DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

FEB 2 3 2001

Mr. Drew Johnson
Director, Regulatory Affairs
Advanced Neuromodulation Systems, Inc.
6501 Windcrest Drive, Suite 100
Plano, TX 75024

Re: Reclassification Order:
Docket No. 00P-0788
Petition for Reclassification: Totally Implanted Spinal Cord Stimulator for Pain Relief
Dated: June 16, 1999
Date of Panel Review: September 17, 1999

Dear Mr. Johnson:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your petition for reclassification of the Totally Implanted Spinal Cord Stimulator for Pain Relief intended for use in the treatment of chronic intractable pain of the trunk or limbs. We apologize for the delay in responding to your petition. After carefully reviewing all relevant information we have concluded that we must deny your petition for the reasons discussed below.

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (act) (21 U.S.C. 360c(f)(1)), devices that were not in commercial distribution prior to May 28, 1976 (the date of enactment of the Medical Device Amendments of 1976 (the amendments)), generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking. Those devices remain in class III and require premarket approval, unless and until: (1) the device is reclassified into class I or II; (2) FDA issues an order classifying the device into class I or II in accordance with new section 513(f)(2) of the act (21 U.S.C. 360c(f)(2)), as amended by the Food and Drug Administration Modernization Act of 1997 (FDAMA); or (3) FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act (21 U.S.C. 360c(i)), to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and Part 807 of the regulations (21 CFR Part 807).

As you know, on June 16, 1999, you submitted a petition requesting reclassification of the Totally Implanted Spinal Cord Stimulator for Pain Relief from class III into class II. The petition was submitted under section 513(f)(2) of the act, now section 513(f)(3) of the act, as amended by FDAMA, and 21 CFR 860.134 of the agency's regulations. In accordance with section 513(f)(1) of the act, the Totally Implanted Spinal Cord Stimulator for Pain Relief was automatically classified into class III because the device was not within a type of device introduced or delivered for introduction into interstate commerce for commercial distribution

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before May 28, 1976, and had not been found to be substantially equivalent to a device placed in commercial distribution after May 28, 1976, that had been reclassified into class II or class I. In order to reclassify the Totally Implanted Spinal Cord Stimulator for Pain Relief intended for use in the treatment of chronic intractable pain of the trunk or limbs into class II, there must be valid scientific evidence establishing that the proposed class has sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

Pursuant to 21 CFR 860.125 and 860.134, FDA consulted with the Neurological Devices Panel (the Panel) on September 17, 1999. The Panel recommended that the device be reclassified from class III into class II because the Panel believed that special controls would provide reasonable assurance of the safety and effectiveness of the device. The Panel's recommendation was based on the information and data contained in the reclassification petition, the summary and analysis of the data as set forth in the petition, information presented during the open public hearing, the open Panel discussion at the meeting, and the Panel members' own personal knowledge of, and clinical experience with, the device. The Panel recommended the following special controls to reasonably assure the safety and effectiveness of the device: guidance documents, consensus standards, post-market surveillance, pre-clearance manufacturing inspections, device tracking, and patient registries.

The recommendations of the Panel, along with our tentative conclusions, were published in the Federal Register of September 6, 2000 (65 FR 54053) (enclosed) and interested persons were invited to comment by October 6, 2000. Subsequently, the comment period was extended to November 4, 2000. FDA received 22 comments from individual practitioners, a manufacturer, and the petitioner in response to the notice of panel recommendation. A summary of these comments is enclosed as Appendix A. FDA's receipt of these comments prompted a closer examination of our tentative findings as stated in 65 FR 54053.

After careful consideration of all the relevant information, FDA has determined that you have not demonstrated that there exists valid scientific evidence establishing that special controls, when combined with the general controls of the act, are sufficient to provide reasonable assurance of the safety and effectiveness of the Totally Implanted Spinal Cord Stimulator for Pain Relief. While the special controls that you proposed in your petition, when combined with the special controls identified by FDA, may address specific performance issues related to your device, we have concluded that they do not address all the safety and effectiveness concerns related to the device type.

The Totally Implanted Spinal Cord Stimulator for Pain Relief is in the category of "active implantable devices." Devices of this type are intended to be surgically implanted in the human body for more than 30 days and are designed to achieve their effect through a sustained release of energy. Because of the risks to health presented by these devices, FDA believes that before such devices are reclassified, it is critical that we fully understand all of the factors that contribute to a safe and effective device design as well as the processes by which devices within this device type are manufactured. As indicated above, the special controls that have been

identified may address certain safety and effectiveness concerns related to your device design, but are not sufficient to address others.

FDA identified the following risks to health associated with the use of the Totally Implanted Spinal Cord Stimulator for Pain Relief: lead migration, device failure, tissue reaction, skin erosion, surgical procedure risks, lack of electromagnetic compatibility (EMC), and lack of magnetic resonance (MR) compatibility. Many of these risks to health can be adequately addressed by special controls. For example, lead migration and surgical procedure risks can be minimized by guidance on adequate directions for implantation of the device. Additionally, the lack of EMC and MR compatibility may be adequately addressed by pre-clinical bench testing and possibly consensus standards, as well as through proper labeling. Device failure is, however, the most serious of the risks to health presented by the device type and the risk that supports maintaining the device type in class III. At this time, we do not believe that you have presented sufficient information establishing that special controls, in concert with general controls, can provide reasonable assurance of the safety and effectiveness of the device with respect to device failure.

