DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

P970004

Date · SEP 29 1997

From Deputy Director, Clinical and Review Policy, Office of Device Evaluation, Center for Devices and Radiological Health (HFZ-400)

Subject Premarket Approval of Medtronic, Inc.'s Interstim® Sacral Nerve Stimulation (SNS)™ System - ACTION

To Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Kimber C. Richter
Kimber C. Richter, M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved X Disapproved ____ Date 9/29/97

Prepared by: Laura J. Byrd, CDRH, HFZ-472, 8-26-97, 301-594-2194
Donald J. St. Pierre, CDRH, HFZ-472, 8-26-97, 301-594-2194

DEPARTMENT OF HEALTH AND HUMAN SERVICES

DRAFT

Food and Drug Administration

[Docket No. _____]

Medtronic, Inc.; Premarket Approval of the Interstim® Sacral Nerve Stimulation (SNS)™ System

AGENCY: Food and Drug Administration, HHS

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Medtronic, Inc., Minneapolis, MN, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of the Interstim® Sacral Nerve Stimulation (SNS)™ System. After reviewing the recommendation of the Gastroenterology and Urology Devices Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter of September 29, 1997, of the approval of the application.

DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Laura J. Byrd,

Center for Devices and Radiological Health (HFZ-472),

Food and Drug Administration,

9200 Corporate Blvd.,

Rockville, MD 20850,

301-594-2194.

SUPPLEMENTARY INFORMATION: On January 30, 1997, Medtronic, Inc., Minneapolis, MN 55432, submitted to CDRH an application for premarket approval of the Interstim® Sacral Nerve Stimulation (SNS)™ System. The device is an implantable sacral nerve electrical stimulation system and is indicated for the treatment of urinary urge incontinence in patients who have failed or could not tolerate more conservative treatments.

On August 6, 1997, the Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee, an FDA advisory committee, reviewed and recommended approval of the application. On September 29, 1997, CDRH approved the application by a letter to the applicant from the Deputy Director of Clinical and Review Policy of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity for Administrative Review

Section 515(d)(3) of the act, (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under 21 CFR part 12 of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 21 CFR 10.33(b). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h) (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: _____

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

SEP 29 1997

Ms. Kathy Herzog
Senior Product Regulation Manager
Medtronic, Inc.
Interstim Venture
7000 Central Avenue, N.E.
Minneapolis, Minnesota 55432-3576

Re: P970004
Medtronic® Interstim® Sacral Nerve Stimulation (SNS)™ System
Filed: January 30, 1997
Amended: February 27, May 27, July 2 and 8, and September 26, 1997

Dear Ms. Herzog:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Medtronic® Interstim® Sacral Nerve Stimulation (SNS)™ System which includes the Model 3886 or 3080 Lead, Model 7495 Extension, Model 7424 Implantable Pulse Generator (IPG), Model 7455 Memory Module, Model 7432 Console Programmer, Model 7452 Control Magnet, Model 3625 Test Stimulator (Screener), and Model 3065U PNE Kit and Accessories. This device is indicated for the treatment of urinary urge incontinence in patients who have failed or could not tolerate more conservative treatments. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act. Physicians must be trained in the diagnosis and treatment of lower urinary tract symptoms.

In addition to the postapproval requirements in the enclosure, the postapproval reports must include the annual progress reports on the following postapproval study:

> Your postapproval study should collect 5-year follow-up data to evaluate the long-term effects of the Sacral Nerve Stimulation (SNS)™ System treatment on a minimum of 152 patients. The postapproval study should assess the rates of adverse events that occurred during the 5-year follow-up period, focusing on those events which require surgical intervention, and evaluate the long-term effect of sacral nerve stimulation on urinary urge incontinence.

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by

requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Ms. Laura J. Byrd at (301) 594-2194.

Sincerely yours,

Kimber C. Richter

Kimber C. Richter, M.D.
Deputy Director
Clinical and Review Policy
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure
1) Conditions of Approval

Issued: 5-2-95

CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. **This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.**

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mixup of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

(1) may have caused or contributed to a death or serious injury or

(2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-531)
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, Room 240
Rockville, Maryland 20850
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

Generic Name: Implantable Electrical Stimulator for Incontinence

Trade Name: Medtronic® Interstim® Sacral Nerve Stimulation (SNS)™ System
Medtronic Itrel II Stimulation System for SNS
Medtronic Model 3886 or Model 3080 SNS Leads
Medtronic SNS Accessories

Applicant: Medtronic, Inc.
Medtronic Synectics Division (Urology Business)
8299 Central Avenue N.E.
Spring Lake Park, MN 55432

PMA Number: P970004

Date of Notice of Approval to Applicant: SEP 29 1997

II. INDICATIONS FOR USE

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

III. CONTRAINDICATIONS

Patients are contraindicated for implantation of the SNS System if they have not demonstrated an appropriate response to test stimulation.

Patients are contraindicated for implantation of the SNS System if they are unable to properly operate the Itrel II Implantable Pulse Generator (IPG).

Refer to the labeling for a list of the precautions.

IV. DEVICE DESCRIPTION

The Medtronic SNS System is intended to manage urinary urge incontinence via electrical stimulation of the sacral nerves (typically S2 or S3). The therapy is non-destructive and reversible, and allows physicians to non-invasively program stimulation parameters.

The Medtronic SNS System consists of the Medtronic Itrel II Stimulation System, SNS Leads, and SNS Accessories. The accessories are used to perform temporary sacral nerve stimulation, either for test stimulation prior to chronic implant, or during implant of the chronic system to assess lead placement and patient responses. The Itrel II System, in

conjunction with an SNS lead, is used to deliver chronic stimulation therapy. The chronic use components of the Medtronic SNS System consist of the Itrel II Stimulation System and an SNS Lead as follows:

Medtronic Itrel II Stimulation System

- Model 7424 Itrel II Implantable Pulse Generator (IPG) (implantable)
- Model 7495 Extension (implantable)
- Model 7432 Console Programmer (external device)
- Model 7455 Memory Module (external device)
- Model 7452 Control Magnet (external device)

Medtronic SNS Leads

- Model 3886 Lead (implantable) or
- Model 3080 Lead (implantable)

Temporary SNS use components consist of the following accessories:

SNS Accessories

- Model 3625 Screener (external device)
- Temporary Peripheral Nerve Evaluation (PNE) Lead (temporary implant)
- Foramen Needles (temporary internal placement)
- Cables (external device)

Other than the SNS Accessories (PNE lead, foramen needles, cables), the other components have prior marketing approval. The Itrel II System components are currently commercially available for Spinal Cord Stimulation (SCS) for the treatment of chronic intractable pain of the trunk and limbs (P840001/S3 and S15). The Model 3886 Leads are currently commercially available for SCS for the treatment of chronic, intractable pain (K923931). The Model 3080 Leads are currently commercially available for SCS and Peripheral Nerve Stimulation (PNS) for the treatment of chronic, intractable pain (K924522). The Model 7495 Extension is currently commercially available for SCS (P840001/S15 and K903690). The Model 3625 Screener is currently commercially available for SCS and PNS for the treatment of chronic, intractable pain of the trunk or limbs (K903690, K884898, K881491, etc.).

V. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

A. *Peripheral Nerve Evaluation (PNE)*

A total of 458 patients were evaluated for adverse events in the PNE stage of the clinical investigation of the Medtronic SNS System. There were a total of 664 PNE procedures conducted on these 458 enrolled patients. Of the 664 PNE procedures, 96 of them resulted in 118 device- and therapy-related adverse events. This yields a PNE procedure adverse event rate of 14.5%. The studies that were conducted recorded the following device and therapy related events:

Device Related: 26 (3.9%) events experienced in 664 PNEs (or 26/118 (22.0%) PNE events) were device-related and were documented in 25 (5.5%) of the 458 patients enrolled.

Therapy Related: 92 (13.9%) events experienced in 664 PNEs (or 92/118 (78.0%) PNE events) were therapy-related and were documented in 81 (17.7%) of the 458 patients enrolled.

Table 1: PNE-Related Adverse Events

PNE-Related Adverse Events 664 PNE Procedures, 458 Enrolled Patients				
Event Type	**PNE Adverse Events**	**# of Patients***	**# of Events**	**Events Resolved**
Device-Related	• PNE lead disconnection at proximal end of auxiliary screener cable/PNE lead interface	16 (3.5%)	17	17
	• Detachment of distal PNE electrode from PNE lead	2 (0.4%)	2†	1
	• Dislodged ground pad	2 (0.4%)	2	2
	• Obstructed foramen needle	1 (0.2%)	1†	1
	• Unable to pass PNE lead through needle	1 (0.2%)	1	1
	• Sensation of transient electric "shock"	1 (0.2%)	1†	1
	• Incorrect connection of auxiliary screener cable	1 (0.2%)	1†	1
	• Broken screener	1 (0.2%)	1†	1
Therapy-Related	• PNE lead migration	56 (12.2%)	66	66
	• Temporary pain	16 (3.5%)	17	16
	• Infection/skin irritation at PNE site	4 (0.9%)	4	4
	• Adverse change in bowel function	3 (0.6%)	3	3
	• Adverse change in voiding function	1 (0.2%)	1	1
	• Irritation at ground pad site	1 (0.2%)	1	1
Totals			118	116

* Some patients experienced more than 1 adverse event.
† Six of the 26 reported device-related events occurred as a result of mishandling.

B. *Chronic SNS Devices*

A total of 157 patients were evaluated for adverse events in the chronic implant stage of the clinical investigation of the Medtronic SNS System. Of the 157 patients implanted, 73 patients (46.5%) experienced 125 adverse events. This yields a patient adverse event rate of 46.5%. The studies that were conducted recorded the following device- and therapy-related adverse events:

Device Related: 3 (2.4%) of the 125 adverse events reported were device-related (lead fracture) and were documented in 1 (0.6%) of the 157 implanted patients (or occurred to

1/73 (1.4%) implanted patients that experienced a device- or therapy-related adverse event).

Therapy Related: 122 (97.6%) of the 125 adverse events reported were therapy-related and were documented in 72 (45.9%) of the 157 implanted patients (or occurred to 72/73 (98.6%) implanted patients that experienced a device- or therapy-related adverse event).

Of the 3 device-related and 122 therapy-related adverse events reported in the 157 chronic implant procedures, 75 (60.0%) required surgical intervention (i.e., repositioning or replacement) which affected 51 (32.5%) of the 157 implanted patients. This yields a patient surgical revision rate of 32.5%.

Table 2: Post-Implant Adverse Events

Post-Implant Adverse Events 73 of 157 Implanted Patients				
Event Type	**Events**	**# of Patients***	**# of Events**	**Events Resolved**
Device-Related	• Lead Fracture†	1 (0.6%)	3	2
Therapy-Related	• Pain at implant site (back, buttocks, legs)	30 (19.1%)	33	30
	• Pain at IPG site	25 (15.9%)	27	22
	• Lead migration	11 (7.0%)	14	12
	• Infection/skin irritation	9 (5.7%)	11	10
	• Technical problem	8 (5.1%)	11	9
	• Sensation of transient electric 'shock'	8 (5.1%)	10	10
	• Adverse change in bowel function	8 (5.1%)	8	8
	• Allergic reaction	1 (0.6%)	1	1
	• Aggravation of baseline symptoms	1 (0.6%)	1	0
	• Other Numbness (2) Vaginal cramping (1) Inability to have orgasm (1) Menstrual bleeding (1) Trauma to IPG (1)	6 (3.8%)	6	5
Totals		73*	125	109

*Some patients experienced more than 1 adverse event.
†All 3 device-related events involved the loss of stimulation as a result of damage to the implanted lead. Medtronic is providing additional training to the physician on lead placement techniques.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Non-surgical treatment options for urge incontinent patients include diet modification, pharmacologics, and behavioral techniques such as timed voiding, pelvic muscle exercises, non-implantable electrical stimulators, and biofeedback. Surgical interventions include augmentation cystoplasty, bladder denervation, and bladder removal/urinary diversion. Patients who fail conservative treatments, and elect not to undergo surgery, default to managing their incontinence through the use of external collecting devices (Foley catheters with a urine bag, penile clamps) or absorbent products (pads and diapers).

VII. MARKETING HISTORY

The Medtronic Itrel II Stimulation System has been commercially available in the US and areas outside the US for Spinal Cord Stimulation (SCS) for the treatment of chronic pain since 1988. Commercial experience for the Medtronic SNS leads includes sales of these leads outside the US for SNS since 1994. Of the SNS Accessories, the Model 3625 screener has been commercially available in the US and outside the US for SCS and PNS for the treatment of chronic pain since 1988. The remaining bulk accessories have been commercially available outside the US since 1994 for use in SNS applications.

VIII. SUMMARY OF STUDIES

A. Non-Clinical Laboratory Studies

1. In-Vitro (Bench) Testing

Summary of Testing: Itrel II Stimulation System

The components of the Itrel II system are commercially available for SCS for the treatment of chronic intractable pain of the trunk and limbs (P840001/S3, approved 5/31/85 and S15, approved 8/2/89). Testing for these currently commercially available components, which are physically identical when used for the SNS indication, was referenced to the previous regulatory submissions.

Summary of Testing: Model 3886 and Model 3080 Leads

The Model 3886 and 3080 leads are part of a family of helical coil-type leads manufactured by Medtronic. The Model 3487A PISCES-Quad SCS lead is the core technology for this family of helical coil-type leads. The 3886 and 3080 SNS leads share common design, materials, and manufacturing methods to the 3487A lead. The 3487A lead is commercially approved for SCS (K881491, etc.) for the treatment of chronic intractable pain of the trunk and limbs, and has been marketed for this indication since 1988.

Because of the similarities in lead design, materials, manufacturing, and use, qualification testing for the Model 3487A is relevant to qualification of the Model 3886 and 3080 leads. Additional testing was performed on the Model 3886 and 3080 leads to augment the 3487A test experience as applicable for their respective designs.

Testing of the Model 3487A lead consisted primarily of design verification and component testing required to establish an adequate device design for the intended use of SCS. Table 3 provides a list of tests which were successfully completed on the Model 3487A lead and are valid and applicable to the Model 3886 and 3080 SNS leads.

