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March 16, 2000

Ms. Jan L. Scudiero
Division of General and Restorative Devices
9200 Corporate Boulevard, HFZ-410
Rockville, MD

Re: Petition for Reclassification of Totally Implanted Spinal Cord Stimulator for use in the Treatment of Chronic Intractable Pain – **00P-0788 / CCP 1**

Dear Ms. Jan Scudiero:

On June 11, 1999, in accordance with applicable provisions of the Federal Food, Drug, and Cosmetic Act (the "Act"), the Food and Drug Administration (FDA) filed the above referenced petition submitted by Advanced Neuromodulation Systems, Inc. (ANS).

The objective of this petition was to seek reclassification of the Implantable Pulse Generator (IPG), which like the currently available Class II externally powered implantable device is not intended for a life sustaining or life supporting purpose. ANS proposed to reclassify the device for use in the treatment of chronic intractable pain which is the same indication for use as the current Class II radio frequency (RF) device.

Consistent with the provisions of Section 513 of the Act, the FDA determined that the petition did not contain any deficiencies and scheduled a meeting of the appropriate Advisory Panel. Prior to the publicly announced September 17, 1999 panel meeting, panel members were provided with a copy of the petition and comments in opposition which were submitted by Medtronic, Inc. (Medtronic), manufacturer of the only IPG device in current US commercial distribution. Medtronic representatives expressed their views during a presentation at the panel meeting and had ample opportunity subsequent to the panel meeting to express further comment during the 210 day statutory time period for review by the FDA.

00P-0788

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ANS very recently learned of the January 31, 2000 letter from Medtronic which the Dockets Management Office of the FDA has filed under the reference OOP-0788. The Medtronic letter requests that FDA deny the ANS petition.

The present request by Medtronic must be rejected by the FDA for two reasons. It does not provide any new information that is relevant to the safety and effectiveness review responsibility of the FDA for a Class II device and it is not timely.

ANS is surprised by this request and puzzled by the absence of relevant substance in the letter. However, ANS shall use this opportunity to provide preliminary comments and to emphasize for the public benefit that it is the desire and intent of ANS to manufacture for distribution a device for which ANS is confident that there is reasonable assurance of device safety and effectiveness. ANS welcomes its responsibility to comply with the pervasive, but reasonable special controls applicable to Class II devices.

ANS sought reclassification in accordance with section 513(f) of the Act because it believes that imposition of and compliance with appropriate special controls is adequate to justify the planned commercial distribution through issuance of an order by the FDA. The "order" is the functional equivalent of a premarket approval (PMA), because the premarket, 510(k), notification applicant can not lawfully market a device until the FDA issues an order.

During 1980, Medtronic itself specifically recognized that a totally Implantable Spinal Cord Stimulation System did not justify need for a PMA. On October 29, 1980, the FDA disagreed but offered that Medtronic could petition for reclassification from the Class III (PMA) requirement. (See Attachment A, FDA Section 510(k) response). It appears that Medtronic elected not to seek reclassification; yet fifteen years later Medtronic sought classification information which resulted in issuance of the December 29, 1995 letter from Susan Alpert, Ph.D., MD. Medtronic, the FDA, or any other petitioner could have initiated the reclassification of the Implantable Pulse Generator (IPG). ANS has undertaken to do this,

because we believe that compliance with special controls applicable to Class II devices are adequate to provide reasonable assurance of IPG safety and effectiveness.

At a later date, ANS may elect to provide a more detailed response to the Medtronic letter; but, at present, ANS believes it is appropriate to comment in general on four topics. These relate to Procedure, Statutory Requirements, Special Controls, and Prescription Device Use.

PROCEDURE:

On September 3, 1999, unknown to ANS, Medtronic submitted a lengthy response to the ANS June 11, 1999 petition. This was provided in whole to members of the advisory panel, and ANS had only a limited opportunity to comment on the Medtronic response prior to the September 17, 1999 Advisory Panel meeting.

Representatives of Medtronic addressed panel members during the panel meeting and had the opportunity to supplement their comments at any time after the meeting. This was not done until four months later when the January 31, 2000 Medtronic letter was delivered to the FDA.

This Medtronic letter repeats information that was provided by Medtronic prior to and at the Advisory Panel meeting. There is nothing of substance that is new, and much of the letter consists of criticism of the performance of panel and FDA personnel. None of these criticisms support a failure to comply with an explicit requirement in the Act.

STATUTORY REQUIREMENTS:

The function of the premarket, 510(k), notification is to determine whether a PMA is necessary to support lawful commercial distribution. Prior to passage of the Medical

Device Amendments of 1976 (the “1976 Amendments”), there were no IPG devices; therefore, the Act automatically required application of Class III controls. But, the Act also provided opportunity for reclassification, which Medtronic elected not to pursue in 1980.

