August 16, 2019

Zimmer Biomet Spine, Inc.
Mike Medina, M.S.
Senior Director, Global Regulatory and Clinical Affairs
10225 Westmoor Drive
Westminster, Colorado 80021

Re: H190005
HUD Number: DEV-2018-0410
Trade/Device Name: The Tether™ - Vertebral Body Tethering System
Product Code: QHP
Filed: June 4, 2019

Dear Mr. Medina:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your humanitarian device exemption (HDE) application for The Tether™ - Vertebral Body Tethering System. This device is indicated for skeletally immature patients that require surgical treatment to obtain and maintain correction of progressive idiopathic scoliosis, with a major Cobb angle of 30 to 65 degrees whose osseous structure is dimensionally adequate to accommodate screw fixation, as determined by radiographic imaging. Patients should have failed bracing and/or be intolerant to brace wear. We are pleased to inform you that the HDE is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

The sale and distribution of this device is 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 probable benefit 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 5 years.

Continued approval of the HDE is contingent upon the submission of periodic reports, required under 21 CFR 814.126, at intervals of one year from the date of approval of the original HDE. This report, identified as "Annual Report" and bearing the applicable HDE 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 814.126.

In addition to the above, and in order to provide continued reasonable assurance of the safety and probable benefit of the HDE device, an HDE holder is required to maintain records of the names and addresses of the facilities to which the humanitarian use device (HUD) has been shipped, correspondence with reviewing institutional review boards (IRBs), as well as any other information requested by a reviewing IRB or FDA.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Each report, identified as an "HDE Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable HDE reference number, should be submitted to the address below.

Based on the protocol summary received on June 4, 2019, The Tether™ – Vertebral Body Tethering System Registry PAS: The Tether™ – Vertebral Body Tethering System Registry is a multi-center, single-arm, prospective post-approval US registry study to provide ongoing safety and probable benefit assessment of The Tether™ – Vertebral Body Tethering System in treatment of skeletally immature patients with idiopathic scoliosis. Skeletal maturity will be assessed using both the Risser grade and Sanders score. It is planned that all patients treated in the first 18-months (up to a maximum of 200 patients) should be enrolled and followed through 60-months from the time of each patient's index surgery, with interim visits at immediate post-operative up to 6-weeks, 6-months, 12-months, 24-months and 60-months post-procedure. Two-hundred (200) patients will be enrolled in this study, with at least 50 patients enrolled by 24-months, 100 patients enrolled by 36-months (should enrollment still be ongoing), and 200 patients enrolled by 48-months (should enrollment still be ongoing). This study will include a minimum of 10 US centers with sequential enrollment from each site that agrees to participate.

The primary safety endpoints are serious adverse events (SAEs), and device- or procedure-related AEs. Additional safety analyses will include the rate of AEs, including by relatedness to device or procedure and severity, time-to-event, including means and ranges if applicable, and rate of reoperation, including by type of reoperation.

The primary probable benefit endpoint is maintenance of major Cobb angle less than or equal to 40 degrees at 60-months post-surgery. Secondary endpoints will be analyzed up to 60-months post-surgery, and will include the following:

1. Curve progression no greater than 10 degrees of any secondary curve above or below the implant, or development of a new curve equal to or greater than 40 degrees.

2. Device integrity failures including cord breakage and screw migration.

3. Composite endpoint analysis (maintenance of major Cobb angle less than or equal to 40 degrees AND freedom from SAEs during The Tether™ – Vertebral Body Tethering System procedure and procedure/device related SAEs following surgery).

4. Analysis of the failure attributable to conversion to another spinal implant OR major Cobb angle that exceeded 40 degrees at defined follow-up visit OR any progression of the major curve at defined follow-up compared to baseline OR death OR permanent disability.

These safety and probable benefit data will be collected from each patient at pre-operative, immediate post-operative up to 6-weeks, 6 months, 12-months, 24-months, and 60-months post-operatively. This study is estimated to last a total of 84-months.