Table 3: Design Qualification Tests Completed on Model 3487A

Category	Test Description
Mechanical:	Visual Inspection ("cosmetic")
	Coiled Wire Coating Dimensional Adherence
	Full Lead Dimensional Adherence
	Lead Stiffness
	Static Crush Strength
	Weld Strength
	Welded Connections
	Insertion/Withdrawal
	Moisture Resistance
Electrical:	DC Resistance and Continuity
Toxicological:	Residual DMAC (USP N-Dimethyl Acetamide)
Stress/Wear:	Conductor Coil Winding
	Flex Testing of Conductor Coils
	Flex Testing (whole lead)
Environmental Durability:	Environmental Durability (thermal cycling)
	Saline Soak ("life" test)
Shelf Life/Packaging:	Mechanical Vibration
	Mechanical Shock
	Storage Temperature
	Package Drop Test (2 series)
	Vehicle Stacking
	Loose Load and Vehicle Vibration
	Outer Package Evaluation
	Package Leak Test
	Peel Strength
Sterilization:	Sterilization Suitability
Manufacturing:	Laser Welding
	Dimensional Verification
	Electrical Qualification

Biocompatability testing was performed on the Model 3487A lead that is valid and applicable to the Model 3886 and 3080 leads because the materials used to manufacture the leads are identical. Testing that demonstrated the materials to be biocompatible and suitable for human use included: Hemolysis; Tissue Culture/MEM Elution; USP Pyrogen Test; modified USP Class V [modified USP Class V testing utilized cottonseed oil and sodium chloride extraction mediums for both the mouse and rabbit models; polyethylene glycol (PEG-400) and alcohol, with sodium chloride were not used for extraction testing]; 12-week intramuscular implant; Ames Mutagenicity; and Guinea Pig Maximization Test.

Model 3886 Testing

The Model 3886 lead is identical to the Model 3487A lead except for the electrode spacing (6 mm spacing on the 3487A, 3 mm spacing on the 3886). Due to similarities in design, materials, and intended use, the Model 3886 lead is qualified by similarity to the Model 3487A lead. Electrode spacing is not an aspect of the lead that is a cause or factor in device failures or reasons for explant. To document the effect of reduced electrode spacing, lead stiffness and dimensional adherence tests were performed on the Model 3886 lead at the electrode end.

Model 3080 Testing

Due to similarities in design, materials, and intended use, the Model 3080 lead is qualified by similarity to the Model 3487A lead. In addition, due to the same electrode spacing on the Model 3080 and 3886 leads, the electrode spacing on the Model 3080 is qualified by similarity to the Model 3886 lead. The only difference between the Model 3080 and 3886 leads is the pre-attached anchor behind electrode #3.

Therefore, the following additional tests were used to qualify the Model 3080 lead: tensile testing of lead to anchor interface; torsional testing of lead to anchor interface; flex testing of lead to anchor interface; and dimensional control of anchor placement.

SNS Accessories

The SNS accessories include the Model 3625 Screener, temporary PNE screening lead, foramen needles, and cables.

The Model 3625 Screener is currently commercially available for SCS and PNS for the treatment of chronic, intractable pain of the trunk or limbs (K903690, K924522, K903690, K884898, K881491, etc.). The screener is qualified for use for SNS by testing completed for the SCS and PNS applications of the device. The screener is used in an identical manner for SCS, PNS, and SNS applications.

The PNE lead uses the same basic design and materials as another commercially available Medtronic temporary lead, the Model 6500 Temporary Cardiac Pacing Lead (K862970). Since the PNE lead uses the same materials used in the Model 6500, the biocompatibility testing completed for the Model 6500 materials applies to the PNE lead.

However, because the PNE lead is used for a different anatomical location than the Model 6500 lead, cardiac muscle vs. sacral foramen, flex testing and pull testing were performed on the PNE lead to qualify the design for implant in the sacral foramen for up to seven (7) days. The test results demonstrate that the PNE lead meets performance requirements.

Bulk accessory packages, specifically the foramen needles (Model 041828 and 041829), PNE lead (Model 041830), and Patient Cable (Model 041831), were also subjected to package qualification testing of completed, sterilized packages which were climate conditioned (temperature and humidity extremes) and then subjected to the complete series of packaging and sterilization testing.

All packages met the requirements of the test and passed the post-test visual inspection. Bioburden, pyrogens, and ethylene oxide residuals (where applicable) were all found to be within acceptable limits.

Based on the qualification testing of all three leads, 3487A, 3886, and 3080, and on commercial experience with these leads, the safety, effectiveness, and performance of the leads have been demonstrated and, in combination with the SNS clinical experience, justify the use of the Model 3886 and 3080 leads for the indication of sacral nerve stimulation for the treatment of urinary urge incontinence.

The non-clinical laboratory, in-vitro (bench) studies and relevant commercial experience demonstrate that the Medtronic Itrel II Stimulation System with the Model 3886 and 3080 SNS Leads and SNS Accessories for SNS is safe for human use. These in-vitro studies included, as appropriate: System Component Testing; Biocompatibility Tests; Shelf Life and Packaging Validation; Sterilization Validation; and Manufacturing Validation Tests.

2. In -Vivo Animal Studies

An animal study was conducted to evaluate the effects of implantation and stimulation with the Medtronic 3886 lead and the Itrel II Stimulation System, when implanted in the sacral foramen of pigs. A total of three pigs were evaluated. Each pig was implanted with two Model 3886 leads, one in the left sacral foramen (control, non-stimulated), and one in the right sacral foramen (connected to an extension and IPG, stimulated). Impedance values were measured and recorded over time to evaluate the tissue response to the stimulated lead. In addition, histology sections of the left and right sacral nerves and surrounding tissues were studied from each pig and compared to determine any effects of lead implant and stimulation on surrounding tissue.

The results of this study indicate that there were no significant adverse effects on the sacral nerve or surrounding tissue from implantation or stimulation of the sacral nerve with the Model 7424 Itrel II IPG, Model 7495 Extension, and Model 3886 (applicable also to Model 3080) lead when stimulated at recommended human stimulation parameters.

B. Clinical Studies

Sacral nerve stimulation is the application of electrical stimulation to the sacral nerves via a totally implantable system including a lead, a power source (the implantable pulse

generator or IPG), and an extension which connects the lead to the IPG. The therapy is based on the observation that electrical stimulation of sacral nerves can modulate neural reflexes that influence bladder, sphincter, and pelvic floor behavior.

The SNS treatment involves 2 stages. The first stage is a minimally invasive trial screening period PNE that allows patients to temporarily experience the effects of stimulation on their incontinence and make an informed choice about the risks and benefits of pursuing the therapy. The second stage, if the PNE is successful, is the surgical implantation of the SNS System.

1. Study Design/Methods

This study is a prospective, randomized clinical trial which was conducted with 16 investigators worldwide to evaluate the safety and effectiveness of the Medtronic SNS System for the treatment of urinary voiding dysfunction. The study included an extensive baseline evaluation, temporary trial stimulation (PNE), and randomization to either an immediate implant or delayed implant group. The delay group served as the control arm of the study and all qualified delay group patients were offered the opportunity for device implantation after 6 months follow-up.

Based on the baseline data, patients were categorized into one of three patient groups: urge incontinence, voiding difficulty, or urgency/frequency syndrome. Key voiding diary variables were established for assessing the effectiveness of the therapy for each of the patient groups. For the urge incontinent population, effectiveness was determined based on the effect of SNS therapy on:

- leaking episodes/day
- severity of leaking episodes
- absorbent pads/diapers replaced due to leaking/day.

Follow-up evaluations took place at 1, 3, 6, and 12 months post-implant and every 6 months thereafter through study completion. Delay Group patients were followed at 3 and 6 months post-randomization, then if appropriate, crossed over to the implant arm of the study. Voiding diaries were collected at baseline and all scheduled follow-ups. In addition, urodynamic testing was conducted at baseline and 6 months, and two types of quality of life assessments were administered at baseline and at each follow-up visit after 3 months.

Finally, another test, the Therapy Evaluation Test, was performed at 6 months post-implant which consisted of turning the stimulation off, collecting voiding diaries, and then turning stimulation back on. In this paired comparison, patients served as their own control and results were compared to the baseline data for each patient.

2. Clinical Study Results

Introduction

Clinical study results are analyzed on two patient populations for effectiveness and safety in the study. Effectiveness is based on results with the urge incontinent patients only (n = 155). Safety is assessed based on a larger population which included all patients enrolled in the study regardless of their presenting symptoms (PNE, n = 458; Implant, n = 157).

Effectiveness

One hundred fifty-five (155) patients were enrolled as urge incontinent patients in the clinical study. Of these, 98 patients met the criteria for randomization and entered the Implant and Delay arms of the study.

Baseline Characteristics - Urge Incontinent Patients

Table 4: Baseline Characteristics

Enrollment Statistics n=155	Urge Incontinent
Gender:	
Female	125 (80.6%)
Male	30 (19.4%)
Age at PNE (mean ± SD, range)	46.6 ± 13.0 (20.2 - 78.9)
Years of urinary symptom duration prior to study enrollment (mean ± SD, range)	9.0 ± 7.4 (0.6 - 35.4)
Medical Procedures:	914
Non-surgical	706
Surgical	208

Results from the baseline voiding diaries in this group of patients documented severe, frequent episodes of urge incontinence. At baseline, the 155 urge incontinent patients documented the following:

- 8.9 leaking episodes/day
- leak severity ranking of 1.9 ± 0.6
  - rank of 1 (mild) is defined as drops of urine
  - rank of 2 (moderate) is defined as 1-2 tablespoons per leaking episode
  - rank of 3 (heavy) is defined as soaking a pad or outer clothing with urine
- 4.8 absorbent pad/diapers replaced due to leaking episodes/day.

PNE Results (n=155)

All 155 urge incontinent patients underwent a PNE procedure, and 98 patients were subsequently qualified for randomization into the Implant and Delay groups of the study.

Of the 57 patients who did not qualify for randomization, 14 did not complete PNE voiding diaries and were exited from the study. Of the 43 who completed PNE diaries but did not qualify for randomization, reductions in urge incontinent symptoms were <50% as compared to baseline status, and therefore did not meet the inclusion criteria.

Treatment vs. Control (78 Randomized Patients)

This analysis was conducted on 78 randomized urge incontinent patients who had completed 6 months of follow-up prior to database closure, and 1 patient who was explanted prior to 6 months. (Three Implant Group patients were followed to 6 months but their voiding diaries were not received prior to database closure.) The resulting group of 76 urge incontinent patients included 34 Implant Group and 42 Delay Group patients.

The results of statistical analysis for each of the 3 key diary variables are summarized below.

Leaking Episodes/Day

For the 34 Implant Group patients, the frequency of leaking episodes was reduced significantly from 9.7 ± 6.3 at baseline to 2.6 ± 5.1 at 6 months post-implant ($p<0.0001$). At 6 months, 47% (n = 16) of the Implant Group patients were completely dry, and an additional 29% (n = 10) of the Implant Group patients documented ≥ 50% reduction in their incontinent episodes. Fifteen percent (15%, n = 5) of the Implant Group patients documented an overall reduction in their incontinent episodes, albeit not at a rate that exceeded 50%. Nine percent (9%, n = 3) of the Implant Group patients documented either no change or a slight increase in the number of leaking episodes at 6 months.

As expected, the majority of Delay Group patients retained their baseline incontinent behavior through 6 months. The average number of leaking episodes in these patients significantly increased from 9.3 at baseline to 11.3 at 6 months ($p=0.0002$). At 6 months, 74% (n = 31) of the 42 Delay Group patients documented either no change or a slight increase in the number of leaking episodes through the 6 month delay period, 21% (n = 9) of the Delay Group patients documented < 50% improvement in leaking episodes, 5% (n = 2) of the Delay Group patients documented a ≥50% reduction in leaking episodes through 6 months, and no Delay Group patients were dry at 6 months.

Statistical analysis of these data compared the distributions of improvement rankings in leaking episodes from baseline to 6 months in the two groups (Implant and Delay). Results of this analysis indicate that the distribution of improvement rankings in the Implant Group was significantly different from the distribution of improvement rankings in the Delay Group ($p<0.0001$). The results demonstrated significant reductions in leaking episodes in the Implant Group as compared to the Delay Group.

Severity of Leaking Episodes

Analysis of the diary results for severity of leaking episodes demonstrated significant reductions in the average severity of leaking episodes at 6 months in the Implant Group patients when compared to the Delay Group patients.

The average severity ranking of leaks in the Implant Group patients was significantly reduced from 2.0 ± 0.7 at baseline to 0.8 ± 0.9 at 6 months ($p<0.0001$).[1] For 60% of patients ($n = 18/30$) who reported moderate or heavy leaking episodes at baseline, such episodes were completely eliminated at 6 months post-implant. An additional 20% of the patients ($n=6/30$) documented $\geq 50\%$ reduction in the frequency of moderate or heavy leaking episodes at 6 months post-implant. At 6 months post-implant, heavy leaking episodes which soaked the patient's pad/diaper or outer garment were eliminated in 77% of patients ($n = 20/26$) reporting heavy episodes at baseline. An additional 15% of the patients ($n = 4/26$) documented $\geq 50\%$ reduction in the frequency of heavy leaking episodes at 6 months post-implant.

Statistical analysis compared the distribution of reduction in moderate and/or heavy leaking episodes from baseline to 6 months between the two groups (Implant and Delay). Analysis of results indicated that the distribution of leak severity for the Implant Group was significantly different from the Delay Group ($p<0.0001$). Therefore, the Implant Group results demonstrated significantly greater reductions in moderate and/or heavy leaks as compared to the Delay Group.

Absorbent Pads/Diapers Replaced Due to Leaking/Day

Analysis of the diary results for the number of absorbent pad/diapers replaced per day due to leaking demonstrated significant reductions in the average number of pads replaced per day at 6 months in the Implant Group patients when compared to the Delay Group patients.

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[1] A severity ranking of 1 (mild) is equivalent to drops of urine leaked; a severity ranking of 2 (moderate) is equivalent to 1-2 tablespoons of urine leaked; and a severity ranking of 3 (heavy) is equivalent to soaking the pad/diaper or outer garment.

Of the urge incontinent patients in the Implant Group, the number of absorbent pads/diapers replaced per day were significantly reduced from an average of 6.2 ± 5.0 at baseline to 1.1 ± 2.0 at 6 months ($p<0.0001$). Fifty percent (50%) of the Implant Group patients (n = 15/30) eliminated absorbent pad/diaper replacement completely, and an additional 37% of the patients (n = 11/30) reported ≥ 50% reduction in their absorbent pad/diaper replacement at 6 months post-implant. Seven percent (7%) of the Implant Group patients (n = 2/30) reported an overall reduction in pad replacement, albeit not at a rate that exceeded 50%, and the remaining 7% (n = 2/30) reported no reduction in absorbent pad/diaper replacement through 6 months post-implant.