Implanted devices which are used for life supporting or life sustaining purposes are expected to be subject to Class III (PMA) controls. However, the FDA has classified many neurological, orthopedic, and dental devices into Class II recognizing that these controls are adequate to prove reasonable assurance of device safety and effectiveness¹.

In 1984, regulations requiring Medical Device Reporting (MDR) were promulgated and manufacturers of devices in commercial distribution were required to report certain events. The MDR regulation did not apply to devices subject to the Investigational Device Exception (IDE) regulation and therefore were not captured in the FDA database. Reference to omissions by ANS of MDR information in regards to the Neuromed device is therefore misleading.

In 1990, the Safe Medical Devices Act of 1990 (the “1990 SMDA”) was enacted into law. This greatly expanded the authority of the FDA and burdens on manufacturers. Before 1990, the 510(k) applicant could market a device after 90 days irrespective of FDA’s opinion of the classification status of the device. After the “1990 SMDA”, lawful commercial distribution required a written order from the FDA. Without this order, lawful commercial distribution could not commence.

¹ The FDA has classified approximately 1800 types of devices using the same panel procedure and documentation method it has applied to the IPG petition.

The Class II performance standard limitation was replaced by special controls which provided the FDA with broad discretionary authority. In addition, manufacturers could be subject to “pre-production design validation” requirements.

The FDA flexibility to apply the additional controls provided by the “1990 SMDA” were enhanced by the Food and Drug Modernization Act of 1997 (the “FDAMA”) which authorized the FDA to consider the least burdensome means of demonstrating substantial equivalence as part of the 510(k) premarket notification submission. Contrary to the Medtronic assertion, application of special controls to Class II devices does not authorize or require that either the FDA or the applicant utilize Medtronic IPG data to demonstrate substantial equivalence.

SPECIAL CONTROLS:

Manufacturers of Class II (Special Controls) devices are subject to biennial inspection, compliance with the comprehensive Quality System Regulation (QSR), and every other control that is applicable to a Class III device. Moreover, the FDA can apply a variety of additional controls – which may not apply to Class III devices – such as performance standards, post market surveillance, patient registries, guidelines (including clinical data), recommendations, and other appropriate actions.

The selection of appropriate special controls by the FDA is to assure that as part of 510(k) notification submission review every reasonable level of inquiry is applied to assure support for issuance of a 510(k) clearance “order”.

PRESCRIPTION DEVICE USE:

The IPG is to be made available only to licensed practitioners who have the necessary skill, experience, and competence to select the IPG that is appropriate to the needs of

their patients. At present, only the Medtronic device is available in the US.

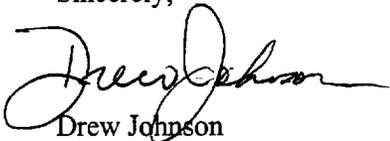
Consequently, the benefit of competitive selection opportunity is not available.

ANS is confident of its ability to provide a safe and effective IPG to physicians for acceptable indications for use cleared through an order by the FDA. ANS also believes that marketplace competition subject to regulatory oversight by the FDA will stimulate improvements for a device that is not intended for a life supporting or life sustaining use. ANS believes that consumers, industry and the FDA are stakeholders in the reclassification process. Consistent with Congress's intent that devices not be over-regulated, The Food Drug and Cosmetic Act provides procedures for reclassifying devices to ensure they are in the appropriate Class and not over-regulated. Unjustified over-regulation increases the time to market for products that could be commercially available helping to improve the quality of life of patients.

In summary, ANS urges the FDA to reject this belated and redundant effort by Medtronic to prevent the lawful reclassification of the IPG device. The decision by Cordis approximately fifteen (15) years ago to discontinue distribution of an IPG device and by Neuromed in 1994 to terminate its clinical investigation are not relevant to reclassification. Furthermore, ANS made it clear during the panel presentations that the MDR search " was refined by identifying those reports referring to IPG systems currently in commercial distribution" thus illuminating the Cordis device since that division of Cordis ceased to exist in about 1985 (See Attachment B Panel Meeting Presentation Slides). Much of the Medtronic representations about these devices consist of hearsay. Likewise, much of the rhetoric employed by Medtronic engages in speculation and efforts to attribute meanings to the positions expressed by or implied of other individuals without receiving confirmation from these individuals. For example, attacks on performance of the industry representative, FDA personnel, or other Advisory Panel Members/presenters is unnecessary and irrelevant to the real issue; namely, the identification of applicable special controls for the reclassification of the IPG.

ANS welcomes further inquiry from the FDA, reserves the opportunity to submit additional comments, and urges the FDA to complete the reclassification of the IPG in accordance with provisions of the Act as clearly supported by the administrative record.

