outcome measures at both baseline and follow-up visits. This set is defined for each outcome measure at each follow-up visit.
- As Treated analysis set: Includes only those complete case subjects who received stimulation in the period prior to the visit. This set is defined for each outcome measure at each follow-up visit. Subjects will be excluded from the As Treated analysis sets if they meet 1 or more of the following:
    - If the subject received zero therapy sessions in the 2 weeks prior to the visit.
    - If the subject experienced a consecutive 4 week period with zero therapy sessions in the 3 months prior to the visit.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a pivotal study performed in the US. Tables 8-10 below show the baseline demographics of the 'All Implanted' subjects.

Table 8: Baseline Demographics (All Implanted Analysis Set)

Subject Characteristics	All Implanted (N=126)
Age (years)	
Measure Available	126
Mean (SD)	62.6 (13.68)
Median	65
Min to Max	27.0 to 90.0
Sex (n, %)	
Measure Available	126
Female	120 (95%)
Male	6 (5%)
Ethnicity (n, %)	
Measure Available	126
Not Hispanic or Latino	120 (95%)
Hispanic or Latino	5 (4%)
Not Reported	1 (1%)
OAB Treatment History, n (%)	
Measure Available	126
OAB Medication(s)	126 (100%)
Conservative Therapy	124 (98%)
Botox	23 (18%)
PTNS/PTNM	11 (9%)
Sacral Neuromodulation	4 (3%)
Race (n, %)	
Measure Available	126
White	109 (87%)

Subject Characteristics	All Implanted (N=126)
Black or African American	16 (13%)
American Indian or Alaska Native	1 (1%)
Unknown	1 (1%)
BMI (kg/m^2)	
Measure Available	126
Mean (SD)	34.8 (8.61)
Median	33.3
Min to Max	20.8 to 63.1
BMI>40	35 (28%)
BMI>30	84 (67%)

Abbreviations: BMI, body mass index.
Note: A subject may have more than one race.

Table 9: Baseline OAB Characteristics (All Implanted Analysis Set)

Symptom	N	Mean (SD)	Median	Min to Max
UUI (episodes/day)	126	5.1 (3.46)	4.5	0.6 to 25.3
UF [subjects with UF≥10 only] (episodes/day)	59	12.9 (2.59)	12.1	10.0 to 22.3
OAB-q HRQL Total Score	126	45.6 (20.91)	44	6.4 to 98.4
UPS Degree of Urgency (n, %)	126	1.3 (0.50)	1	1.0 to 3.0

Table 10: Other Medical History (All Implanted Analysis Set)

Subject Characteristics	Implanted (N=126)
Steroid Use Within the Last Year, n (%)	
Measure Available	126
No	78 (62%)
Yes	48 (38%)
Smoking Status, n (%)	
Measure Available	126
Never	75 (60%)
Former	35 (28%)
Current	16 (13%)
Medical History, n (%)	
Measure Available	126
Hypertension	65 (52%)
Depression	57 (45%)
Constipation	33 (26%)
Diabetes Mellitus	22 (17%)
Chronic Urinary Tract Infections	17 (13%)

Note: A subject may have more than one medical history item.

Implant procedures were performed in hospital operating rooms (29%), ambulatory surgical centers (35%), and outpatient clinic procedure rooms (37%).

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the 'All Implanted' cohort of 126 patients. available for the 12-month evaluation. The key safety outcomes for this study are presented below in Tables 11 to 16.

Among the 126 implanted subjects, 107 (85%) experienced a total of 437 adverse events (AEs) within 12 months of implantation, including 45 serious AEs in 18.3% of subjects, with 1 device/procedure-related serious AE (Clostridium difficile colitis). Another AE was reported before 6-months post-implantation where the implant wound infection resulted in device explant. The FDA considers this AE as a serious device-related AE (SADE) (Table 12 below does not include this SADE). The most reported serious adverse events after device implant were pyelonephritis (2%), angina pectoris (2%), and pneumonia (2%). A total of 30 anticipated device effects (ADEs) or device/procedure related AEs were reported in 20% (25/126) of subjects through the 12-month visit. ADEs occurred at the highest rate immediately after implant with 25% of all ADEs occurring in the first month, and 53% within the first 3 months. Overall, the most frequently reported ADEs in the first 6 months were related to infection and pain. The most reported infections were implant site infection (4%) and incision site cellulitis (2%). The most reported preferred terms related to pain were implant site pain (3%) and medical device site pain (2%). Suspected implant-related infections at the implant site (inclusive of multiple preferred terms) were reported at a rate of 7% (9/126). All resolved with antibiotic treatment except for one which resolved after explant (1%). All ADEs were mild (grade 1) or moderate (grade 2) on the Common Terminology Criteria for Adverse Events (CTCAE) grading scale.