Statistical analysis compared the change in the number of absorbent pads replaced per day due to leaking episodes from baseline to 6 months between the two groups (Implant and Delay). Results of this analysis indicate that the distribution of absorbent pad/diaper replacement in the Implant Group was significantly different from the Delay Group ($p<0.0001$). Therefore, the results demonstrated a significant reduction in number of absorbent pad/diapers replaced per day due to leaking episodes for the Implant Group as compared to the Delay Group.

Therapy Evaluation Test

To further document the effects of SNS on voiding function, 57 implanted urge incontinent patients completed the Therapy Evaluation Test where stimulation therapy was temporarily programmed OFF by the investigator after 6 months post-implant. Therapy Evaluation Test results were available from 52 out of 57 patients. The purpose of the test was to compare the effects of SNS on urge incontinent behavior in a stimulation OFF vs. stimulation ON mode.

Statistical analysis of voiding diary results collected during the Therapy Evaluation Test demonstrated a return to baseline symptoms of severe urge incontinence when stimulation therapy was turned OFF at 6 months post-implant. When stimulation was turned OFF, statistically significant increases were documented in the number of leaking episodes/day ($p<0.0001$), severity of leaking episode rankings ($p<0.0001$), and absorbent pads/diapers replaced due to leaking/day ($p<0.0001$).

These results demonstrated that urge incontinent symptoms significantly increased (worsened) after stimulation was temporarily turned OFF at 6 months post-implant. Statistical comparisons of Therapy Evaluation Test results (stimulation OFF) with baseline diary parameters (no stimulation) indicated that these increases were clinically and/or statistically comparable to the severe incontinent symptoms at baseline. Thus, discontinuation of stimulation therapy resulted in statistically and clinically significant increases in incontinent symptoms with, in essence, a return to baseline dysfunctional behavior. This indicated that reductions in urinary urge

incontinent symptoms reported with stimulation ON is attributable to SNS therapy alone. In addition, these results demonstrated the effects of SNS are reversible.

All patients resumed SNS stimulation following the Therapy Evaluation Test.

Results for All 58 Implanted Urge Incontinent Patients Followed for 6 Months Post-Implant

A total of 63 patients were implanted and followed to 6 months post-implant in the study (36 Implant Group and 27 Delay Group). Voiding diary results were obtained from 56 of the 63 patients. (Two additional patients were explanted prior to the 6 month follow-up visit and were included in all statistical analyses to conservatively evaluate the 6 month results.) Therefore, at the time of database closure, voiding diary results were evaluable from 58 of 65 implanted patients.

The results of statistical analysis for each of the 3 key diary variables are summarized below.

Leaking Episodes/Day

The group of 58 implanted urge incontinent patients demonstrated a significant reduction in the frequency of leaking episodes from an average of 10.7 ± 6.3 at baseline to 2.8 ± 4.8 at 6 months post-implant ($p<0.0001$). At 6 months, 47% ($n = 27$) of the implanted patients were completely dry, and an additional 28% ($n = 16$) demonstrated ≥50% improvement in their incontinent episodes. Sixteen percent (16%, $n = 9$) of the implanted patients demonstrated an overall reduction in their incontinent episodes, albeit not at a rate that exceeded 50%. Seven percent (7%, $n = 4$) of the implanted patients demonstrated no change or a slight increase in the number of leaking episodes at 6 months. Two patients were explanted prior to the 6 months post-implant visit.

Severity of Leaking Episodes

Analysis of the diary results from all implanted urge incontinent patients demonstrated significant reductions in the average severity ranking of leaking episodes. The average severity ranking of leaks was significantly reduced from 2.0 ± 0.6 at baseline to 0.8 ± 0.8 at 6 months post-implant ($p<0.0001$).

At baseline, the group of implanted urge incontinent patients documented an average of 7.2 ± 5.5 moderate and/or heavy leaks/day. This was significantly reduced down to 1.2 ± 2.5 moderate and/or heavy leaks at 6 months post-implant ($p<0.0001$). Of all implanted patients, 79% ($n=42/53$) demonstrated either complete elimination of moderate and/or heavy leaking episodes (62%) ($n = 33/53$) or reduced the frequency of these types of leaks by ≥50% (17%) ($n = 9/53$) at 6 months post-implant.

At baseline, the group of implanted urge incontinent patients documented an average of 3.8 ± 4.0 heavy leaks/day. This was dramatically reduced to 0.3 ± 0.1 heavy leaks at 6 months post-implant ($p<0.0001$).

Ninety percent (90%) (n=42/47) of the implanted patients who experienced heavy leaking episodes (soaking the patient's pad/diaper or outer garment) either completely eliminated these types of leaks (77%) (n=36/47) or reduced the frequency of these types of leaks by ≥ 50% (13%) (n=6/47) at 6 months post-implant.

Absorbent Pads/Diapers Replaced Due to Leaking/Day

At baseline, the group of implanted urge incontinent patients documented an average of 6.4 ± 4.6 absorbent pads/diapers replaced due to leaking/day. At 6 months post-implant, the frequency of absorbent pad/diaper replacement for these patients was significantly reduced to 1.2 ± 2.1/day ($p<0.0001$).

Fifty-seven percent (57%) (n=30/53) of the implanted patients eliminated replacement of absorbent pads/diapers completely, and an additional 26% (n= 14/53) of the patients demonstrated ≥50% reduction in the frequency of absorbent pads/diapers replaced per day at 6 months post-implant. Note: 5 patients did not replace pads/diapers due to leaking at either baseline or 6 months.

Effectiveness at 12 Months Post-Implant (n=38)

A total of 43 patients had completed 12 months of post-implant follow-up at the time of database closure. Two additional patients were permanently explanted before 6 months. As with the 6 month analysis, these 2 explanted patients were included in the 12-month statistical analysis to allow the most conservative evaluation of the chronic effectiveness data. Of the resulting group of 45 patients, 7 were not evaluable leaving 38 patients with evaluable 12-month data for evaluation (24 Implant Group and 14 Delay Group).

The results of statistical analysis for each of the 3 key diary variables are summarized below.

Leaking Episodes/Day

The frequency of leaking episodes was significantly reduced from an average of 11.1 ± 6.4 at baseline to 2.5 ± 3.7 at 12 months post-implant ($p<0.0001$). At 12 months, 45% (n=17) of the implanted patients were completely dry, and an additional 34% (n=13) demonstrated ≥50% improvement in their incontinent episodes.

Severity of Leaking Episodes/Day

Data analysis of the diary results for the 38 implanted urge incontinent patients demonstrated significant reductions in the average severity ranking of leaking episodes when comparing baseline with 12-month results. The average severity ranking of leaks in implanted patients was significantly reduced from 2.0 ± 0.7 at baseline to 0.8 ± 0.9 at 12 months ($p<0.0001$).

The group of 33 implanted urge incontinent patients who documented moderate and/or heavy leaking at baseline documented an average of 7.5 ± 5.8 moderate and/or heavy leaks/day. This was dramatically reduced to 1.3 ± 2.9 moderate and/or heavy leaks/day at 12 months post-implant ($p<0.0001$). Seventy-nine percent (79%) of the 33 implanted patients demonstrated either complete elimination of moderate and/or heavy leaking episodes (64%, n=21) or reduced the frequency of these types of leaks by ≥50% (15%, n=5) at 12 months post-implant.

Of the 38 implanted patients, 30 experienced heavy leaking at baseline or at 12 months. These 30 patients documented an average of 4.3 ± 4.4 heavy leaks/day at baseline. This was significantly reduced to 0.8 ± 2.2 heavy leaks at 12 months post-implant ($p<0.0001$). Of those 30 patients, 80% either completely eliminated these types of leaks (70%, n=21) or reduced the frequency of these types of leaks by ≥ 50% (10%, n=3) at 12 months.

Absorbent Pads/Diapers Replaced due to Leaking/Day

Of the 38 implanted patients evaluated at 12 months, 33 patients reported replacement of pads/diapers due to leaking at baseline. Five (5) patients reported they did not use pads/diapers for the management of leaking at baseline or thereafter.

At baseline, the group of 33 patients documented an average of 6.4 ± 4.5 absorbent pads/diapers replaced due to leaking/day. At 12 months, the frequency of absorbent pad/diaper replacement was dramatically reduced to 1.5 ± 2.7/day ($p<0.0001$). Of these patients, 55% (n=18) eliminated replacement of absorbent pad/diapers completely, and an additional 21% (n=7) demonstrated ≥ 50% reduction in the frequency of absorbent pads/diapers replaced due to leaking at 12 months post-implant.

Improvements were also noted through 12 months post-implant in the remaining voiding diary parameters that include: increases in the average volume voided/void ($p=0.032$), reduction in the number of voids/day ($p=0.007$), increases in the maximum voided volume ($p=0.007$), and significant increases in the percent of the time the patient felt empty post-void ($p<0.0001$).

Effectiveness at 18 Months Post-Implant (n=21)

A total of 23 patients have completed 18 months of post-implant follow-up at the time of database closure. Follow-up voiding diaries were not received for 2 of the patients at the time of database closure. Therefore, chronic effectiveness of SNS therapy was demonstrated by comparing voiding diary results for 21 of the 23 urge incontinent patients. The 21 patients included 14 Implant Group patients and 7 Delay Group patients. Two Delay Group patients were explanted before 18 months but they were included in the statistical analysis to allow the most conservative evaluation of the chronic effectiveness data.

Of the 21 implanted patients followed for 18 months post-implant, 52% (n=11) remained completely dry, and an additional 24% (n=5) demonstrated ≥50% improvement with respect to the number of leaking episodes. Eighty-one percent (81%) of the implanted patients experienced either complete elimination of moderate and/or heavy leaking episodes (62%, n =13) or documented ≥50% reduction in these types of leaks (19%, n=4). Eighty-four percent (84%, n=16) of patients had completely eliminated heavy leaking at 18 months.

The results of the statistical analysis of voiding diary data in the group of 21 implanted urge incontinent patients further demonstrated chronic effectiveness of SNS for the management of urinary urge incontinence through 18 months post-implant.

Secondary Outcome: Urodynamic Evaluation

The findings from the urodynamic testing performed on the group of 78 randomized urge incontinent study patients confirm that SNS does not compromise urologic function through 6 months.

Secondary Outcome: Quality of Life

Improvement in quality of life, as documented with the SF-36 Health Status Questionnaire, was demonstrated through 6 months in patients implanted with the SNS System. The individual SF-36 concept scores were summarized into the Standardized Mental Component Scale and Standardized Physical Component Scale for analysis.

Evaluation of 6 month results of the Standardized Mental Component Scale revealed no significant differences between the Implant Group and the Delay Group. However, statistically significant differences were noted in the Standardized Physical Component Scale at 6 months in favor of the Implant Group patients. These data suggest that, on average, Implant Group patients experienced more positive changes in physical health status at 6 months as compared to the Delay Group patients.

The Beck Depression Inventory was administered at baseline and 6 months as an additional quality of life tool. No clinically significant differences were documented between the two groups (Implant and Delay).

The value of these data are limited because a validated, domain specific (for UI) Quality of Life questionnaire was not used in the clinical study. These data were not given much weight in the effectiveness evaluation for this device.

Safety

Safety of SNS for urge incontinence is based on pooling of safety data from the entire study population of 458 patients for temporary SNS stimulation (PNE procedure) and all 157 implanted patients for chronic SNS stimulation.

Table 5: PNE Safety Experience

Patients enrolled	458
Total PNE procedures conducted	664
PNE procedures that resulted in an event	96
PNE procedure adverse event rate	14.5%
# of PNE device- & therapy-related events	118
PNE event resolution	98.3% (116/118)

Repeat PNE procedures were performed for a variety of reasons including inadequate response to stimulation, incomplete voiding diaries, and inadequate improvement in symptoms at a particular sacral foramen site. Refer back to Table 1 for a listing of all PNE adverse events experienced, # of patients affected, # of events, and event resolution.

Table 6: Implant Safety Experience

Patients implanted	157
# of patients that experienced an event	73
Patient adverse event rate	46.5%
# of post-implant device & therapy-related events	125
Post-implant event resolution	87.2% (109/125)
# of post-implant events that required surgical intervention	75
# of patients affected	51
Patient surgical revision rate	32.5%
# of revision surgeries	79
Range of surgical revisions needed	1-5
Surgical event resolution	92.0% (69/75)

Refer back to Table 2 for listing of all post-implant adverse events experienced, # of patients affected, # of events, and event resolution.

See Table 7 for a listing of all post-implant device- and therapy-related adverse events experienced, # of patients affected, # of events, time to event onset, # of events that required either surgical intervention, non-surgical intervention, or no

intervention. Note: 30 of the 36 events that required non-surgical intervention (i.e., IPG reprogramming or medical intervention) and all events that required no intervention were resolved as of database closure.

IX. CONCLUSIONS DRAWN FROM THE STUDIES

The laboratory, animal, and clinical data provide reasonable assurance of the safety and effectiveness of the Medtronic® Interstim® Sacral Nerve Stimulation (SNS)™ System, when used as indicated in accordance with the directions for use.

X. PANEL RECOMMENDATION

The Gastroenterology and Urology Devices Advisory Panel met to discuss the application on August 6, 1997. The Panel recommended that the application be approved subject to submission to, and approval by, the Center for Devices and Radiological Health (CDRH) of revised physician labeling, revised patient labeling, a formal physician training program, an agreement to conduct a post-marketing study, and a summary of the effectiveness results for the voiding difficulty and frequency/urgency indications. The Panel recommended that the labeling be modified to state that the use of the Sacral Nerve Stimulation (SNS)™ System must be prescribed and administered under the direct supervision of a qualified and trained physician, after appropriate urologic evaluation of the patient. The Panel also agreed with the proposal to conduct a post-approval study to evaluate the long-term effects of treatment on 152 patients, followed for 5 years post-treatment. This study is designed to record the adverse events among these subjects, as well as the long-term effect of sacral nerve stimulation on voiding dysfunction.

XI. CDRH Decision

CDRH agreed with the Panel's recommendations that the PMA be approved subject to conditions, and concurred with each of the conditions recommended by the Panel.

FDA issued a status letter, dated August 8, 1997, to Medtronic, Inc., and another letter dated, August 21, 1997, advising that the PMA was approvable subject to the conditions listed above as recommended by the Panel and required by FDA. In an amendment received by FDA on September 26, 1997, Medtronic, Inc., submitted the required information. CDRH determined that the applicant's response adequately addressed the Panel's and FDA's concerns. To fulfill the conditions of approval, the sponsor will conduct a study to address FDA's and Panel's concerns.

