



DEC 17 2007

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Synthes Spine, Inc.
c/o Mr. John J. Walsh, J.D.
Vice President, Regulatory and Clinical Affairs
1302 Wrights Lane East
West Chester, Pennsylvania 19380

Re: P070001
ProDisc™-C Total Disc Replacement
Filed: January 3, 2007
Amended: January 16, February 9, February 12, March 6, March 7, March 8, May 11,
June 15, June 29, July 2, August 9, August 17, September 5, September 12, October 4,
October 18, October 25, October 29, November 1, and December 7, 2007
Product Code: MJO

Dear Mr. Walsh:

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 ProDisc™-C Total Disc Replacement. This device is indicated for skeletally mature patients for reconstruction of the disc from C3-C7 following single-level discectomy for intractable symptomatic cervical disc disease (SCDD). Symptomatic cervical disc disease is defined as neck or arm (radicular) pain and/or a functional/neurological deficit with at least one of the following conditions confirmed by imaging (CT, MRI, or X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or loss of disc height. The ProDisc™-C Total Disc Replacement is implanted via an open anterior approach. Patients receiving the ProDisc™-C Total Disc Replacement should have failed at least six weeks of non-operative treatment prior to implantation of the ProDisc™-C Total Disc Replacement. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions described below and in the "Conditions of Approval" (enclosed).

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, 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.

In addition to the periodic report (often referred to as annual report) requirements outlined in the enclosure, you have agreed to provide the following data in a separate postapproval study report:

1. You have agreed to conduct a post-approval study (PAS) to evaluate the long-term safety and effectiveness of the ProDisc™-C Total Disc Replacement. This study will involve investigational and control patients from the pivotal investigational device exemption (IDE) study, as well as patients who received the ProDisc™-C as part of the Continued Access arm. This PAS will evaluate the long-term safety and effectiveness of the ProDisc™-C Total Disc Replacement by following 209 subjects from the randomized clinical trial (103 ProDisc™-C patients, and 106 control subjects) out to 7 years (i.e., 84 months). All 99 Continued Access subjects will also be evaluated through 7 years (i.e., 84 months) post-surgery.

The PAS will evaluate Overall Success, defined as:

- improvement in the Neck Disability Index (NDI) $\geq 20\%$ at 84 months compared to the score at pre-operative baseline
- neurological status improved or maintained (motor, sensory, reflexes) as compared to the pre-operative baseline
- no removals, revisions, re-operations or additional fixation were required to modify any implant
- no adverse events occur which are related to the treatment, ProDisc™-C, or its implantation or anterior cervical discectomy and fusion (ACDF) surgery, or its associated implants or graft material

This analysis will utilize a non-inferiority margin of 10%

You also have agreed to conduct an additional analysis evaluating Overall Success with NDI success defined as an improvement in the NDI score ≥ 15 points at 84 months compared to the score at pre-operative baseline (instead of an improvement of $\geq 20\%$). This analysis will use a non-inferiority margin of 10%.

The PAS will also evaluate all adverse events as well as adjacent segment degeneration both symptomatically and using radiographs; radiographic parameters including implant migration, subsidence, radiolucency, disc height, motion/fusion status patient satisfaction and quality of life (SF-36), and heterotopic ossification; neck and arm pain on a Visual Analog Scale (VAS); and the correlations of range of motion (ROM) with NDI and VAS scores.

Please be advised that FDA expects a minimum follow-up of 80% at the 7-year time point to provide sufficient data to adequately power your study.

PAS reports will be submitted every six months for the first two years and then annually until the study is completed.

2. You have agreed to perform a 5-year enhanced surveillance study of the ProDisc™-C Total Disc Replacement to more fully characterize adverse events when the device is used in the intended patient population under general conditions of use. You will collect, analyze, and submit all adverse events and complaints received by the company for the ProDisc™-C Total Disc Replacement, as well as information on the total number of devices shipped and implanted. The study will commence at the time of PMA approval. The Enhanced

Surveillance Study reports will be submitted every six months for the first two years and then annually through the fifth year after approval.

3. You have agreed to submit amended labeling (via a PMA supplement) with the results of the PAS and enhanced surveillance study outlined in items 1-2 above upon completion of the studies, and/or at earlier timepoints, as needed.

Expiration dating for this device has been established and approved at 6 months.

CDRH does not evaluate information related to contract liability warranties, however you should be aware that any such warranty statements must be truthful, accurate, and not misleading, and must be consistent with applicable Federal and State laws.

CDRH will notify the public of its decision to approve your PMA by making available 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 <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch, (HFA-305), Food and Drug Administration, 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 requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with any postapproval requirement constitutes a ground for withdrawal of approval of a PMA. 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. The labeling will not routinely be reviewed by FDA staff when PMA applicants include with their submission of the final printed labeling 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 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

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If you have any questions concerning this approval order, please contact Mr. Sergio M. de del Castillo at 240-276-3751.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Mark N. Melkerson", with a long horizontal flourish extending to the right.

Mark N. Melkerson
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

CONDITIONS OF APPROVAL

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) or (f). 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 that require a PMA supplement cannot be briefly summarized; therefore, 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 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 (see below). 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.

Alternate submissions permitted under 21 CFR 814.39(f) for manufacturing process changes include the use of a 30-day Notice. The manufacturer may distribute the device 30 days after the date on which the FDA receives the 30-day Notice, unless the FDA notifies the applicant within 30 days from receipt of the notice that the notice is not adequate.

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 mix-up 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. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

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 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 a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc.

Any written report is to be submitted to:

Food and Drug Administration
Center for Devices and Radiological Health
Medical Device Reporting
PO Box 3002
Rockville, Maryland 20847-3002

Additional information on MDR is available at <http://www.fda.gov/cdrh/devadvice/351.html>