Through 12 months, 3 subjects had their devices explanted: 2 explants were due to ADEs (1 due to infection, and 1 due to implant leg pain), and the other explant was due to a planned surgery. One subject had a device revision (explant with reimplant on the same day) due to an ADE (burning/blue bruising at implant post charging) post INS charging. Eight subjects had the implant removed at 12 months due to lack of effectiveness. There were no reported ADEs of device migration or erosion, and there were no unanticipated adverse device effects through 12-month follow-up.

Table 11: Adverse Event Summary (All Implanted Analysis Set, N=126)

	# of events at 6 months	# of subjects (n) (%) at 6 months	# of events at 12 months	# of subjects (%)at 12 months
Total AE	227	90 (71.4%)	437	107 (84.9%)
SAE	17	12 (9.5%)	45	23 (18.3%)
SADE	1	1 (0.8%)	1	1 (0.8%)
ADE	23	21 (16.7%)	30	25 (19.8%)

Table 12: Device/Procedure Related Adverse Events by Type (All Implanted Analysis Set, N=126)

	Implant to 6 months		Implant to 12 months	
	ADE events (subjects (n), % of subjects)	**SADE events (subjects (n), % of subjects)**	**ADE events (subjects (n), % of subjects)**	**SADE events (subjects (n), % of subjects)**
Total	23 (21, 16.7%)	1 (1, 0.8%)	30 (25, 19.8%)	1 (1, 0.8%)
Procedure	10 (10, 7.9%)	1 (1, 0.8%)	10 (10, 7.9%)	1 (1, 0.8%)
Device	9 (9, 7.1%)	0 (0, 0.0%)	15 (14, 11.1%)	0 (0, 0.0%)
Therapy	5 (5, 4.0%)	0 (0, 0.0%)	6 (6, 4.8%)	0 (0, 0.0%)

Note: An event can be classified as more than 1 relatedness category, and a subject may have more than 1 event, so the sum of the related components may not add to the total.

Table 13: Device/Therapy Related Adverse Events – Implant to Month 12 (All Implanted Analysis Set, N=126)

System Organ Class Preferred Term	**Events (Subjects (n), % of Subjects)**	
	Implant to Month 6	**Implant to Month 12**
All Adverse Events	(N = 126) 13 (12, 9.5%)	(N = 126) 20 (16, 12.7%)
Musculoskeletal and connective tissue disorders		
Limb discomfort	1 (1, 0.8%)	1 (1, 0.8%)
Muscle tightness	1 (1, 0.8%)	1 (1, 0.8%)
Pain in extremity	1 (1, 0.8%)	2 (2, 1.6%)
General disorders and administration site conditions		
Implant site bruising	1 (1, 0.8%)	1 (1, 0.8%)
Implant site pain	2 (3, 1.6%)	4 (4, 3.2%)
Medical device pain	0 (0, 0%)	1 (1, 0.8%)
Medical device site pain	2 (2, 1.6%)	3 (3, 2.4%)
Oedema peripheral	1 (1, 0.8%)	1 (1, 0.8%)
Gastrointestinal disorders		
Anal incontinence	1 (1, 0.8%)	1 (1, 0.8%)
Injury, poisoning and procedural complications		
Incision site complication	1 (1, 0.8%)	1 (1, 0.8%)
Incision site swelling	1 (1, 0.8%)	2 (1, 0.8%)
Product issues		
Device inappropriate shock delivery	1 (1, 0.8%)	2 (2, 1.6%)

Note: The event count may not be the same as the subject count, as a subject may have had more than 1 similar event. The sum of individual preferred terms may not add to the total of all adverse events, as a subject may have had more than 1 event.

Table 14: Procedure Related Adverse Events – Implant to Month 12 (All Implanted Analysis Set, N=126)

System Organ Class Preferred Term	**Events (Subjects (n), % of Subjects)**	
	Implant to Month 6	**Implant to Month 12**
All Adverse Events	(N = 126) 10 (10, 7.9%)	(N = 126) 10 (10, 7.9%)
Infections and infestations		
Clostridium difficile colitis	1 (1, 0.8%)	1 (1, 0.8%)
Implant site infection	5 (5, 4.0%)	5 (5, 4.0%)
Incision site cellulitis	3 (3, 2.4%)	3 (3, 2.4%)
Wound infection	1 (1, 0.8%)	1 (1, 0.8%)

Note: The event count may not be the same as the subject count, as a subject may have had more than 1 similar event. The sum of individual preferred terms may not add to the total of all adverse events, as a subject may have had more than 1 event.

