DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

July 24, 2014

Medtronic Sofamor Danek USA, Incorporated
Mr. Raphael McInnis
Manager, Regulatory Affairs
1800 Pyramid Place
Memphis, Tennessee 38132

Re: P090029
PRESTIGE® LP Cervical Disc
Filed: December 22, 2009
Amended: February 4, March 8, March 18, September 2 and December 21, 2010; January 20 and August 12, 2011; March 1, 2012; May 31 and December 11, 2013
Procode: MJO

Dear Mr. McInnis:

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 PRESTIGE® LP Cervical Disc. This device is indicated in skeletally mature patients for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy (arm pain and/or a neurological deficit) with or without neck pain, or myelopathy due to a single-level abnormality localized to the level of the disc space and at least one of the following conditions confirmed by imaging (CT, MRI, X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height as compared to adjacent levels. The PRESTIGE® LP Cervical Disc is implanted using an anterior approach. Patients should have failed at least 6 weeks of non-operative treatment or have had the presence of progressive symptoms or signs of nerve root/spinal cord compression in the face of continued non-operative management prior to implantation of the PRESTIGE® LP Cervical Disc. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at eight years. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study reports (PAS). Two (2) copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below.

1. *Prestige LP Cervical Disc –Extended Follow-up:* This study will be conducted as per protocol dated April 14, 2014, Version P03-03-PAS (email). This study will consists of the extended prospective follow-up of the premarket cohort for 10-years post-implant to evaluate the longer term safety and effectiveness of the Prestige LP Cervical Disc, by following all available Prestige LP patients (original n=280 pivotal investigation patients and approximately n=50 continued access patients) from the pivotal investigational device exemption (IDE) study. At the 120-month (±4 month) visit, you will collect the following data: Neck Disability Index; The Short Form (36) Health Survey; adverse events and outstanding adverse events forms; radiographic images (AP-lateral, lateral, right/left AP lateral bend, lateral flexion/extension) with independent review of medical images; neurological data; postoperative subject survey; postoperative Gait Assessment and Foraminal Compression test; postoperative Neck and Arm Pain Questionnaire; patient satisfaction, medication usage and postoperative treatment for pain management, patient disposition; and work status. Specimens for metal ions will be collected for all the metal ion cohort patients and any patient with an explant or revision. Radiographic information collected will include: range of motion on flexion/extension films (angulation and translation as well as the correlation of range of motion with outcomes), disc height (functional spinal unit), device conditions (bending, breakage, migration, and fracture); and bridging bone (stability over time and correlation with patient characteristics and postoperative outcomes).

You will also collect radiographic and clinical data on adjacent level surgeries and adjacent level range of motion on flexion/extension films (angulation and translation).

The primary objective of the study is to evaluate the overall success at 7 years. A patient will be considered an overall success if all of the following conditions are met:
Postoperative Neck Disability Index score improvement of at least 15-points from preoperative; maintenance or improvement in neurological status; Disc height success; no serious adverse event classified as implant associated or implant/surgical procedure associated; and no secondary surgical procedure classified as a "failure."
An alternate overall success determination will also be made without the inclusion of disc height into the aforementioned criteria.

You will also summarize and analyze the data as follows:

- Non-inferiority analysis comparing success rates between the PRESTIGE® LP Cervical Disc device group and the control group at 7 years— a Bayesian logistic regression model adjusting for the propensity score as the covariate will be carried out.

- All additional statistical comparisons between groups, at 7 year only, outlined in the original IDE study will utilize Bayesian statistical methods for the post- approval study.

- Time-to-event analyses and comparisons using the Cox regression model adjusting for the propensity score as the covariate for serious, possibly device-related adverse events; device failures, if any; second surgeries that are classified as failures at the target level; and additional surgical interventions at adjacent levels.

- Sensitivity analyses to assess the effect of missing data. These analyses will assume various proportions of successes and failures for overall success in the two groups for lost-to-follow-up, additional analyses will be carried out using Frequentist methods to assess the demographics characteristics, baseline information and the last observed overall success status of patients who become lost-to-follow-up compared to those who remain in the study.

FDA will expect 80% follow-up at 10-years to provide sufficient data to evaluate safety and effectiveness.

2. *Prestige LP Cervical Disc –ESS:* You have agreed to a study outline on January 24, 2014 (email). This is a 10 year Enhanced Surveillance Study (ESS) of PRESTIGE® LP Cervical Disc to fully characterize adverse events and complaints when the device is used in the intended use population in the United States and in the rest of the world.

You will collect, analyze, and submit all adverse event data including subsequent surgeries, heterotopic ossification, device malfunction, and other serious device-related complications. Information will be actively collected from annual surgeon surveys and on the company website. Information will also be collected passively through complaints, MDRs, and literature reviews.

All of the surgeons who have been trained on the use of PRESTIGE® LP Cervical Disc Prosthesis in the U.S. will be surveyed annually and the number of surveys issued and received will be reported. If a survey response includes any information related to an adverse event, you will collect additional data as specifically outlined in the ESS protocol and report that data to FDA.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval study. Your PMA supplement should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

3. *Prestige LP Cervical Disc –Device Failure:* You have agreed to a study outline on February 05, 2014 (email). This study will characterize the long-term modes and causes of failure. It will be conducted for a 10 year duration with a detailed analysis of all PRESTIGE® LP Cervical Disc explanted and retrieved components which were returned to the company. Your analysis will include the following details:

    a. Explant and histologic analyses conducted by third-party vendor, metal ion analysis for explants obtained during extended follow-up investigation

    b. Internal device analysis, without histologic and metal ion analysis for all other post-market explants

    Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval study. Your PMA supplement should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

Please be advised that the results from these studies should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement.

FDA would like to remind you that you are asked to submit separate PAS Progress Reports every six months during the first two years of the study and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm).

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Before making any change affecting the safety or effectiveness of the device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

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. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in 6 copies, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

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10903 New Hampshire Avenue
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If you have any questions concerning this approval order, please contact David Hwang, Ph.D. at (301) 796-3217.

Sincerely yours,

Mark N. Melkerson -S

Mark N. Melkerson
Director
Division of Orthopedic Devices
Office of Device Evaluation
Center for Devices and
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