Sincerely,



Drew Johnson
Director, Regulatory Affairs

cc: Philip Phillips, FDA
James Dillard, FDA
Russ Pagano, FDA
Lyle D. Jaffe, FDA

Attachment A: FDA "Totally Implanted Stimulation System" NSE letter to Medtronic
Attachment B: ANS September 17, 1999 Panel Meeting Presentation Slides

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
SILVER SPRING, MARYLAND 20910

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OCT 29 1987

Mr. Russell W. Felkey
Sr. Product Regulation Manager
Medtronic, Inc.
3055 Old Highway Eight
P.O. Box 1453
Minneapolis, MN 55440

Re: K802516 - Medtronic Totally
Implantable Spinal Cord
Stimulation System

Dear Mr. Felkey:

The Food and Drug Administration (FDA) has completed its review of your premarket notification submission K802516 under Section 510(k) of the Federal Food, Drug, and Cosmetic Act.

Based upon our review, we have concluded that the Medtronic Totally Implantable Spinal Cord Stimulation System is not substantially equivalent to any device that was in commercial distribution before May 28, 1976, or to any device introduced since that date which has been classified in Class I (General Controls) or Class II (Performance Standards). This decision is based on the fact that your design is based on a totally implanted device as compared to the R-F coupled principle employed in the design of the pre-enactment device, and also based on major differences in the electrical stimulation parameters being employed.

Therefore, your device is classified by statute in Class III (Premarket Approval), under section 513(f) of the Act.

Premarket Approval. Section 515(a)(2) of the Act requires Class III devices to have an approved premarket approval application before they can be legally marketed, unless the device is the subject of an investigational device exemption under Section 520(g) or unless the device has been reclassified.

To prepare a premarket approval application, statutory provisions appearing in Section 515(c) of the Act must be followed. Until regulations for premarket approval applications have been promulgated, we suggest you follow the pertinent parts of the regulations for new drug applications in 21 CFR, Part 314, as guidelines.

Investigational Use. In the absence of an approved premarket approval application, a Class III device may be distributed only for investigational use. Enclosed for your information, is the final regulation for investigational devices which was published in the Federal Register on January 14, 1980. We believe the regulations set forth desirable procedures and safeguards for the conduct of clinical investigations. The label for such devices must indicate that the devices are for investigational use only.

Page 2 - Mr. Russell W. Felkey

Petition for Reclassification. If you believe that your device should not have to undergo premarket approval before it is commercially distributed, you may petition FDA for reclassification of your device under Section 513(j)(7) of the Act.

Premarket approval applications, investigational device exemption requests, and petitions for reclassification should be submitted to:

Food and Drug Administration
Bureau of Medical Devices
Document Control Center (HFK-20)
8757 Georgia Avenue
Silver Spring, Maryland 20910

Any commercial distribution of this device prior to approval of an application for premarket approval or the effective date of any order by the FDA reclassifying your device into Class I or II, would be a violation of the Federal Food, Drug, and Cosmetic Act.

Should you require any additional information concerning our decision or the alternatives available to you under the law, please contact:

James R. Veale
Director, Division of Anesthesiology
and Neurology Devices (HFK-430)
Bureau of Medical Devices

Sincerely yours,


Robert S. Kennedy, Ph.D.
Associate Director for
Device Evaluation
Bureau of Medical Devices

Enclosure

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ADVANCED NEUROMODULATION SYSTEMS, INC.

ANS Presentation Agenda

<u>Topic</u>	<u>Min.</u>	<u>Presenter</u>
Introduction/Basis for Reclassification	3	Johnson
Device Similarities and Differences	5	Dr. Barolat
Literature/Risk/Indications Summary	10	Dr. Barolat
MDR Review Summary	5	Dr. Cameron
Proposed Special Controls	5	Johnson
Closing Statement	2	Johnson

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Significant SCS Historical Regulatory Events

- 1979 - FDA formally Classified Implanted Spinal Cord Stimulator devices for pain relief into Class II
- 1980 - A manufacturer (Medtronic) submitted a 510(k) premarket notification to FDA for clearance of their internally powered SCS device as a class II device substantially equivalent to the externally SCS powered device
 - ◆ FDA deemed that a PMA was necessary
- 1981- First implantable power generator (IPG) for SCS approved through a PMA

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Changes to Law

- 1976 Amendments
 - ◆ Modifications have occurred to facilitate FDA/industry flexibility to provide reasonable assurance of safety and effectiveness
- 1990 Amendments
 - ◆ Instituted procedures for establishing a performance standard
 - ◆ Required manufacturer compliance with design controls
 - ◆ Changed the definition of Class II device to include the use of "special controls" as a means of providing reasonable assurance of safety and effectiveness

