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

LDR Spine USA, Inc.
% Noah J. Bartsch, MS, RAC
Director - Clinical/Regulatory/Quality
13785 Research Boulevard, Suite 200
Austin, Texas 78750

August 7, 2013

Re: P110002
Mobi-C® Cervical Disc Prosthesis
Filed: January 14, 2011
Amended: January 14, 2011; February 14, 2011; April 11, 2011; August 1, 2011; April 3, 2012; June 29, 2012; August 27, 2012; September 11, 2012; and, December 14, 2012
Procode: MJO

Dear Mr. Bartsch:

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 Mobi-C® Cervical Disc Prosthesis. 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 radiographic imaging (CT, MRI, X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height compared to adjacent levels. The Mobi-C® Cervical Disc Prosthesis is implanted using an anterior approach. Patients should have failed at least 6 weeks of conservative treatment or demonstrated progressive signs or symptoms despite nonoperative treatment prior to implantation of the Mobi-C® Cervical Disc Prosthesis. 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 five 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" (please use this title even if the specified interval is more frequent than one year) 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.

You have agreed to provide the following data as part of the annual report:

You must attempt to retrieve all explanted Mobi-C® devices (including but not limited to those retrieved from patients in the PAS and ESS) for analysis. All retrievals will be analyzed and reported per the agreed Post-Approval Study and Enhanced Surveillance Study protocols.

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.

In addition to the conditions outline above, you must conduct two post-approval studies to evaluate the long-term safety and effectiveness and the real-world device safety; as described below.

1. *The Extended Follow-up of Premarket Cohort*: Per agreement dated April 24, 2013 (email), this study will consists of the extended follow-up of the premarket cohort up to 7 -years to evaluate the longer term safety and effectiveness of the Mobi-C® Cervical Disc Prosthesis as compared to ACDF, by following the 260 subjects from the pivotal investigational device exemption (IDE) study (179 Mobi-C® subjects, and 81 ACDF subjects) annually through 7 years. At each annual (±4 month) visit, you will collect the following data: Neck Disability Index, neck and right/left arm pain Visual Analog Scale (VAS), health status survey (SF-12), patient satisfaction, neurological status, radiographic information, medication usage and postoperative treatment for pain management, work status, and all adverse events regardless of cause. 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, radiolucency, device displacement, subsidence and

migration, spinal fusion (control arm only), and heterotopic ossification (including grade, stability over time, and correlation with patient characteristics and postoperative outcomes). You will also collect radiographic and clinical data on adjacent level degeneration/disease including surgical and non-surgical adjacent level treatments as well as adjacent level diagnoses, adjacent level range of motion and radiographic changes at adjacent levels.

The primary objective of the study is to evaluate the overall success rate, using Overall Success defined as:

- Pain/Disability Improvement of at least 25% in the Neck Disability Index (NDI) at 5 years and 7 years compared with the score at baseline;

- No device failures (at the index level) requiring revision, re-operation, removal or supplemental fixation;

Absence of major complications is defined as 1) neurological deterioration, 2) radiologic failure (bridging bone and lack of motion at the index level for Mobi-C® subjects; failure of fusion for ACDF subjects), and 3) adverse events determined to be major complications and related to the study device (as determined by the independent CEC oversight committee); and,

Fusion in ACDF control subjects is defined as evidence of bridging trabecular bone and $< 2°$ total angular motion (from flexion to extension) and $< 50\%$ radiolucency along the graft/endplate interface and for Mobi-C® subjects radiologic failure as defined as evidence of continuous bridging bone and $< 2°$ total angular motion (from flexion to extension).

You will also conduct an additional analysis evaluating Overall Success with a second definition, as follows:

- Pain/Disability Improvement of at least 15 points in the Neck Disability Index (NDI) at 5 years and 7 years compared with the score at baseline;

- No secondary surgery at the index level, including revision, removal, reoperation and supplemental fixation;

- No potentially device-related adverse events;

- Maintenance or improvement in all components of neurologic status;

- No Mobi-C® intraoperative changes in treatment.

Success rates between the randomized investigational and control groups will be compared and assessed for non-inferiority based on a ten percent non-inferiority margin for both overall success analyses. Patients who were non-recoverable non-responders prior to 24 months will

carry forward as failures for each subsequent annual visit. Several sensitivity analyses will also be done.

FDA will expect at least 85% follow-up at the 7-year time point to provide sufficient data to evaluate safety and effectiveness.

2. *The Enhanced Surveillance System*: Per agreement dated April 24, 2013 (email), this is a 10-year Enhanced Surveillance Study (ESS) of the Mobi-C® Cervical Disc Prosthesis to fully characterize adverse events and complaints when the device is used in the intended patient population under general conditions of use 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, device removal, or 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 and MDRs, explant analysis, and literature reviews.

   All of the surgeons who have been trained on the use of Mobi-C® Cervical Disc Prosthesis 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.

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.

Within 30 days of your receipt of this letter, you must submit two separate PMA supplements that include complete protocols for each one of your Post Approval Studies. Your PMA supplements should be clearly labeled as a "Post-Approval Study Protocols" and submitted in triplicate to the address below. Please reference the PMA Supplement number above to facilitate processing.

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#2

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.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Amy Graf at (301) 796-5613.

Sincerely yours,

Mark N. Melkerson -S

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