Descriptive statistics and 95% confidence intervals will be presented for all analyses. For continuous variables, means and standard deviations will be shown. For categorical variables, frequencies and percentages will be presented.

Please be advised that failure to comply with any post-approval requirement, including enrollment milestones at the above-referenced timepoints, constitutes grounds for FDA withdrawal of approval of the HDE in accordance with 21 CFR 84.82(c).

Please 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 HDE.

Please be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of an HDE Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (https://www.fda.gov/media/71327/download).

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

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). For more information on these requirements, please see the UDI website, https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

Before making any change affecting the safety or probable benefit of the HDE device, you must submit an HDE supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.108 and 814.39 except a request for a new indication for use of a humanitarian use device (HUD). A request for a new indication for use for an HUD shall comply with the requirements set forth in 21 CFR 814.110 which includes obtaining a new designation of HUD status for the new indication for use and submission of an original HDE application in accordance with §814.104. The application for the new indication for use may incorporate by reference any information or data previously submitted to the agency.

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 for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products, 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product postmarketing safety reporting is available at (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the postmarketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, 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 https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

FDA has determined that this device meets the conditions of either (I) or (II) under section 520(m)(6)(A)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). This device may be sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device (i.e., for profit) as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). The ADN for this device is determined to be 54,320 Vertebral Body Screw/Set Screw Assemblies, 54,320 Anchors, and 8,000 Cords. You must immediately notify the agency by submitting an HDE amendment (21 CFR 814.126) whenever the number of devices shipped or sold in a year exceeds the ADN. FDA may also inspect the records relating to the number of your devices distributed during any calendar year. See section 520(m)(6)(B) of the FD&C Act. If you notify the FDA that the ADN has been exceeded, or if FDA discovers through an inspection that the ADN has been exceeded, then you are prohibited to sell your device for profit for the remainder of the year. See section 520(m)(6)(D) of the FD&C

Act. If additional information arises regarding the ADN for your device, you may submit an HDE supplement (21 CFR 814.108) requesting that FDA modify the ADN based upon this additional information. See section 520(m)(6)(C) of the FD&C Act.

This device is indicated and labeled for use in pediatric patients or in a pediatric subpopulation and is permitted by FDA to be sold for profit in accordance with section 520(m)(6)(A)(i)(1) of the FD&C Act, and therefore will be subject to annual review by the agency's Pediatric Advisory Committee (PAC). As stated in section 520(m)(8) of the FD&C Act, the PAC annually reviews all HUDs described in section 520(m)(6)(A)(i)(1) of the FD&C Act, which are HUDs approved under an HDE that are intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs, and that are exempt from the profit prohibition, in accordance with section 520(m)(6) of the FD&C Act. See section 520(m)(8) of the FD&C Act, as amended by FDASIA.

The PAC reviews these devices to ensure that the HDE remains appropriate for the pediatric populations for which it is approved, in accordance with 520(m)(2) of the FD&C Act. The requirements under section 520(m)(2) of the FD&C Act include that (1) the target population of the device not more than 8,000 individuals in the United States; (2) the device would not be available to a person with the disease or condition without the HDE and there is no comparable device to available to treat or diagnose such disease or condition; and (3) the device does not expose patients to an unreasonable risk or significant risk of illness or injury and the probable benefit to health from the use of the device outweighs risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. The PAC will also conduct periodic review of adverse events for this device.

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 HDE by making available, among other information, a summary of the safety and probably benefit data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals. 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 HDE 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 HDE. 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 HDE submission with a copy of all final labeling. Final 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 labeling is identical to the labeling approved in draft form. If the final

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, unless otherwise specified, to the address below and should reference the above HDE number to facilitate processing.

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

If you have any questions concerning this approval order, please contact Stephanie J. Shedd at 301-796-6416 or Stephanie.Shedd@fda.hhs.gov.

Sincerely,

CAPT Raquel Peat, PhD, MPH, USPHS
Director
OHT6: Office of Orthopedic Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health