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Changes to Law

- **Food and Drug Administration Modernization Act of 1997 (FDAMA)**
 - ◆ **Two key features of FDAMA**
 - **Postmarket controls**
 - **Applied to classification of devices to provide reasonable assurance of safety and effectiveness**
 - **International Standards**
 - **FDA is authorized to recognize standards and require a declaration of conformance as part of the 510(k) clearance process**

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Basis for Reclassification

- **Risks and indications are similar to Class II implanted spinal cord stimulators.**
- **General controls and special controls are available to reasonably assure the device's safety and effectiveness.**
- **Over 10 years of use demonstrates that the device is safe and effective for the treatment of chronic pain of the trunk and/or limbs.**

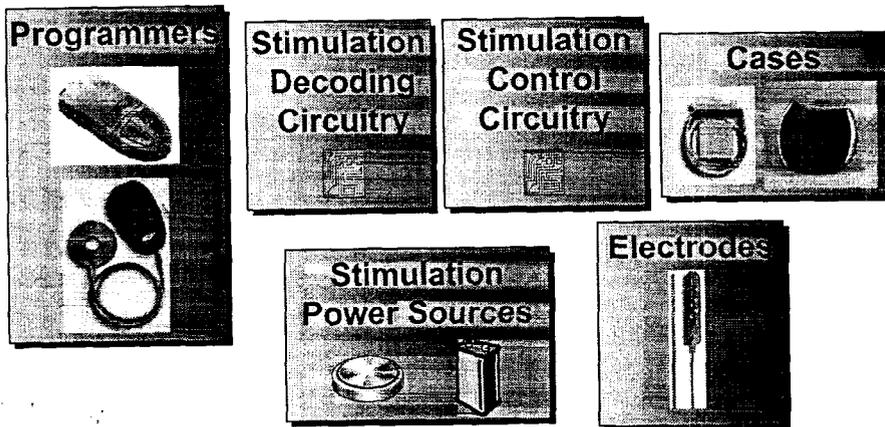
ANS

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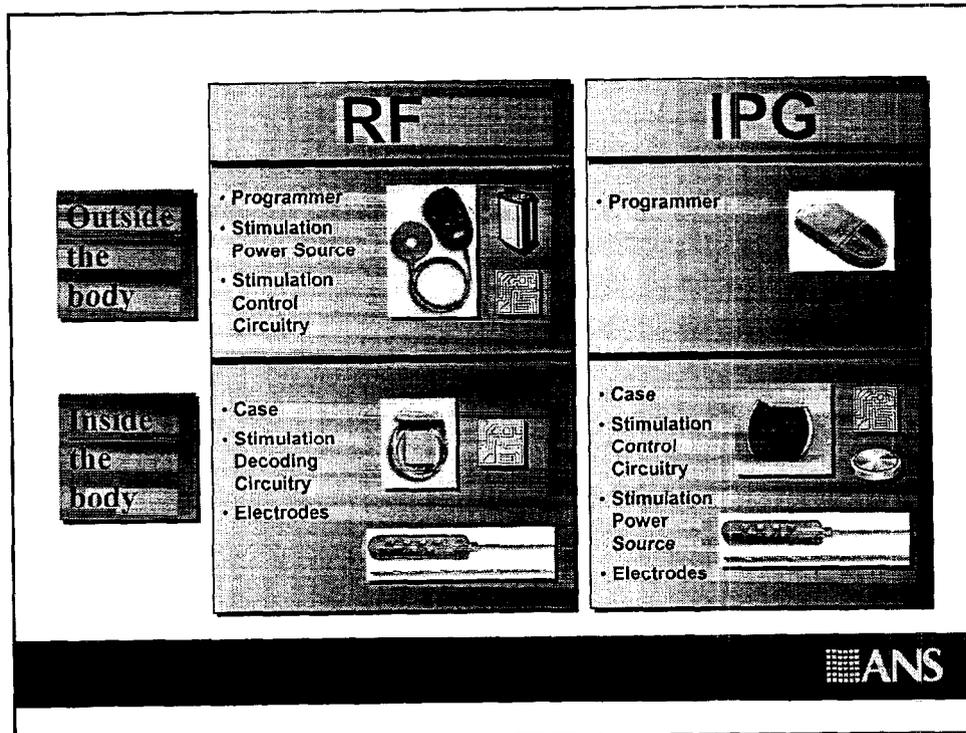
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Components of a Spinal Cord Stimulation System



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**SCS System
Patient Programmmerers**



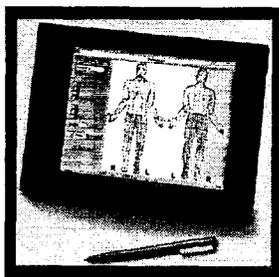
Renew™



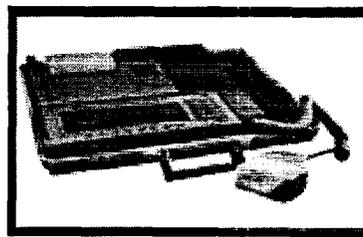
Itrel®

 ANS

**SCS System
Physician Programmmerers**



PainDoc®



Itrel®

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Historical Uses of IPG and RF Devices

- SCS, in general, has been used for over 30 years.
- Current IPG and RF systems have over 10 years of use in the treatment of chronic pain of the trunk and/or limbs.
- The literature has shown that SCS has a 60 percent success rate in the treatment of chronic pain.
- Power source is the main difference.