Following FDA inspections, the manufacturing facilities were determined to be in compliance with the Good Manufacturing Practices (GMP) regulation.

CDRH issued an approval order for the application on September 29, 1997.

Table 7: Post-Implant Adverse Events by Required Intervention

			# of Surgical Interventions Required					Nonsurgical Intervention	No Intervention
Event Type	**Events†**	**Time to Event Onset (median, range in months)**	**Permanent Explant (n=6)**	**Temporary Explantation Reimplantation* (n=4)**	**Device Exchange (n=15)**	**Reposition of Lead/ Extension (n=16)**	**Reposition of IPG (n=23)**	**(n=35)**	**(n=14)**
Device-Related (n=3)	• Lead fracture (3)	**	0	0	2 (1 pending)	0	0	0	0
Therapy-Related (n=122)	• Pain at implant site (back, buttocks, legs) (33)	2.7 (0.0 - 22.3)	3	2	3	5 (1 pending)	0	10	10
	• Aggravation of baseline symptoms (1)	3.8 (3.8 - 3.8)	0	0	0	0	0	1	0
	• Pain at IPG site (27)	3.1 (0.0 - 17.5)	0	0	0	0	22 (3 pending)	2	0
	• Change in bowel function (8)	3.5 (0.0 - 12.5)	1	0	1	3	0	3	0
	• Sensation of transient electric 'shock' (10)	4.9 (1.9 - 13.7)	0	0	0	1	0	5	4
	• Lead migration (14)	5.4 (0.5 - 17.6)	0	0	10	3	0	1	0
	• Infection/Skin irritation (11)	0.6 (0.0 - 13.8)	2	4	0	0	0	7	0
	• Allergic reaction (1)	1.5 (1.5 - 1.5)	0	2	0	0	0	0	0
	• Technical problem (11)	5.8 (0.0 -25.8)	0	0	5 (1 pending)	4	0	1	0
	• Other (6) • Vaginal cramping (1) • Inability to have orgasms (1) • Numbness (2) • Menstrual bleeding (1) • Trauma to IPG (1)	5.9 (0.9 - 29.7)	0	0	0	0	0	6	0
Totals		3.4 (0.0 - 29.7)	6	8* (4 events)	23	17	25	36	14

† Some patients experienced more than 1 adverse event

* Each event required 2 surgeries (1 for explantation, 1 for reimplantation)

** Lead fractured occurred initially at 8.1 weeks post-implant, 4 weeks after replacement, and 10 weeks after replacement

Medtronic

Physician and Hospital Staff Manual

Implantable Pulse Generator Model 7424

Contents

⚠ **Caution:** Federal law (USA) restricts this device to sale, distribution, and use by, or on the order of, a physician.

System Description

The Medtronic Model 7424 Quadripolar ITREL II Implantable Pulse Generator (IPG) (see Figure 1) is a multiprogrammable device designed for use in Sacral Nerve Stimulation (SNS) when connected to an extension and lead. These components comprise the implantable portion of the Medtronic® Interstim® Sacral Nerve Stimulation (SNS) System. The operation of the IPG is supported by a Console Programmer and a Control Magnet (see Figure 2).

The IPG operates on a sealed battery and electronic circuitry to provide controlled electrical pulse stimulation through the implanted extension and lead to the target site, the sacral nerves, for the treatment of urinary urge incontinence.

For a complete list of model numbers and components compatible with the ITREL II IPG, see the ITREL II "Sacral Nerve Stimulation System Components Sheet" packaged with this manual in the IPG shelf box.

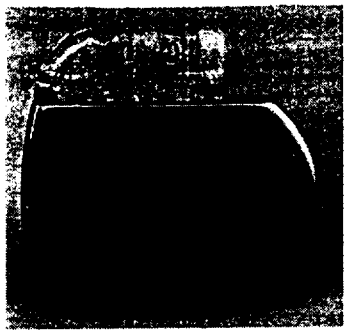


Figure 1. The Implantable Pulse Generator (IPG)

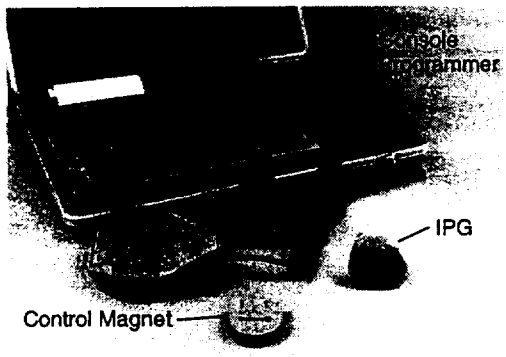


Figure 2. Itrel II IPG and control equipment

Contents of Package

The Model 7424 Quadripolar ITREL II IPG packaging contains:

- One Itrel II IPG
- Two hex wrenches
- Product literature

Indications

The Medtronic® Interstim® Sacral Nerve Stimulation System is indicated for the treatment of urinary urge incontinence in patients who have failed or could not tolerate more conservative treatments.

⚠ **Caution:** All other SNS uses of the ITREL II IPG remain investigational.

Contraindications

Patients are contraindicated for implantation of the SNS System if:

- They have not demonstrated an appropriate response to test stimulation, or
- They are unable to operate the IPG.

Precautions

Physician Training

Physicians—Physicians should be experienced in the diagnosis and treatment of lower urinary tract symptoms and should be trained on the use of the Medtronic® Interstim® SNS System.

Implanting Physicians—Implanting physicians should be trained on the implant and use of the SNS system.

Storage and Sterilization

Storage Temperature—Store the IPG between 125° F (50° C) and 0° F (-18° C). Temperatures outside this range can damage components.

Resterilization Considerations—Refer to the Resterilization section on pages 16-17 for further information.

System and Therapy

Component Failures—IPG systems may unexpectedly cease to function. A system may fail at any time due to random failure of system components or of the battery (prior to depletion). These events, which can include electrical shorts or opens and insulation breaches, cannot be predicted.

Components—The use of non-Medtronic components with this system may result in damage to Medtronic components, loss of stimulation, or patient injury.

Patient Management—To ensure maximum benefits from the IPG system, long-term, post-surgical management of patients is recommended.

Implantation/Explantation

IPG Implant Location—Place the ITREL II IPG away from bony structures (i.e., ribs, pelvic bone), and with the etched identification side facing away from muscle tissue to minimize pain at the IPG site, and to minimize the possibility of skeletal muscle stimulation, which may be perceived as twitching or burning by patients.

Handling Components—The implanted components of this system were designed to perform in the extremely hostile environment of the human body. However, these components may be damaged by excessive traction or sharp instruments. Any component showing signs of damage should not be used. Also, if the IPG is dropped more than 12 inches (30 cm) onto a hard surface, it should not be used.

Connections—Wipe off body fluids on the lead contacts or connector before connecting, as contamination of connections can affect stimulation.

Excess Extension—Do not place any excess extension on top of the IPG's etched side. Wrap excess extension wire around the perimeter of the IPG. This avoids any increase in the subcutaneous pocket depth, helps minimize potential damage during IPG replacement surgery, and helps minimize potential kinking of the extension.

Component Disposal—If explanting an SNS System component, please remember the following guidelines:

- Do not incinerate the IPG; an explosion can result if an IPG is subjected to incineration or cremation temperatures.
- Return all explanted components to Medtronic for analysis and safe disposal.

Medical Environment

Cardiac Pacemakers—Under certain conditions, IPG systems may adversely affect the operation of cardiac demand pacemakers or therapies.

Cardioverter Defibrillators—Under certain conditions, IPG systems may affect the therapies programmed into cardioverter defibrillators.

Diathermy—The effects of diathermy on patients with an implanted IPG system are unknown. It is not recommended to use diathermy directly over an implanted IPG or lead, since internal components may be damaged.

Electrocautery—Electrocautery can cause temporary suppression of IPG output and/or reprogramming of the IPG. If use of electrocautery is necessary, the current path (ground plate) should be kept as far away from the IPG and lead as possible.

External Defibrillators—Safety for use of external defibrillatory discharges on patients with SNS Systems has not been

established. Use of defibrillatory changes in the vicinity of an Itrel II IPG can cause permanent damage to or reprogramming of the IPG. Such reprogramming could cause the stimulation mode and all programmable parameters to reset to the nominal or preset state with the amplitude at zero and the output OFF.

If external defibrillation is necessary, follow these precautions to minimize current flowing through the pulse generator and lead system:

- Position defibrillation paddles as far from the pulse generator as possible.
- Position defibrillation paddles perpendicular to the implanted pulse generator-lead system.
- Use the lowest clinically appropriate energy output (watt seconds).
- Confirm SNS System function following any external defibrillation.

High Output Ultrasonics—Use of high output ultrasonic devices, such as an electrohydraulic lithotriptor, is not recommended for patients with an implanted SNS System. While there is no danger to the patient, exposure to high output ultrasonic frequencies may result in damage to the IPG circuitry. If lithotripsy must be used, do not focus the beam near the IPG.

High Radiation Sources—High radiation sources, such as cobalt 60 or gamma radiation, should not be directed at the IPG. If a patient recquires radiation therapy in the vicinity of the

IPG, place lead shielding over the device to prevent radiation damage.

Magnetic Resonance Imaging—Patients with an implanted device should not be exposed to the electromagnetic fields produced by magnetic resonance imaging (MRI). Use of MRI may potentially result in dislodgment, heating, or induced voltages in the pulse generator and/or lead. An induced voltage through the pulse generator or lead may cause uncomfortable (jolting or shocking) levels of stimulation.

Clinicians should carefully weigh the decision to use MRI in patients with an implanted SNS System, and note the following:

- Managed and radio-frequency (RF) fields produced by MRI may change the pulse generator settings, activate the device, and injure the patient.
- Patients treated with MRI should be closely monitored and programmed parameters verified upon cessation of MRI.

Ultrasonic Scanning—Ultrasonic scanning equipment may cause mechanical damage to an implanted IPG, or implanted lead, if used directly over the IPG, or lead, implant site.

Home or Occupational Environment

Case Damage—If the IPG case is ruptured or pierced after implant due to outside forces, severe burns may result from exposure to battery chemicals.

Equipment Operation—During stimulation, patients should not operate potentially dangerous equipment such as power tools or automobiles.

Home Appliances—Home appliances that are in good working order and properly grounded do not usually produce enough EMI to interfere with IPG operation.

Occupational Environments—Commercial electrical equipment (arc welders, induction furnaces, resistance welders), communication equipment (microwave transmitters, linear power amplifiers, high-power amateur transmitters), and high voltage power lines may generate enough EMI to interfere with IPG operation if approached too closely.

Theft Detectors and Screening Devices—Theft detectors found in libraries, department stores, etc., and airport/security screening devices may cause the stimulation power source of an implantable IPG system to switch ON or OFF. It is possible that sensitive patients, or those with low stimulation thresholds, may experience a momentary increase in perceived stimulation at they pass through these devices. These higher levels of stimulation have been described as "uncomfortable, jolting or shocking."

Patient Magnet—The magnet provided to the patient for device activation and deactivation may damage televisions, computer disks, credit cards, and other items affected by strong magnetic fields.

Adverse Events

The Medtronic Sacral Nerve Stimulation (SNS) System was implanted in 157 patients. These 157 patients were followed for 0-40 months with a mean follow-up time of 14.7 months.

Observed Adverse Events

The following therapy related events were observed in the clinical trial with event rates indicated in parentheses:

- Pain at the implant site (21%)
- Pain at the IPG site (17%)
- Lead migration (9%)
- Infection/Skin irritation (7%)
- Technical problem (7%)
- Increased electrical sensation (6%)
- Adverse change in bowel function (5%)
- Numbness (1.3%)

Adverse events reported in one patient each included: aggravation of baseline symptoms, vaginal cramping, inability to have orgasms, menstrual bleeding, trauma to IPG, and allergic reaction.

There were three device related events in the clinical study. All occurred in one patient and were due to overtightening of the setscrew at the lead/extension connection.

Surgical Revision—Thirty-three percent of implanted patients required surgical intervention to resolve an adverse event. The leading events requiring revision surgery were: pain at the IPG site, pain at the implant site, and lead migration.

Six implanted SNS patients had their systems explanted. Three were explanted due to pain at the implant site, one due to adverse change in bowel function, and two due to infection.

Potential Adverse Events

Potential adverse events which may occur, but were not reported in the clinical study include:

- Nerve injury
- Seroma at the IPG site
- Undesirable stimulation
- Undesirable sensations (permanent)

Clinical Studies

The Medtronic® Interstim® Sacral Nerve Stimulation (SNS) System was evaluated in a multicenter trial at study centers in the United States, Canada, and Europe for the indication of urinary urge incontinence. This device continues under clinical investigation for the indications of voiding difficulty (retention) and urinary urgency/frequency.

Urge Incontinence Study Results

Patients Studied—One hundred fifty-five urge incontinent patients were enrolled in the study (30 males). Mean age was 47 years (range 20 to 79 years). These 155 patients underwent at least one and, in some cases, up to five Peripheral Nerve Evaluation (PNE) procedures. Of these 155 screened patients, 98 had a successful PNE result (experienced at least a 50% improvement in leaking variables). Of these 98 patients who were eligible for implantation, 86 (7 males) were implanted with the SNS System. Fifty-eight patients (6 males) have data at 6 months follow-up and 38 patients (4 males) have data at 12 months follow-up.

Design—The clinical study was a multicenter prospective randomized trial. All of the enrolled patients completed a peripheral nerve evaluation, or PNE procedure. The PNE results were used to determine patient eligibility for randomization.

Patients were randomized into either an immediate implantation of the Medtronic SNS System (treatment arm) or six-month delay from implant (control arm). After completing the six-month delay arm, control group patients could elect to cross over to the treatment arm of the study. All implanted patients were followed at six-month intervals until completion of the study.

Methods—The effect of SNS on urinary urge incontinence was evaluated using a voiding diary as the primary outcome measure.

During the PNE evaluation, voiding diary results completed at baseline and during PNE were compared. If the results showed a minimum 50% improvement in urge incontinence symptoms, the patient was eligible for randomization.

Voiding diaries diaries were completed at baseline and at six months for control group patients and at baseline, one, three, six, and twelve months post implant (and at six-month intervals thereafter) for the treatment group patients. Concomitant medical treatment, such as medications, was allowed in both the control and treatment arms of the study.

Efficacy Results—Voiding diary results showed statistically significant reductions in urge incontinence symptoms in patients implanted with the Medtronic® Interstim® SNS System as compared to baseline. Table 1 shows the percentage of patients who experienced a successful result (≥ 50% improvement in baseline symptoms) as recorded in voiding diaries at 6 and 12 months follow-up post implant. These results were obtained in patients refractory to conservative treatments for urinary urge incontinence.