Table 15: Device/Therapy Related Adverse Events (AE) Over Time through 12-months From Implant Date (All Implanted Analysis Set, N=126)

AE Preferred Term	**Day 0**	**Day 1-7**	**Day 8-30**	**Day 31-90**	**Day 91-180**	**Day 181-365**	**Total AE**
Anal incontinence	0	0	0	0	1	0	**1**
Device inappropriate shock delivery	0	0	0	1	0	1	**2**
Implant site bruising	0	0	0	1	0	0	**1**
Implant site pain	1	0	0	1	0	2	**4**
Incision site complication	0	0	0	0	1	0	**1**
Incision site swelling	0	0	0	1	0	1	**2**
Limb discomfort	1	0	0	0	0	0	**1**
Medical device pain	0	0	0	0	0	1	**1**
Medical device site pain	0	0	0	1	1	1	**3**
Muscle tightness	0	0	1	0	0	0	**1**
Oedema peripheral	0	0	0	1	0	0	**1**
Pain in extremity	0	0	0	0	1	1	**2**
Grand total during the visit window	**2**	**0**	**1**	**6**	**4**	**7**	**20**

Table 16: Procedure Related Adverse Events (AE) Over Time through 12-months From Implant Date (All Implanted Analysis Set, N=126)

AE Preferred Term	Day 0	Day 1-7	Day 8-30	Day 31-90	Day 91-180	Day 181-365	Total AE
Clostridium difficile colitis	0	0	1	0	0	0	**1**
Implant site infection	0	0	2	3	0	0	**5**
Incision site cellulitis	0	0	2	1	0	0	**3**
Wound infection	0	0	1	0	0	0	**1**
Grand total during the visit window	**0**	**0**	**6**	**4**	**0**	**0**	**10**

2. Effectiveness Results

The analysis of effectiveness was based on the 126 evaluable patients at 12-month time point. Key effectiveness outcomes are presented in Tables 17 to 19.

In the table below, the primary effectiveness endpoint (UUI responder rate, ≥ 50% reduction from baseline in UUIs per day) data are provided for different sensitivity analysis in the 'All Implanted' analysis set for 6 and 12-months post implantation. The 12-month data presented below are post-hoc. Within the 12-months after implantation, 5 study subjects used OAB medications.

Table 17: UUI Responder Rate Sensitivity Analyses-6 and 12 months (All Implanted Analysis Set)

All Implanted (N=126)	6 Months	12 Months*
Imputing missing using Multiple Imputation (MI)[a] n/N[b] (%) 95% Lower Control Bound (LCB)	73.5/126 (58.3%) 49.6%	76.2/126 (60.5%)
Imputing missing using MI and OAB medications taken as failures UUI responder rate n/N (%)	72.7/126 (57.4%)	73.1/126 (58%)
Imputing both missing and OAB medications taken as failures UUI responder rate n/N (%)	71/126 (56.4%)	68/126 (54%)

*12-month data are considered post-hoc and no statistical inference can be made from these data.

[a] MI followed ITT principals and was a prespecified primary analysis, which is presented as a sensitivity analysis due to less than 5% missing.

[b] The All Implanted analysis set with MI analysis displays a sample size (n) which is not a whole number. This number has decimals because multiple imputation combines results from multiple imputed datasets, resulting in the average responder count shown.

Table 18: Summary of Secondary Effectiveness Endpoints (All Implanted Analysis Set)

Measure (N = 126)	Change from Baseline to 6 months Mean ± SD (N)	Change from Baseline to 12 months Mean ± SD (N)
UUI episodes (per day)	-2.7 ± 3.10	-2.7 ± 3.20
UF episodes (per day)	-2.5 ± 2.91	-3.0 ± 3.54
Urgency Perception Scale (UPS)	0.4 ± 0.74	0.4 ± 0.72
Quality of Life Questionnaire (OAB-q)	26.9 ± 25.81	25.5 ± 27.04

The sponsor provided a post-hoc analysis with the mean improvement in different symptoms compared to the baseline for the 'All Implanted' population (N =126), calculated from the 3-day patient bladder diary at 12-months follow-up. Table 19 below shows the percentage mean improvement of different symptoms at 12-months of device activation compared to the baseline.