 ANS

Literature Review Background

- MedLine Search 1983–Present
 - ◆ Key words
 - Spinal cord stimulation or dorsal column stimulation
 - Pain
 - ◆ Found 253 articles
 - ◆ 31 articles in English listing complications
 - ◆ Results were grouped according to complications

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IPG and RF System Complications

- Lead migration: 14.20%
- Epidural hemorrhage and/or paralysis: 0.30%
- CSF leakage: 0.30%
- Infection, seroma and/or hematoma: 4.48%
- Undesirable changes in stimulation over time: 0.60%

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IPG and RF System Complications

- Pain over implant sites: 1.03%
- Allergic or rejection response to implanted materials: 0.15%
- Local skin erosion over the receiver: 0.15%
- Device failure: 7.47%
- Other: 0.60%

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Complications Exclusive to IPGs

- Battery Failure: 1.80%

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Indications for SCS from the Literature

- Reflex Sympathetic Dystrophy (Complex Regional Pain Syndrome I)
- Causalgia (Complex Regional Pain Syndrome II)
- Pain due to Peripheral Neuropathy
- Pain Due to Brachial Plexus Injuries
- Cauda Equina Pain
- Pain Due to Nerve Root Avulsion
- Stump Pain

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Indication for SCS from the Literature

- Failed Back Surgery Syndrome Pain
- Pain Due to Spinal Cord Injuries
- Postherpetic Neuralgia Pain
- Phantom Limb Pain
- Pain Due to Tumors
- Ischemic Limb Pain
- Arachnoiditis
- Pain Due to Multiple Sclerosis
- Pain Due to Peripheral Vascular Disease
- Angina Pain

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Proposed Indication for Reclassified IPG Systems

- Same as current RF systems
 - ◆ Spinal cord stimulation is indicated for the treatment of chronic pain of the trunk and/or limbs either as the sole mitigating agent or as an adjunct to other modes of therapy used in a multidisciplinary approach.

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Proposed Contraindications

- Unsuccessful pain relief during stimulation of the spinal cord.
- Inability of the patient to properly operate the system.
- The stimulators are contraindicated for patients with an implantable cardiac pacemaker or cardioverter/defibrillator or those patients who will be exposed to magnetic resonance imaging (MRI).

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Benefits Associated with Totally Implanted SCS Devices

- No external hardware
 - ◆ Cosmetically appealing
 - ◆ No clothing restrictions
- Allows for aquatic activities
 - ◆ Swimming
 - ◆ Bathing
- No antenna results in a more consistent stimulation
 - ◆ Not affected by perspiration
 - ◆ No antenna alignment
- Reduced patient interface

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Closing Comments

In my opinion, considering the similarities of the systems components, reported complications, and indications for use, I believe that the totally implanted spinal cord stimulator for pain relief presents the same risks to patients as the radio-frequency spinal cord stimulator. For practical purposes, the most significant difference between the two devices is the location of the power source. The benefits of the internal power source outweigh the surgical risks to replace the power source in the event of battery failure.

Medical Device Reporting

- Incident Reporting
 - ◆ Incidents are placed into categories at the time of entry not after an analysis
- MDR Categories
 - ◆ Death
 - ◆ Serious Injury
 - ◆ Malfunction
- Analysis of DATA BASE
 - ◆ Requires a detailed review of each report to draw conclusions

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Medical Device Reporting

DETAILED INFORMATION

Access Number: M749965
Date Received: 03/29/96
Product Description: CERVITRODE
Manufacturer Code: QUESMEDI
Manufacturer Name: QUEST MEDICAL, INC.
5000-A OAKES ROAD
FORT LAUDERDALE, FL 33314
Report Type: DEATH
Model Number: UNK
Panel Code: NEUROLOGY
Product Code: GZB
Event Type: FINAL

Event Description: A PT. WHOSE HEALTH WAS DETERIORATING RAPIDLY, WAS IMPLANTED WITH A STIMULATOR ON 1/30/96. AFTER A 15 DAY TRIAL THE PT WAS DIAGNOSED WITH MENINGITIS AND PASSED AWAY ONE WEEK LATER. THE DEVICE HAS NOT BEEN RETURNED TO THE MFR FOR EVAL. BASED ON THE ONLY INFORMATION CO HAS RECEIVED, CO DOES NOT FEEL THAT THERE IS ENOUGH INFORMATION TO SUGGEST THAT CO'S PRODUCT CONTRIBUTED OR CAUSED THE PT'S DEATH. IN CO'S LITERATURE FOR THE PHYSICIAN IT STATES THAT IT IS NOT RECOMMENDED ON PATIENTS WHO HAVE RAPIDLY PROGRESSING DISORDER.