Table 1. Six and twelve month post implant results (% of patients with successful result)

	6 Months Post Implant (n=58 patients)		12 Months Post Implant (n=38 patients)	
Leakage Amount	**Eliminated**	**≥50% Improved**	**Eliminated**	**≥50% Improved**
Any Leak	47% (dry)	75%	45% (dry)	79%
Heavy Leaking	77%	90%	70%	80%

As Table 1 indicates, 75% of implanted patients had ≥ 50% reduction in frequency of leaking episodes, 47% of implanted patients were dry at 6 months.

Of patients who experienced heavy leaking episodes (soak pad or clothing) at baseline, 90% reduced the average severity of leaking to less than two tablespoons, and 77% of patients eliminated heavy leaking episodes at 6 months. These results were sustained at 12 months.

Urodynamic results indicated that sacral nerve stimulation does not adversely affect a patient's ability to void.

Individualization of Treatment

Best results are achieved when the patient is fully informed about the therapy risks and benefits, surgical procedure, follow-up requirements, and self-care responsibilities. Sacral Nerve Stimulation is appropriate for patients who meet the following criteria:

- Patient have urinary urge incontinence
- Patients should have failed more conservative treatment
- Patients should be suitable candidates for surgery.

Use in Specific Populations

The safety and effectiveness of this therapy has not been established for the following:

- Bilateral stimulation
- Patients with neurological disease origins, such as multiple sclerosis or diabetes
- Pregnancy and delivery
- Pediatric use (patients under the age of 16)

Medtronic

Physician and Hospital Staff Manual

Lead Kit
Model 3886
Model 3080

Contents

⚠ **Caution:** Federal law (USA) restricts this device to sale, distribution, and use by, or on the order of, a physician.

System Description

The Medtronic® Model 3886 and 3080 Sacral Nerve Stimulation (SNS) Leads are designed for electrical stimulation of the sacral nerves, when connected to an extension and Implantable Pulse Generator (IPG). Both leads are indicated for the treatment of urinary urge incontinence. The Model 3080 lead features a pre-attached anchor proximal to electrode #3. This feature is the only difference between the two leads. Figure 1 shows the Model 3886 Lead.

Electrical signals are transmitted from the Medtronic® Itrel® II Model 7424 Implantable Pulse Generator (IPG) to the sacral nerve via the Medtronic® Model 3095 Extension and either the Model 3886 or 3080 lead. These components comprise the implantable portion of the Medtronic® Interstim® Sacral Nerve Stimulation (SNS) System.

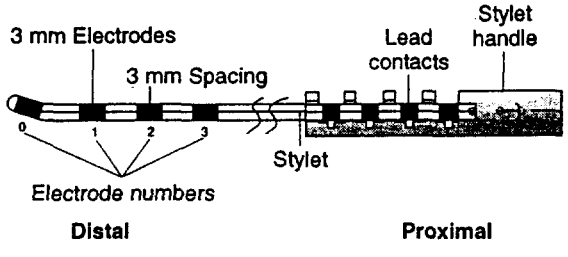


Figure 1. Model 3886 Lead

Contents of Package

The Model 3886/3080 Lead Kit consists of the following items:

- One Model 3886/3080 Lead with inserted stylet
- One pin connector
- One twist-lock screening cable
- One stainless-steel PERCUPASS® II tunneling tool and tunneling tip
- PTFE (Polytetrafluoroethylene) tubes
- One hex wrench
- One boot and anchors

The contents of the inner package are **STERILE.**

Indications

The Medtronic® Interstim® Sacral Nerve Stimulation System is indicated for the treatment of urinary urge incontinence in patients who have failed or could not tolerate more conservative treatments.

⚠ **Caution:** All other uses of the SNS leads ~~for SNS~~ remain investigational.

Contraindications

Patients are contraindicated for implant of the SNS System if:

- They have not demonstrated an appropriate response to test stimulation; or
- They are unable to operate the IPG.

Precautions

Physician Training

Physicians — Physicians should be experienced in the diagnosis and treatment of lower urinary tract symptoms and should be trained on the use of the Interstim® SNS System.

Implanting Physicians — Implanting physicians should be trained on the implant and use of the SNS System.

Storage and Sterilization

Storage Temperature — Store the Model 3886/3080 Lead between -40° F (-40° C) and 167° F (75° C). Temperatures outside this range can damage components.

Resterilization Considerations — Refer to the Resterilization section on pages 15-16 for further information.

System and Therapy

Postural Changes — Postural changes or abrupt movements by patients may cause an increase or decrease in the perceived level of stimulation. Higher levels of stimulation have been described as "uncomfortable, jolting or shocking" by some patients.

Component Failures — The SNS System may unexpectedly cease to function due to battery depletion or other causes. These events, which can include electrical short or open circuits and insulation breaches, cannot be predicted.

Components — The use of non-Medtronic components with this system may result in damage to Medtronic components, loss of stimulation, or patient injury.

Patient Management — To ensure maximum benefits from the IPG system, long-term, post-surgical management of patients is recommended.

Implantation / Explantation

Implant Considerations — Do not implant a component of the system when:

- The storage package has been pierced or altered; or if the component shows signs of damage; or
- The Use Before date has expired, because this can adversely affect storage package sterility.

Handling Components — Handle the implanted components of this system with extreme care. These components may be damaged by excessive traction or sharp instruments.

- Do not bend, kink, or stretch the lead body whether or not the stylet is in place. Do not bend or kink the stylet.
- Do not tie a suture directly to the lead body. Use an anchor supplied in the lead package.
- When handling the lead with forceps, use only rubber-tipped forceps.
- Be extremely careful when using sharp instruments around the lead to avoid nicking or damaging the lead body insulation.

IPG Implant Location — Place the Itrel® II Model 7424 IPG with the etched identification side facing outward, away from the muscle layer of the body. This helps to minimize the possibility of skeletal muscle stimulation that may be perceived as twitching or burning.

55

Connections — Wipe off body fluids on the lead contacts or connector before connecting, as contamination of connections can affect stimulation.

Component Disposal — If explanting an SNS System component, please remember the following guidelines:

- Do not incinerate the IPG; an explosion can result if an IPG is subjected to incineration or cremation temperatures.
- Return all explanted components to Medtronic for analysis and safe disposal.

Medical Environment

Cardiac Pacemakers — Under certain conditions, IPG systems may adversely affect the operation of cardiac demand pacemakers or therapies.

Cardioverter Defibrillators — Under certain conditions, IPG systems may affect the therapies programmed into cardioverter defibrillators.

Diathermy — The effects of diathermy on patients with an implanted IPG system are unknown. It is not recommended to use diathermy directly over an implanted IPG or lead, since internal components may be damaged.

Electrocautery — Electrocautery can cause temporary suppression of IPG output and/or reprogramming of the IPG. If use of electrocautery is necessary, the current path (ground plate) should be kept as far away from the IPG and lead as possible.

External Defibrillators — Safety for use of external defibrillatory discharges on patients with SNS Systems has not been established. Use of defibrillatory discharges in the vicinity of an ITREL II IPG can cause permanent damage to or reprogramming of the IPG. Such reprogramming could cause the stimulation mode and all programmable parameters to reset to the nominal or preset state with the amplitude at zero and the output OFF.

If external defibrillation is necessary, follow these precautions to minimize current flowing through the pulse generator and lead system:

- Position defibrillation paddles as far from the pulse generator as possible.
- Position defibrillation paddles perpendicular to the implanted pulse generator-lead system.
- Use the lowest clinically appropriate energy output (watt seconds).
- Confirm SNS System function following any external defibrillation.

High Output Ultrasonics — Use of high output ultrasonic devices, such as an electrohydraulic lithotriptor, is not recommended for patients with an implanted SNS System. While there is no danger to the patient, exposure to high output ultrasonic frequencies may result in damage to the IPG circuitry. If lithotripsy must be used, do not focus the beam near the IPG.

High Radiation Sources — High radiation sources, such as cobalt 60 or gamma radiation, should not be directed at the IPG. If a patient requires radiation therapy in the vicinity of the IPG, place lead shielding over the device to prevent radiation damage.

Magnetic Resonance Imaging — Patients with an implanted device should not be exposed to the electromagnetic fields produced by magnetic resonance imaging (MRI). Use of MRI may potentially result in dislodgment, heating, or induced voltages in the pulse generator and/or lead. An induced voltage through the pulse generator or lead may cause uncomfortable (jolting or shocking) levels of stimulation.

Clinicians should carefully weigh the decision to use MRI in patients with an implanted SNS System, and note the following:

- Magnetic and radio-frequency (RF) fields produced by MRI may change the pulse generator settings, activate the device, and injure the patient.
- Patients treated with MRI should be closely monitored and programmed parameters verified upon cessation of MRI.

Ultrasound Scanning — Ultrasonic scanning equipment may cause mechanical damage to an implanted IPG or implanted lead if used directly over the IPG or lead implant site.

Effects on Other Medical Devices — The SNS System may affect the operation of other implanted devices, such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems and inappropriate device responses. If the SNS patient requires concurrent implantable pacemaker and/or defibrillator therapy, careful programming of each system may be necessary to optimize the patient's benefit from each device.

Most routine diagnostic procedures, such as fluoroscopy and x-rays, are not expected to affect system operation. However, because of higher energy levels, sources such as transmitting antennas may interfere with the system.

Home or Occupational Environment

Equipment Operation — During stimulation, patients should not operate potentially dangerous equipment such as power tools or automobiles.

Home Appliances — Home appliances that are in good working order and properly grounded do not usually produce enough EMI to interfere with IPG operation.

Occupational Environments — Commercial electrical equipment (arc welders, induction furnaces, resistance welders), communication equipment (microwave transmitters, linear power amplifiers, high-power amateur transmitters), and high voltage power lines may generate enough EMI to interfere with IPG operation if approached too closely.

Theft Detectors and Screening Devices — Theft detectors found in public libraries, department stores, etc., and airport/security screening devices may cause the stimulation power source of an implantable SNS System to switch ON or OFF. It is also possible that sensitive patients, or those with low stimulation thresholds, may experience a momentary increase in their perceived stimulation. For other indications, higher levels of stimulation have been described as "uncomfortable, jolting or shocking" by some patients as they pass through these devices.

Patient Magnet — The magnet provided to the patient for device activation and deactivation may damage televisions, computer disks, credit cards, and other items affected by strong magnetic fields.

Adverse Events

The Medtronic Sacral Nerve Stimulation (SNS) System was implanted in 157 patients. These 157 patients were followed for 0-40 months with a mean follow-up time of 14.7 months.

Observed Adverse Events

The following therapy related events were observed in the clinical trial (with event rates indicated in parentheses):

- Pain at the implant site (21%)
- Pain at the IPG site (17%)
- Lead migration (9%)
- Infection/Skin irritation (7%)
- Technical problem (7%)
- Increased electrical sensation (6%)
- Adverse change in bowel function (5%)
- Numbness (1.3%)

Adverse events reported in one patient each included: aggravation of baseline symptoms, vaginal cramping, inability to have orgasms, menstrual bleeding, trauma to IPG, and allergic reaction.

There were three device related events in the clinical study. All occurred in one patient and were due to overtightening of the setscrew at the lead/extension connection.

Surgical Revision — Thirty-three percent of implanted patients required surgical intervention to resolve an adverse event. The leading events requiring revision surgery were: pain at the IPG site, pain at the implant site, and lead migration.

Six implanted SNS patients had their systems explanted. Three were explanted due to pain at the implant site, one due to adverse change in bowel function, and two due to infection.

Potential Adverse Events

Adverse events which may potentially occur, but were not reported in the clinical study include:

- Nerve injury
- Seroma at the IPG site
- Undesirable stimulation
- Undesirable sensations (permanent)

Clinical Studies

The Medtronic® Interstim® Sacral Nerve Stimulation (SNS) System was evaluated in a multicenter trial at study centers in the United States, Canada, and Europe for the indication of urinary urge incontinence. This device continues under clinical investigation for the indications of voiding difficulty and voiding urgency/frequency.

Urge Incontinence Study Results

Patients Studied — One hundred fifty-five urge incontinent patients were enrolled in the study (30 males). Mean age was 47 years (range 20 to 79 years). These 155 patients underwent at least one, and, in some cases, up to five Peripheral Nerve Evaluation (PNE) procedures. Of these 155 screened patients, 98 had a successful PNE result (experienced at least a 50% improvement in leaking variables). Of these 98 patients who were eligible for implantation, 86 (7 males) were implanted with the SNS System. Fifty-eight patients (6 males) have data at 6 months follow-up and 38 patients (4 males) have data at 12 months follow-up.

Design — The clinical study was a multicenter prospective randomized trial. All of the enrolled patients completed a peripheral nerve evaluation, or PNE procedure. The PNE results were used to determine patient eligibility for randomization.

Patients were randomized into either an immediate implantation of the Medtronic SNS System (treatment arm) or six-month delay from implant (control arm). After completing the six-month delay arm, control group patients could elect to crossover to the treatment arm of the study. All implanted patients were followed at six-month intervals until completion of the study.

Methods — The effect of SNS on urinary urge incontinence was evaluated using a voiding diary as the primary outcome measure.

During the PNE evaluation, voiding diary results completed at baseline and during PNE were compared. If the results showed a minimum of 50% improvement in urge incontinence symptoms, the patient was eligible for randomization.

Voiding diaries were completed at baseline and at six months for control group patients and at baseline, one, three, six, and twelve months post implant (and at six-month intervals thereafter) for the treatment group patients. Concomitant medical treatment, such as medications, was allowed in both the control and treatment arms of the study.

Efficacy Results — Voiding diary results showed statistically significant reductions in urge incontinence symptoms in patients implanted with the Medtronic® Interstim® SNS System as compared to baseline. Table 1 shows the percentage of patients who experienced a successful result (≥ 50% improvement in baseline symptoms) as recorded in voiding diaries at six and twelve months follow-up post implant. These results were obtained in patients refractory to conservative treatments for urinary urge incontinence.

Table 1. Six and twelve month post implant results (% of patients with successful result)

	Six Months Post Implant (n=58 patients)		Twelve Months Post Implant (n=38 patients)	
Leakage Amount	Eliminated	≥50% Improved	Eliminated	≥50% Improved
Any Leak	47% (dry)	75%	45% (dry)	79%
Heavy Leaking	77%	90%	70%	80%

As Table 1 indicates, 75% of implanted patients had ≥ 50% reduction in frequency of leaking episodes, 47% of implanted patients were dry at 6 months.