Table 19: Assessment of Individual Symptoms at 12-months Follow-up (All Implanted, N=126)

Symptom	Baseline mean value of symptom/day (X)	Mean value of symptom/day at 12-months of device activation (Y)	Percentage mean improvement of symptom at 12-months of device activation compared to baseline= $\frac{X-Y}{X} \times 100\%$
UUI episodes/day	5.1	2.5	51%
Urgency episodes/day	9.8	7.9	19%
Urinary frequency (voids/day)	12.9	9.9	23%

As shown in Table 19, the Medtronic Altaviva™ System showed clinically meaningful improvements in UUI related symptoms at 12-months. However, the reduction in urinary urgency and urinary frequency at 12 months are not clinically meaningful. The secondary effectiveness endpoint results related to urinary urgency and urinary frequency episodes are not related to the UUI claim and do not provide evidence supporting the device's safety and effectiveness for the treatment of urinary urgency and frequency.

The sponsor provided additional exploratory effectiveness data analyses for the Complete Case' analysis set, including OAB-q HRQL (Overactive Bladder Questionnaire Health-Related Quality of Life), 100% UUI responder rates. The OAB-q HRQL analysis showed that 71.2% (89/125) of subjects achieved a ≥10 point change at 6 months, which decreased to 69.5% (82/118) at 12 months. For the 100% urgent urinary incontinence (UUI) responder rate, which evaluated

complete resolution of all urgent leaks, 19% (23/123) of subjects showed 100% improvement for urgent leaks at 6 months, with 22% (26/118) at 12 months.

Patient satisfaction and perceived symptom improvement were assessed at 6 and 12 months following therapy. Satisfaction was measured by willingness to recommend the therapy and personal satisfaction with its effects. On the patient satisfaction question rating, 76% of subjects would recommend the therapy to a friend or family member suffering from similar symptoms at both time points, and 74% (91/123) and 65% (77/118) of subjects were satisfied with the Altaviva therapy at 6 and 12 months, respectively. Symptom improvement was evaluated using the validated PGI-I (Patient Global Impression of Improvement) scale. After 6 months of therapy, 82% (101/123) of subjects reported that their condition had improved, and after 12-months 80% (94/118) subjects reported the same.

3. Subgroup Analyses

The following baseline characteristics were evaluated for potential association with safety and effectiveness outcomes (Table 20):

Table 20: Sub-group Analysis for the UUI Responder Rate at 12-months (All Implanted Analysis Set, N=126)

UUI Responder rate at 12 months	**Subgroup 1**	**Subgroup 2**
Subgroup: Sex	**Female (N=120)**	**Male (N=6)**
Measure available (N)	120	6
Responder (n, %)	**74.2 (61.8%)**	**N/A due to n < 10**
Subgroup: Age 65	**Age < 65 (N=58)**	**Age ≥ 65 (N=68)**
Measure available (N)	58	68
Responder (n, %)	**44.3 (76.4%)**	**31.9 (46.9%)**
Subgroup: Race	**Black or African American (N=16)**	**White (N=109)**
Measure available (N)	16	109
Responder (n, %)	**10.2 (63.8%)**	**65.0 (59.6%)**
Subgroup: Ethnicity	**Not Hispanic or Latino (N=120)**	**Hispanic or Latino (N=6)**
Measure available (N)	120	5
Responder (n, %)	**72.2 (60.2%)**	**N/A due to n < 10**

Note: A subject may be included in more than 1 race; some races are not represented for having fewer than 10 subjects.

As shown in Table 20 above, the UUI responder rate in subjects aged 65 years or older is 46.9% while in subject younger than 65, the UUI responder rate was 76.4%. This represents a 29.5% reduction in UUI responder rate in subjects 65 and older compared to subjects who are aged less than 65.

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

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 58 participating investigators, of which 0 were full-time or part-time employees of the sponsor and 5 had disclosable financial interest/arrangements as defined in 21 CFR 54.2(a), (b), (c), and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 5
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data

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

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Gastroenterology / Urology Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The results from the TITAN 2 study show that the Medtronic Altaviva™ System provides a clinically meaningful improvement in UUI symptoms in patients who have failed or could not tolerate more conservative treatments.

The Medtronic Altaviva™ System demonstrated ≥50% reduction in the number of UUI episodes at 12-months post-implantation, relative to the number of UUI episodes at baseline.