MDR.JPG

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Medical Device Reporting

- MDR and MAUDE searches were performed using manufacturer's names and Neuro.
- A total of 1386 reports were found from 1984 through March 1999.
- This search was further refined by identifying those reports referring to IPG systems currently in commercial distribution.
- A total of 408 reports were found and were categorized according to adverse events found in the literature survey.

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Medical Device Reporting "Others"

Center for Devices and Radiological Health

DETAILED INFORMATION

Access Number: M751902
Date Received: 04/08/96
Product Description: ITREL II
Manufacturer Code: MEDREL
Manufacturer Name: MEDREL, INC.
P.O. BOX 8667
HUMACAO, PR 00661
Report Type: SERIOUS INJURY
Model Number: 7424
Catalog Number: NA
Panel Code: NEUROLOGY
Product Code: GZB
Event Type: FINAL
Event Description: THE DEVICE WAS EXPLANTED DUE TO REPORTED "POSSIBLE FAILURE". ANALYSIS IS ONGOING.

ANS

Medical Device Reporting

- The largest category was "Other" (144 reports).
- The second largest category was related to "Undesirable changes in stimulation over time" (106 reports).
- The third largest category was related to Battery Failure (66 reports)
 - ◆ Defined as pre-end of battery life
- The fourth largest category was related to "Device failure" (63 reports).
 - ◆ Lead breakage - 15; Hardware malfunction - 44;
Loose connection - 4

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Medical Device Reporting

- Fourteen reports were related to "Infection."
- Ten reports were related to "Pain at the Implant Site."
- Two reports were related to "Skin Erosion."
- "Lead Migration," "Seroma," and "Allergic Reaction" were listed on separate reports.

 ANS

Medical Device Reporting Limitations

- This review did not include events that went unreported.
- Incomplete reports are listed under the "Other" category.
- The denominator for the number of devices implanted is unknown.
- MDR data for 1991 was unavailable.

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Class II Device Definition

- A device is in Class II if general controls alone are insufficient to provide reasonable assurance of its safety and effectiveness and there is sufficient information to establish special controls, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines, recommendations, and other appropriate actions as the Commissioner deems necessary to provide such assurance.



SPECIAL CONTROLS

A) LEAD MIGRATION		
Potential Labeling Controls	Potential Consensus Standards Controls	Potential Guidance Documents Controls
<ul style="list-style-type: none"> • Identify lead migration as possible adverse event • Directions to secure lead with anchors in Physician's Manual 	<ul style="list-style-type: none"> • EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> • Design Control: Guidance for Medical Device Manufacturers • Medical Device Labeling Suggested Format and Content
B) INFECTION		
<ul style="list-style-type: none"> • Identify infection as possible adverse event 	<ul style="list-style-type: none"> • Sterilization validation per AAMI/ISO 11135 • Sterilization validation per EN 556 • Sterile labeled medical devices EN 558 • EN 45501-1 subset has EN 861-1 "Packaging materials and systems for Medical Devices which are to be sterilized" • EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> • 510(k) Sterility Review Guidance • Medical Device Labeling Suggested Format and Content
B) EPIDURAL HEMORRHAGE		
<ul style="list-style-type: none"> • Identify epidural hemorrhage as possible adverse event • Directions for needle insertion in Physician Manual 	<ul style="list-style-type: none"> • EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> • Medical Device Labeling Suggested Format and Content

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SPECIAL CONTROLS

B) SEROMA

Potential Labeling Controls	Potential Consensus Standards Controls	Potential Guidance Documents Controls
<ul style="list-style-type: none"> • Identify seroma as possible adverse event 	<ul style="list-style-type: none"> • EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> • Medical Device Labeling Suggested Format and Content

B) HEMOTOMA

<ul style="list-style-type: none"> • Identify Hematoma as possible adverse event • Directions for implantation technique in Physician Manual 	<ul style="list-style-type: none"> • EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> • Medical Device Labeling Suggested Format and Content
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B) PARALYSIS

<ul style="list-style-type: none"> • Identify paralysis as possible adverse event • Directions for needle insertion in Physician Manual • Directions for implantation in Physician Manual • Patient size selection guidance in Physicians manual • Identify infection as possible adverse event 	<ul style="list-style-type: none"> • EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> • Medical Device Labeling Suggested Format and Content
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SPECIAL CONTROLS