Of patients who experienced heavy leaking episodes (soak pad or clothing) at baseline, 90% reduced the average severity of leaking to less than two tablespoons, and 77% of patients eliminated heavy leaking episodes at 6 months. These results were sustained at 12 months.

Urodynamic results from the uroflow tests indicated that SNS does not adversely affect a patient's ability to void.

Individualization of Treatment

Best results are achieved when the patient is fully informed about the therapy risks and benefits, surgical procedure, follow-up requirements, and self-care responsibilities. Sacral Nerve Stimulation is appropriate for patients who meet the following criteria:

- Patients have urinary urge incontinence
- Patients should have failed more conservative treatment
- Patients should be suitable candidates for surgery.

Use in Specific Populations

The safety and effectiveness of this therapy has not been established for the following:

- Bilateral stimulation
- Patients with neurological disease origins, such as multiple sclerosis or diabetes
- Pregnancy or delivery
- Pediatric use (patients under the age of 16)

Medtronic

Patient Manual

Implantable Pulse Generator
Model 7424

Q4

Contents

⚠ **Caution:** Federal law (USA) restricts this device to sale, distribution, and use by, or on the order of, a physician.

Introduction

This manual contains important information about your Medtronic® Interstim® Sacral Nerve Stimulation (SNS) System. **Please read this entire manual before using your SNS System.** The manual will help you understand and use your SNS System and the devices that control it.

This manual covers the following topics:

- The parts of your SNS System
- How your SNS System is implanted
- How you can control your SNS System
- Living with your SNS System
- Answers to common patient questions
- A glossary of terms

If you have any questions after reading this manual, or if you have any problems with your SNS System, talk to your doctor. He or she knows your medical history and can give you more detailed information.

Sacral Nerve Stimulation (SNS)

Sacral Nerve Stimulation is a treatment to manage symptoms of urinary urge incontinence. An SNS System sends electric pulses to your sacral nerves. Your sacral nerves are located at the base of your spine in your lower back. Sacral nerves control your voiding function.

SNS Treatment for Your Urinary Urge Incontinence

Your doctor prescribed your Interstim® SNS System to manage your symptoms of urinary urge incontinence.

The Interstim® SNS System is not an appropriate treatment for your condition if:

- You do not receive satisfactory symptom relief during your test stimulation, or,
- You are unable to properly operate the system.

Your Interstim® SNS System

Your SNS System consists of the following parts:

- **ITREL® II Implantable Pulse Generator (IPG)**
  Your IPG produces the electric pulse that stimulates your sacral nerve. See Figure 1 for a picture of an IPG.
- **Lead**
  Your lead is a wire that carries the electric pulse from your IPG and extension to your sacral nerve.
- **Extension**
  Your extension is a wire that carries the electric pulse from your IPG to your lead.

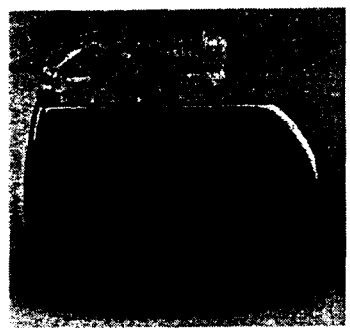


Figure 1. The Implantable Pulse Generator (IPG)

Your IPG

The ITREL® II IPG supplies the energy for nerve stimulation. The IPG contains a special battery and electronics to control stimulation. As with all batteries, the IPG battery will run down. Eventually the IPG will need to be replaced. Surgery is required to remove the old IPG and replace it with the new IPG. Ask your doctor to estimate the battery life for you.

Devices Used to Control Your IPG

The following two devices can control your IPG (Figure 2 shows these devices):

- **The Console Programmer**
  Your doctor uses this device to adjust your IPG settings. The Console Programmer is kept at your doctor's office or the hospital.
- **The Control Magnet**
  You use this special magnet to turn your IPG ON and OFF. You take the Control Magnet home with you. The Control Magnet can also switch the IPG amplitude (stimulation strength) from normal to low if your doctor has programmed these settings into your IPG.

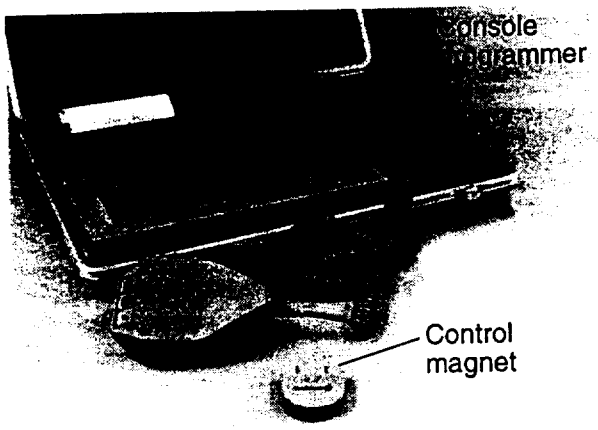


Figure 2. Devices used to control your IPG

You should have received your Control Magnet before leaving the hospital. If you do not have your Control Magnet, do one of the following:

- Contact your doctor.
- Call or write Medtronic. Use the address or telephone number listed on the back cover of this manual.

How Your Interstim® SNS System Is Implanted

Your doctor will usually implant your Interstim® SNS System during one operation. You will be under anesthesia. Doctors usually implant the SNS System in three parts, as follows:

Lead Implant

The doctor does the following to implant the lead:

1. Makes an incision in your lower back.
2. Places one end of the lead next to a sacral nerve.
3. Places the main part of the lead under your skin, from your lower back to your side, above your hip bone.
4. Makes an incision in your side to connect the lead to the extension.

Extension Implant

The doctor places the extension under your skin from your hip bone to your lower abdomen. The extension connects to the lead at your side and to the IPG in your abdomen.

IPG Implant

The doctor does the following to implant the IPG:

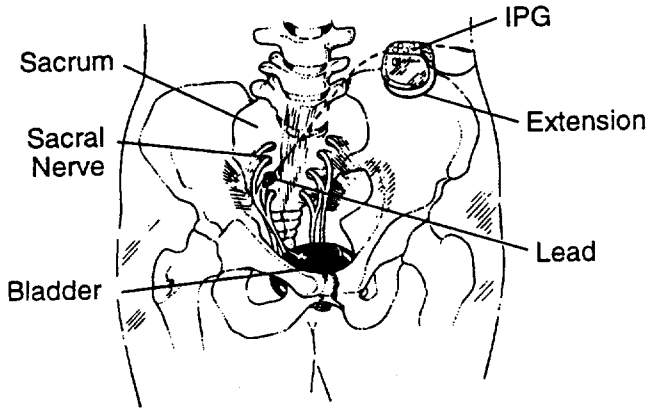
1. Makes a small incision (a pocket) in your lower abdomen. The doctor will try to place the IPG in an area you feel is most comfortable and looks the best.
2. Connects the IPG to the extension.
3. Places the IPG inside the pocket.

See Figure 3 on page 8 for a diagram of the likely location of implants in your body.

You will have a total of three incisions to implant the SNS System:

- One incision in your lower back where the lead is implanted.
- One incision at your side where the lead connects to the extension.
- One incision in your abdomen where the extension connects to the implanted IPG.

After implanting the Interstim® SNS System, your doctor programs the IPG. He or she uses the Console Programmer to program the best stimulation settings for you. Your doctor will need your input to decide what settings are right for you.



Front view

Figure 3. Your implanted SNS System

Using Your Control Magnet

You can control your implanted IPG by using your Medtronic® Model 7452 Control Magnet. There are times when you will need to do this, such as when you are driving a car, or other motor vehicles, or using possibly harmful equipment, such as power tools.

Your Control Magnet can switch your IPG output ON or OFF. When you switch the IPG ON using your Control Magnet, the stimulation resumes at the level at which your IPG was set before your it was switched OFF.

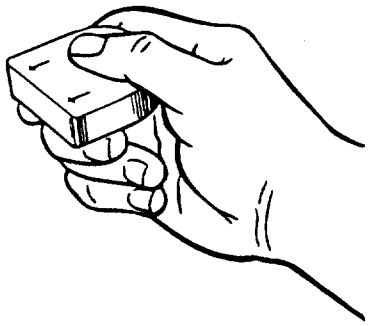
If your doctor has programmed a special setting, your Control Magnet can also switch the IPG amplitude (stimulation strength) between normal (for active times) and low (for less active times).

Your doctor should tell you about any special settings programmed into your IPG.

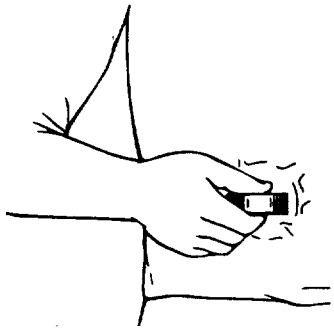
Note: Your implant site and the location of your IPG may be different from the examples shown in the following instructions. Have your doctor show you how to center the Control Magnet over your IPG.

To Switch the IPG ON or OFF

1. Grasp the Control Magnet with the flat end away from you.



2. Center the Control Magnet over your IPG for one to two seconds.

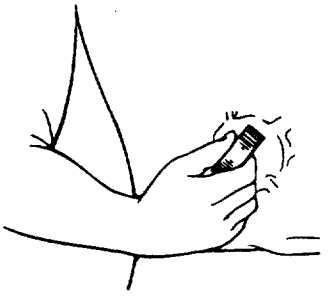


You can find out if your IPG is ON by reading the section Checking to See if Your IPG is ON on page 28.

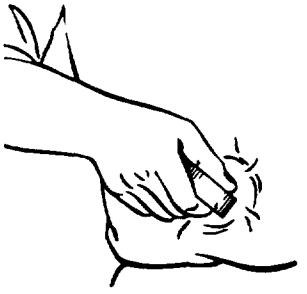
3. Remove the Control Magnet. This action switches the IPG ON or OFF.

If the Control Magnet Fails to Switch the IPG ON or OFF

1. Repeat Steps 2 and 3 from the previous section (To Switch the IPG ON or OFF), holding the Control Magnet against the IPG in a slightly different position.
2. Try a "1 o'clock" or "4 o'clock" position.



1 o'clock position



4 o'clock position

To Switch Between Normal and Low Amplitudes

Note: You can switch between normal and low amplitudes only if your doctor has programmed a low amplitude value for you. If your doctor has not, you are going to switch to a low amplitude value of zero, which does not provide any stimulation. To recover, you need to apply the Control Magnet for six seconds to return to normal amplitude.

1. Grasp the Control Magnet with the flat end away from you.
2. Center the Control Magnet over your IPG for six or more seconds.
3. Remove the Control Magnet. This action switches the amplitude between normal and low.

If the Control Magnet Fails to Switch the Amplitude Between Normal and Low

1. Repeat Steps 2 and 3 from the previous section (To Switch Between Normal and Low Amplitudes), holding the Control Magnet against the IPG in a slightly different position.
2. Try a "1 o'clock" or "4 o'clock" position.

If your doctor has programmed the IPG with the SoftStart™/Stop feature (see page 39 in the glossary), the Control Magnet automatically starts this feature when you turn the IPG ON. You should allow a few seconds for the SoftStart™/Stop feature to increase the stimulation to the point where you can feel it.

Carrying Your Control Magnet

⚠ **Caution:** Do not place the Control Magnet in a pocket or purse on the same side as your implanted IPG. This Control Magnet position can turn your IPG ON and OFF.

Be careful when carrying the Control Magnet. Medtronic suggests that you carry the Control Magnet in the pocket opposite your IPG.

Caring for Your Control Magnet

Be careful not to drop your Control Magnet, because it may break on a hard surface. A broken Control Magnet will have reduced strength. If you have broken or lost your Control Magnet, contact your doctor or Medtronic to replace it.

In an emergency, if you break or lose your Control Magnet, any large magnet (such as a horseshoe magnet) can be used temporarily. Contact your doctor or Medtronic, as soon as possible, to get a new Control Magnet.

Avoiding Damage to Personal Items

Do not store the Control Magnet within two inches of a watch or clock. The Control Magnet will stop them.

The magnetic field may cause damage to the following items or erase information from them. Avoid placing the Control Magnet within six inches of the following items:

- Items with a magnetic strip such as bank or credit cards
- Magnetic media such as video or audio cassette tapes or computer disks
- Home electronic items such as a personal computer, VCR, television, or camera.

Living With Your Interstim® SNS System

Medications

Your doctor will decide if you need medications. He or she may prescribe medications in addition to your Interstim® SNS System. It is important that you follow your doctor's schedule for taking the medicine.

Activities and Exercise

On the advice of your doctor, and as you begin to feel better, you should be able to gradually resume your normal lifestyle. Such activities may include:

- Traveling
- Bathing, showering, and possibly swimming
- Sexual activity
- Returning to your job or work
- Resuming hobbies or recreation such as walking, hiking, gardening, bowling, golfing, fishing, or hunting.

It is important that you follow your doctor's advice. Ask your doctor about any particularly strenuous activities, such as lifting heavy objects.

Changes in Stimulation

Changes in stimulation may happen for many reasons including:

- Changes in body position
- Changes due to other devices
- Changes due to the SNS system
- Changes due to a low IPG battery.

Each of these is discussed as follows:

- **Stimulation changes due to body position**

The lead of your Interstim® SNS System is implanted near a sacral nerve in your lower back. When you move your body, the position of the lead relative to the nerve may change slightly. If this happens, you may sense an increase or decrease in your stimulation. You may also feel that the IPG is turning ON or OFF. You may even feel a burst (a jolt or shock) of stimulation when you move. When this happens, your IPG amplitude is not changing. You are still

receiving the correct amount of energy. The closeness of the lead to the sacral nerve makes it feel like more, or less, stimulation.

Jolting or shocking could cause you to lose control of your car, other motor vehicles, or equipment. This loss of control could hurt you or others. To help ensure your safety, turn your IPG OFF when driving a car, or other motor vehicles, or using other possibly harmful equipment, such as power tools. Remember to turn the IPG to ON again when you are done.

Warning

⚠ Do not use possibly harmful equipment (that is, cars, power tools, etc.) when your ITREL II IPG is ON.

A change in your body position may cause you to feel a sudden increase in stimulation (a jolt or shock). This can cause you to lose control of your car, other motor vehicles, or any equipment you are using.

To prevent this, you must turn OFF your IPG when you use a car, or other motor vehicles, or any other possibly harmful equipment, such as power tools.