For the 'All Implanted' analysis set, 58.3% (73.5/126) and 60.5% (76.2/126) of subjects at 6 months and 12 months post-implant, respectively, were responders (≥ 50% reduction from baseline in UUI episodes per day).

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory as well as data collected in a clinical study conducted to support PMA approval as described above.

In the TITAN 2 study of the Medtronic Altaviva™ System, there was one serious device-related AE (Clostridium difficile colitis), through 12 months post-implant. One AE was reported before 6-months post-implantation where the implant wound infection resulted in device explant. The FDA considers this AE as a serious device-related AE. At 12 months post implant, 30 device/procedure related adverse events in 25 of 126 subjects (19.8%) were seen in the study, of which 28 (93%) were resolved with minimal, local, or noninvasive intervention. At the twelve-month endpoint, the most common device-related AEs in the study were, implant site infection (4%), implant site pain (3.2%), incision site cellulitis (2.4%), medical device site paint (2.4%), pain in extremity (1.6%) and the inappropriate shock delivery by the subject device (1.6%). No INS fracture or migration related adverse events were reported in this study.

In total, 3 subjects underwent explantation prior to the 12-month visit for the following reasons: wound infection, the need for another surgery around the implant site, and burning sensation, while one death occurred due to gastrointestinal bleeding that was unrelated to any device/procedure related adverse events. After 12-month follow-up, 8 subjects explanted the Altaviva™ INS due to lack of efficacy.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The results from the clinical study show that the Medtronic Altaviva™ System provides a clinically meaningful improvement in UUI in patients who have failed or could not tolerate more conservative treatments. For the All Implanted analysis set, 58.3% and 60.5% of subjects at 6 month and 12 months post-implant, respectively, were responders (≥ 50% reduction from baseline in UUIs per day). Additionally, the subject device offers a 15-year device and battery longevity while providing clinically relevant stimulation. This exceeds the typical 3–5-year lifespan of comparable devices currently on the market, which may lower the need for revision or device/battery replacement surgeries. There is uncertainty in the long-term, real-world effectiveness of the subject device in comparison to other legally marketed similar devices for treatment of UUI. Although the device achieved the sponsor's prespecified performance goal of 40%, the lower bound of the UUI responder rate (49.6%) only marginally met the FDA's recommended 50% threshold, raising uncertainty about the robustness of the treatment effect over time. Another point of uncertainty was the reduced effectiveness of the device in patients over 65. The UUI

responder rate was reduced by 29.5% in this patient population compared to the patients aged less than 65 years. The UUI responder rate dropped below the 50% (i.e., 46.9%) threshold in in patients over 65. Given these uncertainties, a post-approval study is required to obtain additional information about the long-term effectiveness of the Medtronic Altaviva™ System and its long-term clinical performance in patients over 65 years of age.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. In the clinical study, there was one serious device-related AE (Clostridium difficile colitis), through 12 months post-implant. However, one AE was reported before 6-months post-implantation where the implant wound infection resulted in device explant, which FDA considered a serious device-related AE. At 12 months post implant, 30 device/procedure related adverse events in 25 of 126 subjects (19.8%) were seen in the study, of which 28 (93%) were resolved with minimal, local, or noninvasive intervention. At the twelve-month endpoint, the most common device-related AEs in the study were, implant site infection (4%), implant site pain (3.2%), incision site cellulitis (2.4%), the inappropriate shock delivery by the subject device (1.6%) and fecal incontinence (0.8%). There is uncertainty about the risk of long-term occurrences of device/procedure related AEs, such as implant site infection, inappropriate electrical shock delivery, and fecal incontinence. Given this uncertainty, a post-approval study is required to obtain additional information about the long-term rates for device/procedure related AEs.

1. Patient Perspective

   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for treatment of urinary urge incontinence (UUI) in patients who have failed or could not tolerate more conservative treatments, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

The results from the non-clinical and clinical evaluations support that a significant portion of the patient population for whom the device is intended can be expected to achieve clinically significant results.

The safety and effectiveness of the Medtronic Altaviva™ System for treatment of urinary urge incontinence was based a pivotal study evaluating the Medtronic Altaviva™ System indicating that the benefit of the Altaviva tibial neuromodulation therapy outweighs the

associated risks. Based on the clinical study results, it is reasonable to conclude that the clinical benefits of the use of the Medtronic Altaviva™ System in the treatment of UUI, in terms of reduction in the number of UUI episodes, outweigh the risks.