C) CSF LEAKAGE

Potential Labeling Controls	Potential Consensus Standards Controls	Potential Guidance Documents Controls
<ul style="list-style-type: none"> • Identify CSF leakage as possible adverse event • Directions for implantation and insertion technique in Physician Manual 	<ul style="list-style-type: none"> • EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> • Medical Device Labeling Suggested Format and Content

D) UNDESIRABLE CHANGES IN STIMULATION

(Intermittent Stimulation, Over Stimulation and/or Shock)

<ul style="list-style-type: none"> • Identify undesirable changes in stimulation as possible adverse event • Warning regarding Anti-Theft Devices • Cautions regarding effects of postural changes 	<ul style="list-style-type: none"> • EN/IEC-60801 series • EN 1441 Medical Device Risk Analysis • EN 45502-1 Active Implantable Medical Device -General Requirements for Safety, Marking ... • ANSI/AAMI NS14 -1995 Implantable Spinal Cord Stimulators 	<ul style="list-style-type: none"> • FDA letter to industry "Important Information on Anti-Theft and Metal Detector Systems....Spinalcord Stimulators", Sept 28, 1998 • Guidance for Content of Premarket Submissions for Software Contained in Medical Devices • General Principles of Software Validation
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Totally Implanted Spinal Cord Stimulator Reclassification

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SPECIAL CONTROLS

E) PAIN AT THE IMPLANT SITE

Potential Labeling Controls	Potential Consensus Standards Controls	Potential Guidance Documents Controls
<ul style="list-style-type: none"> Identify implant site pain as possible adverse event Directions for needle insertion in Physician Manual 	<ul style="list-style-type: none"> EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> Medical Device Labeling Suggested Format and Content

F) ALLERGIC OR REJECTION RESPONSE TO IMPLANTED MATERIALS

<ul style="list-style-type: none"> Identify immune response as possible adverse event 	<ul style="list-style-type: none"> EN ISO 10993-1 Biological Evaluation of Medical Devices - Part 1 EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> Medical Device Labeling Suggested Format and Content
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G) LOCAL SKIN EROSION

<ul style="list-style-type: none"> Identify skin erosion response as possible adverse event Directions for implantation in Physician Manual Patient size selection guidance in Physician manual 	<ul style="list-style-type: none"> EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> Medical Device Labeling Suggested Format and Content
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SPECIAL CONTROLS

H) DEVICE FAILURE (Lead Breakage, Hardware Malfunction, and/or Loose Connection)

Potential Labeling Controls	Potential Consensus Standards Controls	Potential Guidance Documents Controls
	<ul style="list-style-type: none"> ANSI/AAMI NS14-1995 Implantable Spinal Cord Stimulators EN 45502-1 Active Implantable Medical Device -General Requirements for Safety, Marking ... 	<ul style="list-style-type: none"> Design Control Guidance for Medical Devices Guidance for Content of Premarket Submissions for Software Contained in Medical Devices General Principles of Software Validation

I) OTHER (Psychosis)

<ul style="list-style-type: none"> Recommend patients have Psychological Screening prior to Implant in Physician Manual Contraindications: Patients are contraindicated for internalization if they are clearly unsuccessful during screening procedure, or if they are unable to properly operate the system 		
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J) BATTERY FAILURE

<ul style="list-style-type: none"> Disclose expected battery life in patient & Physician Manuals 	<ul style="list-style-type: none"> EN 1441 Medical Device Risk Analysis 	<ul style="list-style-type: none"> Medical Device Labeling Suggested Format and Content Design Control Guidance for Medical Devices
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Labeling Special Controls

- **Warning/Precautions/Adverse Events**
 - ◆ Safety has not been established for pregnancy or pediatric use.
 - ◆ Patients should not drive or use dangerous equipment during stimulation.
 - ◆ Systems may be affected by or adversely affect cardiac pacemakers, cardioverter/defibrillators, external defibrillators, MRI, diathermy, ultrasonic equipment, electrocautery, radiation therapy, theft detectors, security systems, and aircraft communication systems.

(Continued)



Labeling Special Controls

- **Warning/Precautions/Adverse Events** *(Continued)*
 - ◆ Adverse events may include: hematoma, epidural hemorrhage, paralysis, seroma, CSF leakage, infection, erosion, allergic response, hardware malfunction or migration, pain at implantation site, loss of pain relief, chest wall stimulation, surgical risks, and an undesirable change in stimulation described by some patients as uncomfortable, jolting, shocking.
 - ◆ Patient selection criteria include physiological origin of pain, appropriate surgical candidate, detoxification from narcotics, and availability of long-term postsurgical management.



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Labeling Special Controls

- Prescription device labeling statement
 - ◆ Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.