■ **Stimulation changes due to other devices**

Your IPG has built-in features to protect it from interference produced by other electrical devices. Most of the electrical items you encounter in a normal day will not harm your IPG. Special circuits inside the IPG protect it from extreme electrical stress.

However, your Interstim® SNS System may interact with certain **strong** magnetic fields. This can increase stimulation to your sacral nerve. Also, in addition to your Control Magnet, some strong magnetic fields can also switch your IPG output from ON to OFF or OFF to ON.

Most household appliances, office machines, and personal radios **do not** produce magnetic fields strong enough to cause these problems. If you maintain a normal distance (about an arm's length), most devices will not affect your IPG.

The following devices should **not** interfere with your SNS System:

- Microwave ovens
- Televisions, AM/FM radios, stereos, cellular phones
- Tabletop appliances, such as toasters, blenders, electric can openers, food processors
- Hand-held items, such as hair dryers, shavers
- Appliances including washers, dryers, electric stoves
- Electric blankets and heating pads
- Vacuum cleaners, electric brooms
- Personal computers, electric typewriters, copiers, and FAX machines

However, if you place devices with small permanent magnets (some stereo speakers, radios, and telephones have them) **within inches** of your IPG, the device could turn the IPG ON or OFF.

The following devices have enough magnetic energy to increase stimulation to your sacral nerve and/or to turn your IPG ON or OFF if you are near them:

- Theft detectors
- Airport/security screening devices
- Large stereo speakers with magnets
- Magnetic Resonance Imaging (MRI) equipment
- Manufacturing and heavy industrial equipment
- Electric arc welding equipment
- Electric induction heaters used in industry to bend plastic
- Electric steel furnaces
- Power lines
- Electric substations and power generators

Warning

⚠ The following devices may briefly cause an increase in your stimulation level as you pass through them:

- Theft detectors with gateways through which you walk. These are often in places like public libraries and department stores.
- Airport/security screening systems.

Use care when approaching these devices. If you feel unwanted stimulation (a jolt or shock) as you approach a device, you may want to show your ITREL II IPG identification card (see the section Your ITREL® IPG Identification Card on page 26) to the appropriate people and ask them to let you bypass the device.

If you suspect an electrical device or magnet is interfering with your IPG:

1. Move away from the electrical device or magnet or, if possible, turn the electrical device off.
2. Using your Control Magnet, if necessary, switch your IPG back to the desired ON or OFF state.

When switched ON with the Control Magnet, your IPG will resume stimulation at the level at which it was set before it was switched OFF.

Carry your ITREL II IPG identification card at all times. Show your identification card to the appropriate people if you wish to bypass security devices or theft detectors.

- **Stimulation changes due to the SNS System**

When your IPG is switched ON, you may notice a brief tingling feeling. If you think your IPG is ON but your symptoms do not improve, contact your doctor and/or check to see if your IPG is ON. (See page 28 for how to check to see if your IPG is ON.) The IPG may simply require readjustment by your doctor to a different treatment setting. However, there may be a problem with the extension, lead, or IPG. Your doctor should be able to determine the cause of the problem and correct it.

- **Stimulation changes due to a low IPG battery**

Your doctor may be able to predict the life of your IPG battery. As with all batteries, it will run down. As the battery runs down, the stimulation may not be as effective in managing your symptoms. These changes are normal and are no cause for alarm. When you feel this change in stimulation, tell your doctor. Make an appointment with your doctor to have your IPG battery checked if you and your doctor have not already done so.

Medical Appointments

Follow-up Appointments for Your SNS System

It is important that you go to all your follow-up appointments. Your doctor may send you to a special clinic for brief routine checkups. These visits will help to determine if your SNS System is providing the desired treatment.

Please inform your doctor if your address changes. Also, if you change doctors, be sure to have your medical history sent to the new doctor.

Other Medical and Dental Procedures

Always tell any medical personnel that you have an implanted SNS System. Tell your dentist you have an implanted SNS System, so he or she can take proper precautions.

Under certain conditions, IPG systems may affect cardiac demand pacemakers or therapies.

With proper precautions, most medical procedures are unlikely to interfere with your SNS System. However, some of the following procedures may affect your SNS implant:

- **X-rays**
  Diagnostic x-rays do not cause a problem. However, some x-ray procedures that require enclosure of the area where your IPG is implanted may require adjustment of the x-ray equipment.
- **Ultrasound**
  Therapeutic ultrasound should not be used anywhere near the SNS implant sites.

- **Diathermy treatments**
  Diathermy treatments (sometimes used for muscle relaxation) may affect or damage parts of your SNS System.
- **Magnetic Resonance Imaging (MRI)**
  Magnetic Resonance Imaging (MRI) is not recommended. Use of MRI on components of an IPG system may result in movement or heating of the IPG and/or the lead. It may cause "uncomfortable, jolting or shocking" levels of stimulation.
- **Heart defibrillators**
  Electrical shocks from defibrillators may damage the IPG.

Your ITREL® II IPG Identification Card

After your implant, your doctor will give you a temporary identification card. This card has important information about your implant. A few weeks after your implant, Medtronic will send you a permanent, plastic-coated identification card to replace the temporary one.

You should carry this identification card at all times. In the event of an accident, the card will tell anyone taking care of you that you have an implanted medical device. The card supplies basic information about your IPG and identifies your doctor.

Your card is especially important if you travel by air because airport security devices may interfere with your IPG. Also, the security devices may detect the metal in your IPG. Show your identification card to the appropriate airline people to bypass the security device.

If you lose your identification card at any time, contact:

Medtronic® Interstim®
Patient Registration Service
800 53rd Ave. NE
Minneapolis, MN 55421-1200
(612) 514-5000
(800) 328-0810
(24-hour consultation service)

Checking To See If Your IPG Is ON

You can check to see if your IPG is ON by using the following test. Check with your doctor first if you don't know your stimulation amplitude.

1. Turn on a small AM transistor radio to the lowest setting on the tuning dial, about 540 kHz (but not on a station).
2. Adjust the volume to its loudest setting.
3. Hold the radio over the implanted lead at the implant site. If the IPG is ON, and the IPG amplitude is 1.5 volts or more, the radio should emit a strong ticking or clicking sound over the radio static. If your doctor has programmed your IPG to cycle, the sound will cycle ON and OFF.
4. If you don't hear any ticking or clicking from the radio, your IPG may be OFF. Use your Control Magnet to try turning your IPG ON.
5. If you still do not hear ticking or clicking from the radio, contact your doctor.

Replacement Surgery

Because the IPG battery is sealed inside the IPG case, it cannot be replaced separately. Therefore, when it is time to have your battery replaced, your doctor will remove the entire IPG and replace it with a new IPG. During replacement surgery, your doctor will also check your implanted extension and lead. If the extension and lead are working properly, your doctor will simply connect the new IPG. If the extension and lead are not working properly, your doctor may need to replace them as well.

Clinical Studies

In a clinical study, 86 urge incontinent patients were implanted with the Medtronic® Interstim® SNS System. Results were measured six, twelve, and eighteen months after implant.

Of the 58 implanted patients who were evaluated at six months, 47% of patients eliminated all leakage of urine. Approximately three out of every four patients reduced the number of leaks by at least 50%. In addition, three out of four patients who had heavy leaking eliminated these types of leaks.

Data at twelve and eighteen months showed similar results.

Adverse Events

In a clinical study, a total of 157 patients were implanted with the Medtronic® Interstim® SNS System.

The most common complications reported by patients are listed below. The event rates are shown in parentheses:

- Pain in the back, buttocks, or legs (21%)
- Pain at the IPG site (17%)
- Movement of the lead away from the nerve (9%)
- Infection/Skin irritation (7%)
- Technical problem (7%)
- Temporary sensation of electric shock (6%)
- Adverse change in bowel function (5%)
- Numbness in the leg (1.3%)

Adverse events reported in one patient each included: worsening of baseline symptoms, vaginal

cramping, inability to have orgasms, heavy menstrual bleeding, trauma to IPG site, lead conductor fracture, and allergic reaction.

Adverse events may be resolved with surgery, medical therapy (e.g., medications), or no treatment. Thirty-three percent of patients had additional surgery to resolve an adverse event.

Potential Adverse Events

No patient in the clinical study reported any of the events listed below. However, these events could possibly occur.

- Nerve injury
- Swelling at the IPG site
- Undesirable stimulation
- Undesirable sensations (permanent)

Common Questions

- What is SNS?

  SNS (Sacral Nerve Stimulation) is a medical treatment for symptoms of urinary urge incontinence. An SNS System sends electric pulses to your sacral nerves. The sacral nerves control your bladder, bowel, and pelvic organs.

- **What is an IPG?**

  An IPG, or Implantable Pulse Generator, is the device that creates electrical pulses to send to the sacral nerves. In Sacral Nerve Stimulation, an IPG is part of a system that treats urinary urge incontinence. The IPG contains a special battery and electronics to create the pulses.

- **Will the Interstim® SNS System cure my incontinence?**

  Sacral Nerve Stimulation is not a cure for your urinary urge incontinence. However, SNS has been proven effective for managing symptoms of urinary urge incontinence. The degree to which symptoms are relieved varies from patient to patient.

- **What does stimulation feel like?**

  The feeling of stimulation varies from patient to patient. You may feel a brief tingling when stimulation is first turned ON. You may feel some level of stimulation whenever your IPG is ON. Some patients describe higher levels of stimulation as "uncomfortable, jolting or shocking."

- **Will I be able to increase or decrease the strength of stimulation?**

  If your doctor has programmed the normal and low amplitude settings, you may select them with your Control Magnet. Otherwise, your doctor or a clinician uses the Console Programmer to change the strength of stimulation.

- **Will I be able to turn the IPG ON and OFF?**

  Yes. You can use the Control Magnet provided with your system to switch your IPG ON and OFF.

- **Should I void with the IPG ON or OFF?**

  Ask your doctor for specific instructions.

- **What if I have trouble turning my IPG ON?**

  First, wait at least eight seconds after your last try to turn ON your IPG. When you try again, be sure you hold your Control Magnet directly over the implanted IPG. If you still cannot turn ON your IPG, call your doctor or Medtronic at the telephone number listed on the back cover.

- **How long will the IPG battery last?**

  The battery life of the IPG depends on how long you use it each day, and how strong the stimulation must be to manage your symptoms. Once your doctor determines your IPG settings, he or she can give you a better estimate of your IPG's battery life.

- **Can the battery be recharged?**

  No.

- **How is the battery replaced?**

  To replace the battery, your doctor must replace the entire IPG. This requires surgery.

- **Will the Interstim® SNS System limit my activities?**

  Generally, no. However, you should consult your doctor about performing any particularly strenuous activities.

- **How large is the IPG?**

  The IPG is oval, about 0.5 inches thick, 2.5 inches long, and 2 inches wide. The IPG weighs 49 grams.

- **Will the IPG show through my clothes?**

  Your doctor will place the IPG in a place that is most comfortable and looks the best. However, depending on your body build, the IPG may be noticeable as a small bulge under the skin.

- **What happens if the IPG stops working?**

  The stimulation will stop and your symptoms may return. If you can't determine the possible cause and correct the situation, contact your doctor.

- **What should I do if the stimulation changes or becomes uncomfortable?**

  Turn the IPG OFF with your Control Magnet and contact your doctor.

- **What does it mean if I can only feel the stimulation sometimes?**

  Your doctor may have programmed your stimulator output to cycle. This means that the IPG turns OFF and ON at regular intervals. As long as the system controls your symptoms, there is no cause for concern.

- **Is it normal for the stimulation feeling to increase or decrease when I change position?**

  Generally, the feeling of stimulation will be constant. However, abrupt movements or changes in posture could make it feel like it is increasing or decreasing. Some patients describe higher levels of stimulation as "uncomfortable, jolting or shocking." As long as the system controls your symptoms, this is no cause for concern. If your symptoms worsen or the feeling of stimulation stops entirely, contact your doctor.

- **Does the IPG make any noise?**

  No.

- **Will a microwave oven interfere with the IPG?**

  No.

- **Will there be any problems when I pass through theft detectors and screening devices?**

  Theft detectors found in places like public libraries and stores, and airport/security screening systems may cause the IPG to switch ON or OFF. Some patients may feel a momentary increase in their stimulation. Some patients describe higher levels of stimulation as "uncomfortable, jolting or shocking."

  Also, the security devices may detect the metal in your IPG.

- **Can stimulation be used during pregnancy?**

  The safety of Sacral Nerve Stimulation for use during pregnancy or delivery has not been established. If you learn, or suspect, that you are pregnant, turn your IPG OFF and call your doctor.

- **How often should my doctor check the IPG?**

  Generally, the IPG should be checked about once every six months. However, your doctor may want to see you more or less often, depending on your situation.

- **Whom should I contact in case I have a problem?**

  Your first call should be to your doctor. If you are unable to contact your doctor, please contact Medtronic at the telephone number listed on the back cover of this manual.

Glossary

amplitude. A measure of the electrical intensity or strength of a stimulating pulse.

interference. Anything that reduces the effectiveness of the IPG or a programming transmission.

lead. An implantable thin wire with one or more electrodes at its tip. The lead delivers electrical stimulation to the sacral nerve.

sacral nerves. Nerves located near the base of the spinal cord in your lower back. Sacral nerves are involved with bladder, bowel, and pelvic control.

Sacral Nerve Stimulation (SNS). A therapy that sends small electrical pulses to your sacral nerves to manage symptoms of urinary urge incontinence.

SoftStart™/Stop stimulation. A feature that allows stimulation to begin and end gradually. The SoftStart feature prevents a sudden burst of stimulation when the IPG turns ON. SoftStart does this by gradually increasing the amplitude of the stimulating pulses. The Stop feature also causes a gradual decrease of the amplitude of stimulation down to zero when the IPG output is turned OFF, or when the OFF cycle begins.

urge incontinence. The involuntary loss of urine associated with an abrupt, strong desire to void (urgency).

Medtronic

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800 53rd Avenue NE
Minneapolis, MN 55421-1200
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(24-hour consultation service)

September 1997
UC9702690EN 197231-001

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Medtronic

Patient Manual

Peripheral Nerve Evaluation Kit Model 3065U

Contents

⚠ **Caution:** Federal law (USA) restricts this device to sale, distribution, and use by, or on the order of, a physician.

Introduction

Peripheral Nerve Evaluation (PNE) is a method your doctor can use to assess your urinary urge incontinence. The results of the PNE can help your doctor decide if Sacral Nerve Stimulation (SNS) treatment will improve your symptoms.

This Booklet

This booklet describes the steps of a PNE. It also outlines the things you need to do to help your doctor with the process. A glossary is included to define some technical terms. We hope this information answers most of your questions. Please discuss any other questions or concerns with your doctor.