As you know, device failure is frequently the result of improper device design and manufacture. Device failure most often involves battery depletion, lead breakage, hardware malfunction, and loose connections that lessen or eliminate stimulation and result in ineffective pain control. Device failure always requires re-operation with all of the attendant risks of secondary surgery. In addition, certain malfunctions, such as a damaged or improperly sealed implanted pulse generator case, can also result in battery leakage that could potentially cause tissue damage, as well as a secondary surgery.

During its deliberations, the Panel expressed concern about the risk to health presented by the device failure issue and recommended that the agency conduct a "pre-approval inspection" for premarket notifications for the Totally Implanted Spinal Cord Stimulator for Pain Relief, if the device was to be reclassified. In the September 6, 2000 notice of panel recommendation, we stated that we believed that design controls, in accordance with the Quality Systems (QS) regulation, could adequately address the risk of device failure. In light of this Panel recommendation, as well as the comments that FDA received in response to the notice (see Appendix A), we consulted with our manufacturing experts in the Office of Compliance. After further review, we have now determined that you have not identified special controls that provide reasonable assurance that a device of this type, even when manufactured in compliance with the QS regulation, will not fail at an unacceptable rate. Furthermore, routine pre-clearance inspections are not feasible, nor are they appropriate, for a class II device. Section 513(f)(5) of the act states that FDA may not withhold a determination on a premarket notification for failure to comply with the good manufacturing practice requirements, unless FDA finds that there is a substantial likelihood that the failure to comply with the QS regulation will potentially present a serious risk to human health. Moreover, as stated above, we have concluded that compliance with the QS regulation is not sufficient to provide reasonable assurance of the safety and effectiveness of this device, particularly with respect to device failure.

In summary, you have not identified special controls that address all of the risks associated with the Totally Implanted Spinal Cord Stimulators for Pain Relief thereby assuring the safety and effectiveness of these devices when used under the conditions of its intended use. Further, at this time, we do not believe that special controls, such as bench and animal testing, can substitute for actual clinical trials designed to demonstrate the safety and effectiveness of these devices. Lastly, the risks to health associated with the manufacturing process can only be addressed through the degree of regulatory oversight afforded to class III devices. It is for all of these reasons that we have determined that premarket approval continues to be necessary to ensure the safety and effectiveness of devices within this device type.

Although we have concluded that there is not sufficient information supporting reclassification of the device at this time, our review of your petition will result in a least burdensome path through the PMA process. That is, the special control that was identified in our September 6, 2000 Federal Register notice should be used in any future PMA submissions so that the risks to health associated with the Totally Implanted Spinal Cord Stimulator for Pain Relief are addressed in the most streamlined manner possible. As an example, please consider testing your device for conformance with the relevant FDA recognized consensus standards. If your device conforms to a particular recognized standard, you could elect to submit a "declaration of conformity" to the standard in a PMA in lieu of the actual test data.

A notice announcing the availability of this letter will be published in the Federal Register. A copy of this letter and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061 Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

If you have any questions concerning this denial of petition, please contact Mr. Mark N. Melkerson, Deputy Director, Division of General, Restorative, and Neurological Devices at 301-594-1184.

Sincerely yours,

Bernard E. Statland, M.D., Ph.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosures

Appendix A

Summary of Comments

This appendix summarizes the 22 comments received on the notice of panel recommendation: Reclassification of the Totally Implanted Spinal Cord Stimulator (65 FR 54053, September 6, 2000).

Fifteen clinicians opposed reclassification of the device. In summary, they stated that the device and the procedure to implant it are complex and that reclassification of the device would eliminate some critical checks and balances that promote patient safety. One clinician expressed concern that there was not a long history of use with the device and that there was a potential for "off label" use if the device was reclassified.

A manufacturer of the device raised the following eight issues in opposition to reclassifying the device:

1. Based on prior interactions with the manufacturer, the agency appeared in favor of class III regulation of the device rather than reclassification into class II.

2. The petitioner withheld adverse data and information from the petition and did not identify all of the risks associated with use of the device.

3. There was a lack of manufacturing information presented in the petition. The manufacturer thought there would be problems in manufacturing the devices under class II controls.

4. The Panel recommended preclearance premarket manufacturing inspections as one of the special controls. The Panel should have only recommended reclassification if it determined that class III controls were unnecessary to ensure safety and effectiveness, and thus the Panel failed to meet this legal requirement.

5. The data and information provided by the petitioner did not meet the criteria for valid scientific evidence under 21 CFR 860.7(c)(2).

6. They disagreed with the agency's position that many of the recommended special controls were not needed. The comment addressed each of the specific special controls the Panel recommended.. These special controls included guidance documents, consensus standards, postmarket surveillance, pre-approval manufacturing inspections, device tracking and patient registries.

7. The proposed special control guidance document was inadequate.

8. They raised procedural issues, such as panel training and placement of information on the public docket.

Six comments supported reclassification of the device. In summary, they stated that FDA and the Panel correctly identified and characterized all of the risks to health associated with use of the device. They believed that the special control guidance addressed all the elements necessary to allow the medical device industry to design and manufacture safe and effective devices of this generic type. In addition, they stated that reclassification of the device would stimulate innovative competition within the marketplace place which will result in development of even more effective implantable devices for the relief of chronic pain.