Labeling Special Controls Unique to the Internal Battery

- Manufacturers shall provide:
 - ◆ A chart or calculation in the physician manual which illustrates the range of the estimated service life of the device for various output selections.
 - ◆ A low-battery indicator on patient programmer user interface.
 - ◆ An end-of-battery life indicator on patient programmer user interface.



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Battery Failure Modes and Special Controls

- Controls
 - ◆ Design Controls
 - ◆ EN 1441 Std.
 - ◆ EN 45502-1 Std.
 - ◆ MIL Spec 883
 - ◆ Labeling



Battery Failure Modes and Special Controls

Battery Failure Mode	Risk	Control	Control Description
Explosion	Death, patient injury, reoperation	<ul style="list-style-type: none"> • Section 25 of EN45502-1 • Section 26.2 of EN45502-1 	<ul style="list-style-type: none"> • The device shall not be affected by atmospheric pressure changes during normal operation. • The device shall not be affected by temperature changes during normal operation.

Battery Failure Mode	Risk	Control	Control Description
Leakage	Death, no stim, change in stim, intermittent stim, reoperation	<ul style="list-style-type: none"> • Section 16.2 of EN45502-1 • MIL 883 Method 1014.10 	<ul style="list-style-type: none"> • No leakage current greater than 1 μA shall be sustained during device use. • Device housing must be hermetically sealed.

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Battery Failure Modes and Special Controls

Battery Failure Mode	Risk	Control	Control Description
Heat	Burn, undesirable pain, reoperation	Section 17.1 of EN45502-1	No outer surface of the device shall be greater than 2° C above the normal body temperature when implanted.

Battery Failure Mode	Risk	Control	Control Description
Power Depletion	Return of pre-implant pain, intermittent stim, reoperation	<ul style="list-style-type: none"> • Section 19.2 of EN45502-1 • Section 19.3 of EN45502-1 • Section 28.19 of EN45502-1 	<ul style="list-style-type: none"> • The device shall include a replacement indicator. • No single component failure shall cause an unacceptable hazard. • Lifetime of the power source shall be estimated and documented.

Standards Special Controls

- **ANSI/AAMI NS14-1995, "Implantable Spinal Cord Stimulators"**
 - Established safety and performance requirements for internally and/or externally powered spinal cord stimulators.
- **EN 45502-1, "Active Implantable Medical Devices-Part 1: General requirements for safety, marking, and information to be provided by the manufacturer"**
 - An international standard that specifies general requirements for active implantable medical devices to provide basic assurance of safety for both patients and users.

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Standards Special Control

- EN 1441 Medical Devices- Risk Analysis
 - ◆ Specifies a procedure for the manufacturer to investigate, using available information, the safety of medical device, including *in vitro* diagnostic devices or accessories.
 - ◆ Use to identify hazards and estimate the risk associated with the device.
 - ◆ Assists in areas where relevant standards are not applicable or not used.



FDA Guidance Documents Special Controls

- Premarket Notification 510(k) Regulatory Requirements for Medical Devices
- Design Control Guidance for Medical Devices
- General Principles of Software Validation
- Guidance for Content of Premarket Submissions for Software Contained in Medical Devices
- Medical Device Labeling Suggested Format and Content
- 510(k) Sterility Review Guidance





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Petition – 00P- 0788 / CCP 1**

1561 70 MAR 17 1998

Attached is the ANS response to comments submitted to the FDA on January 31, 2000 by Medtronic, Inc. regarding their opposition to the ANS petition to reclassify the Totally Implanted Spinal Cord Stimulator for Pain Relief from Class III to Class II.

3 additional hard copies of the ANS response are being sent to you via Federal Express mail to arrive at your office the morning of March 17, 2000. I am also sending individual copies via Fed Ex to James Dillard, Philip Phillip, Russell Pagano, and Lyle D. Jaffe to arrive on March 17, 2000.

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Drew Johnson.

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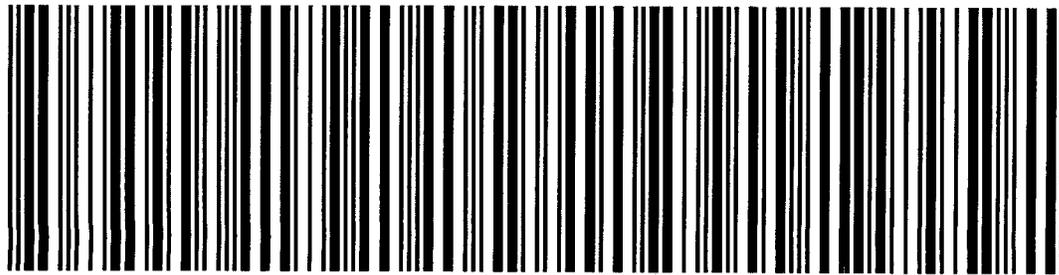
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