During Your PNE

Parts of the PNE may cause you some soreness or pain. You will be given a local anesthetic to lessen any soreness or pain.

You may need to restrict some activities during the PNE. Your doctor will discuss this with you.

Complications may occur, such as movement of the lead away from the nerve, infection, or skin irritation at the implant site. Your doctor will discuss possible complications with you.

The Results of Your PNE

If your PNE is successful, your doctor may recommend a permanently implanted SNS System to help you manage your symptoms. If your PNE is not successful, your doctor will discuss other treatments with you.

An Overview of Your Peripheral Nerve Evaluation

Your Peripheral Nerve Evaluation has several steps:

1. **Finding a sacral nerve to stimulate**

   You will be given a shot of a local anesthetic to numb your lower back. Then your doctor locates your sacral nerves by inserting a test needle into your lower back. He or she tests the nerves with the test needle. This helps your doctor choose the best nerve to receive electric stimulation.

   See pages 4-6 for more details about this process.

2. **Placing the screening lead**

   Your doctor replaces the test needle with a thin wire called a screening lead. This lead will carry electric pulses to your sacral nerve.

   See pages 6-7 for more details about this process.

3. **Connecting and using the external test stimulator**

   Your doctor connects the lead to an external device called a test stimulator. The test stimulator provides electric pulses to stimulate your nerve. Your doctor will show you how to use the test stimulator.

   See pages 7-8 for more details about the test stimulator.

4. **What you need to do during your PNE**

   You will return home. During this time you may be asked to record your urinary symptoms in a voiding diary. If so, you will be given a voiding diary.

   See pages 8-11 for details on what you need to do, and avoid doing, while at home.

5. **After your peripheral nerve evaluation**

   Within one week you will return to your doctor. He or she will remove the lead and discuss the results with you.

   See pages 12-13 for details on what happens after your PNE.

Details of the Steps of Your Peripheral Nerve Evaluation

1. Finding a sacral nerve to stimulate

Your sacral nerves are located in your lower back. Sacral nerves control your bladder, bowel, and pelvic organs. Sacral nerves are protected by a bony plate called the sacrum. Your doctor finds the sacral nerves through holes in the bone called the foramina. Figure 1 shows the location of sacral nerves in your body.

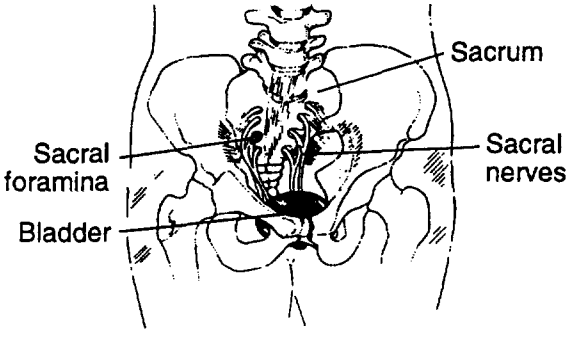

Figure 1. Sacral nerves location

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a) Your doctor finds the best sacral nerve to stimulate by inserting a special test needle into your lower back. To lessen any pain, he or she will first inject you with a local anesthetic to numb the area. You may feel a mild burning during the injection. This feeling should quickly disappear. Once your skin and surrounding tissues are numb, your doctor will insert a special test needle. Figure 2 shows a test needle being inserted.

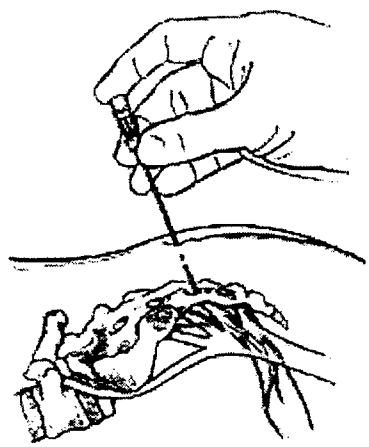


Figure 2. Finding a sacral nerve to stimulate

b) Your doctor stimulates your nerves by sending a small electric pulse through the test needle. He or she looks for certain nerve responses to see if the needle is stimulating the correct nerve.

Your doctor may ask you to describe what you feel. The strength of the stimulation should be such that your pelvic muscles achieve a strong, but comfortable contraction. You will most likely feel a pulling sensation in the rectum. Men will usually feel the stimulation in the scrotum. Women will usually have a similar feeling in the vagina. Occasionally, patients feel additional sensations, such as tingling, in the penis or clitoris, the urethra, or the bladder. Also, stimulating the sacral nerves may cause movement of the toes and sometimes the entire leg.

2. Placing the screening lead

a) Once your doctor finds the best sacral nerve to stimulate, he or she places a thin wire, called a screening lead, through the test needle.

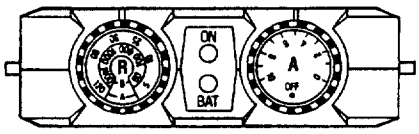
b) Next, your doctor carefully removes the needle, leaving the screening lead near the nerve. He or she secures the lead to your skin with a bandage. (Part of the wire will be outside of your body but covered by the bandage.)

Your doctor may also take an X-ray to record the lead position.

3. **Connecting and using the external test stimulator**

   Your doctor will connect the test stimulator to the temporary screening lead and a ground pad. The test stimulator is a device about the size of a small portable radio. You can wear it on your belt or carry it in your pocket. The test stimulator sends out electrical pulses that stimulate your sacral nerve.

   The test stimulator has an ON/OFF control knob marked A for amplitude. This control knob is like the volume control on a radio—you adjust it to the desired intensity or amplitude of stimulation. The other control knob, marked R for rate, is set by your doctor. **Do not change this R setting.** Your doctor will show you how to use the test stimulator. Figure 3 shows the external test stimulator.



Top view

Figure 3. The external test stimulator

The ground pad is a small black patch that adheres to your skin. Your doctor will place the ground pad on your lower back, where it is most comfortable for you. If the ground pad comes off your skin, turn the test stimulator off. Apply a few drops of water to the gel surface of the ground pad and reapply. Turn the test stimulator back on.

4. What you need to do during your PNE

After your doctor has placed the screening lead and connected the lead to the external test stimulator, you will return home. Please do the following during your PNE:

- **Keep the test stimulator ON**

You should keep the test stimulator ON at all times unless otherwise instructed by your doctor. The only time that you should turn the test stimulator OFF is when driving a car, or other motor vehicles, or using possibly harmful equipment, such as power tools.

See pages 10-11 for more information about possibly harmful equipment.

- **Adjust the test stimulator as needed**

You should set the level of stimulation with the A (amplitude) control knob so that you are comfortable, but aware of the stimulation. The stimulation may feel different with changes in your body

position. Your doctor will help you determine what setting is right for you. If you do not feel the stimulation in your pelvic muscles at any A (amplitude) setting, please contact your doctor.

- **Do not change the test stimulator rate or R control knob**

Your doctor will set the rate or R control knob on the test stimulator. Please do not change this control knob from the setting your doctor has chosen. **Note the setting your doctor has chosen.** Check regularly to see that this setting has not been accidentally changed. **If necessary, move the control knob back to the correct setting.**

- **Follow your doctor's instructions**

Your doctor will give you specific instructions that you should follow during your trial screening period. It is important to follow these instructions. This may include completing a voiding diary to record your urinary symptoms during stimulation. Your doctor will provide you with these voiding diaries and show you how to complete them. If you have any problems or questions during your trial screening, contact your doctor.

- **Resume your daily routine**

After the temporary screening lead is inserted and you return home, resume your daily routine as much as possible. Strenuous activity, such as exercise or heavy physical labor, may cause the temporary screening lead to move away from the sacral nerve. You may need to restrict these types of activities.

If you have any questions about the activities you may or may not do, please ask your doctor.

- **Turn the test stimulator OFF before using possibly harmful equipment**

Warning

⚠ Do not use possibly harmful equipment (that is, cars, power tools, etc.) when your test stimulator is ON.

Should you feel a sudden increase in stimulation (a jolt or shock), this may cause you to lose control of your car or any equipment you are using.

You must turn your test stimulator OFF when you use a car, or other motor vehicles, or any other possibly harmful equipment.

The PNE temporary screening lead is implanted near a sacral nerve in your lower back. When you move your body, the position of the lead relative to the nerve may change slightly. If this happens, you may feel an increase or decrease in your stimulation. You may also feel the test stimulator turning ON or OFF. You may even feel a burst (a jolt or shock) of stimulation when you move abruptly.

Jolting or shocking could cause you to lose control of possibly harmful equipment such as cars, or other motor vehicles, or power tools. This loss of control could hurt you or others. To help ensure your safety, turn your test stimulator OFF when driving a car, or other motor vehicles, or using other possibly harmful equipment.

Turn the test stimulator ON again when you are done driving or using possibly harmful equipment.

- **Do not bathe or shower**

The temporary screening lead is held in place only by a bandage. Because of this, and the increased chance of infection, please do not bathe or shower. You may take sponge baths if you are careful not to get the area around the screening lead wet.

5. **After Your Peripheral Nerve Evaluation**

   a) The PNE temporary screening lead is intended for implant for up to seven days. Your doctor will schedule a return visit to remove the lead from your lower back.

   b) Your doctor will also discuss the results of temporary sacral nerve stimulation on your urge incontinence. Based on the results of your PNE, your doctor may recommend an implantable Sacral Nerve Stimulation (SNS) System to improve your urge incontinence. If your doctor decides an SNS System would help you, your doctor will discuss the risks and benefits of SNS therapy with you.

Some lifestyle factors that you should consider in your decision about SNS treatment include:

- Possible restriction or reduction of your activity level.
- Sensations of jolting or shocking may occur due to movement or when passing through theft detectors or security devices.
- The SNS should be turned off while you use a car, or other motor vehicles, or other possibly harmful equipment, to ensure your safety.

Some health-related factors that you should consider include:

- Safety of using SNS during pregnancy has not been established.
- Under certain conditions the Sacral Nerve Stimulation System may affect heart pacemakers and defibrillators.
- SNS therapy patients should not be exposed to the electromagnetic fields produced by Magnetic Resonance Imaging (MRI).

If you decide that SNS therapy is not right for you, your doctor can discuss other treatments available for your urinary urge incontinence.

Clinical Studies

In a clinical study, a total of 664 PNE procedures were completed in 458 patients. Approximately 63% of urge incontinent patients had a successful result from their PNE.

The most common or clinically significant complications reported by patients during the PNE procedure are listed below. The percentage of PNE procedures where complications occurred are shown in parentheses:

- Lead migration (9.9%)
- Temporary pain (2.6%)
- Lead/screener cable disconnection (2.6%)
- Adverse change in bowel and/or voiding function (0.6%)
- Infection or skin irritation (0.6%)
- Lead electrode left in patient (0.3%)

The lead electrode required surgical removal. All other events were resolved with either no treatment or standard medical treatment (e.g., antibiotics). None of the patients experienced any permanent complication from the PNE procedure.

Potential Adverse Events

Potential adverse events which may occur, but were not reported in the clinical study include:

- Nerve injury
- Swelling at the implant site
- Allergic or immune system response to the implanted materials
- Undesirable sensations that may be either temporary or permanent
- Undesirable changes in stimulation, possibly related to physiological changes, shifts in electrode position, lead migration, loose electrical connections, or lead/screener cable fractures. These changes in stimulation have been described by some patients as, "uncomfortable, jolting, shocking or loss of sensation of stimulation."

Common Questions

- **What is SNS?**

  SNS (Sacral Nerve Stimulation) is a medical treatment for symptoms of urinary urge incontinence. In SNS, a small electric pulse is applied to sacral nerves. The sacral nerves control your bladder, bowel, and pelvic organs.

- **What does stimulation feel like?**

  The feeling of stimulation varies from patient to patient. You may feel a brief tingling when stimulation is first turned ON. You may feel some level of stimulation whenever your test stimulator is ON. Some patients describe higher levels of stimulation as, "uncomfortable, jolting or shocking."

- **Will I be able to increase or decrease the strength of stimulation?**

  Yes. You can adjust the stimulation using the amplitude control knob marked A on the top of the test stimulator.

- **Will I be able to turn the test stimulator ON and OFF?**

  Yes. To turn the test stimulator OFF, turn the control knob marked A for amplitude to OFF. The green ON light will stop flashing. To turn the test stimulator back ON, turn the control knob marked A clockwise and check to see if the green light is flashing.

- **Should I void with the test stimulator ON or OFF?**

  Ask your doctor for specific instructions.

- **Will the PNE limit my activities?**

  Generally, no. However, you should consult your doctor about performing any particularly strenuous activities.

- **What should I do if the stimulation changes or becomes uncomfortable?**

  Turn the test stimulator OFF and contact your doctor.

- **Is it normal for the stimulation feeling to increase or decrease when I change position?**

  Generally, the feeling of stimulation will be constant. However, abrupt movements or changes in posture could make the stimulation feel like it is increasing or decreasing. Some patients describe higher levels of stimulation as, "uncomfortable, jolting or shocking." As long as the stimulation controls your symptoms, this is no cause for concern. If your symptoms worsen or the feeling of stimulation stops entirely, contact your doctor.

- **Does the test stimulator make any noise?**

  No.

- **Can stimulation be used during pregnancy?**

  The safety of SNS for use during pregnancy or delivery has not been established. If you learn, or suspect, that you are pregnant, turn your test stimulator OFF and call your doctor.

- **Whom should I contact in case I have a problem?**

  Your first call should be to your doctor. If you are unable to contact your doctor, please contact Medtronic at the telephone number listed on the back cover of this manual.

Glossary

amplitude. A measure of the electrical intensity of a stimulating pulse.

Peripheral Nerve Evaluation (PNE). A method your doctor can use to assess how Sacral Nerve Stimulation affects your urinary urge incontinence.

rate. The number of times stimulating pulses are delivered each second.

sacral nerves. Nerves located near the base of the spinal cord in your lower back. Sacral nerves control your bladder, bowel, and pelvic organs.

Sacral Nerve Stimulation (SNS). A treatment that sends small electric pulses to your sacral nerves to manage symptoms of urinary urge incontinence.

screening lead. An implantable thin wire. Electric stimulation is delivered to the sacral nerve through the lead.

test stimulator. An external electronic device used to stimulate the sacral nerve.

urge incontinence. The involuntary loss of urine (incontinence) associated with an abrupt, strong desire to void (urgency).

void. Urinate.

voiding diary. A diary used to record the frequency, timing, amount of urine and/or other factors associated with urinary incontinence.

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