XIV. CDRH DECISION

CDRH issued an approval order on September 18, 2025. The final clinical conditions of approval cited in the approval order are described below.

1. 24-month Follow-up of the "Evaluation of Implantable Tibial Neuromodulation (TITAN 2) Pivotal Study"

   This study was initiated prior to device approval and is a single-arm, multi-center clinical study. It was conducted at 25 sites and enrolled 188 subjects. One hundred and twenty six (126) subjects were implanted in this study. The 12-month outcomes from the study were used to support PMA approval. The 24-months follow-up data from this study must be submitted to assess the continued safety and effectiveness of the Medtronic Altaviva™ System. You must report the following clinical outcomes for 24-months follow-up:

Effectiveness

- Primary Effectiveness Endpoint: Percentage of subjects who experience an improvement in urge urinary incontinence (UUI) episodes of at least 50% or greater from baseline (therapy responders)
- Change from baseline in quality of life as measured and assessed by the total overactive bladder (OAB)-q Health Related Quality of Life (HRQL) score
- Change from baseline in mean number of UUI episodes
- Percentage of subjects who experience an improvement in OAB-q HRQL of at least 10 points
- Subgroup analysis of the UUI responder rate for the patient population 65 and older

Safety

- Comprehensive summary of all adverse events (AEs) for the duration of study participation, including all device- or procedure-related AEs and device- or procedure-related serious adverse events
- Revision rates
- Explantation rates

Device Use

- Device parameters including but not limited to voltage, pulse width, frequency, and stimulation duration/day

This PAS Report should be submitted no later than two (2) months after the approval of this PMA.

2. Tibial Neuromodulation (TNM) Post Approval Study

The purpose of this new enrollment PAS is to assess the long-term safety and effectiveness of the Medtronic Altaviva™ System for the treatment of UUI in patients through 5 years of follow-up. This is a prospective, multicenter, single-arm, open-label study. Subjects that have symptoms of UUI will be enrolled. The study will be conducted at approximately 30 institutions in the United States. Eligible subjects must sign a study-specific informed consent form (ICF). Subjects must complete an Enrollment/Baseline Visit, a Device Implant Visit, 1-month, 6-month, 12-month and annual follow-up visits thereafter post implant until the 60-month follow-up visit is complete.

Approximately 256 subjects will be enrolled in the study to achieve a minimum of 170 implanted subjects to account for about 33% attrition between enrollment and implant. At least 90 subjects must be followed to 60 months post implant. Additionally, a least 50% of enrolled subjects must be aged 65 years or older. To ensure that a minimum of 50% of enrolled subjects are aged 65 years or older, enrollment may be opened exclusively to individuals within this age group during the study if needed.

The following must be collected and reported for this PAS:

- Primary Effectiveness Endpoint: UUI responder rate annually through 60 months after implant. A UUI responder is defined as having at least 50% improvement from baseline in daily UUI episodes.

- Additional Effectiveness Endpoints:
  - The following endpoints should be evaluated annually through 60 months:
    - Change from baseline in daily UUI episodes
    - UUI responder rate for subjects aged 65 and older
    - Patient reported impression of improvement as measured with the Patient Global Impression of Improvement (PGI-I) questionnaire
    - Device and system usage data (i.e., stimulation parameters, duration and frequency of stimulation for each subject)

- Safety Endpoints:
  - Procedure-, device-, and/or therapy-related adverse events through 60 months by reporting the number of events, and number and percentage of subjects with events.
  - Serious adverse events through 60 months by reporting the number of events, and number and percentage of subjects with events

  All adverse events data must be collected and recorded regardless of relatedness.

The primary analysis must be conducted on the Intention-to-Treat (ITT) population (all subjects who are implanted), with results based on the voiding diary data and summarized using descriptive statistics. Missing data must be addressed based on the underlying reason for missingness. Subjects with missing data due to lack of efficacy must be classified as treatment failures, while all other missing data must be managed using multiple imputation under a missing-at-random assumption. Additionally, in the ITT analysis set, the sensitivity analysis must be conducted considering all missing data as treatment failures without imputation for each follow-up up visit through 60-months. In the ITT population, the sensitivity analysis must be conducted considering subjects with increase in overactive bladder medication or the subjects receiving additional treatments during the study, as treatment failures without imputation for each follow-up up visit through 60-months. Additionally, specific subgroup analysis must be conducted with the ITT population at each annual follow-up through month 60 on the primary effectiveness endpoint data on age, OAB medication use in subjects by age (older than 65) and sex.

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

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.