**February 17, 2021**

Additive Orthopaedics, LLC
% Janice Hogan
Partner
Hogan Lovells US LLP
1735 Market Street
Suite 2300
Philadelphia, Pennsylvania 19103

Re: H200001
HUD Number: 18-0405
Trade/Device Name: Patient Specific Talus Spacer
Product Code: QNN
Filed: June 30, 2020
Amended: December 4, 2020

Dear Janice Hogan:

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 Patient Specific Talus Spacer. This device is indicated for avascular necrosis of the ankle joint. The anatomical landmarks necessary for the design and creation of the Additive Orthopaedics Patient Specific Talus Spacer must be present and identifiable on computed tomography scan. 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 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 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 6 months from the day computed tomography scans are obtained.

Continued approval of the HDE is contingent upon the submission of periodic reports, required under 21 CFR 814.126, at intervals of one year (unless otherwise specified) 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 accordance with 21 CFR 814.124, an HDE holder is responsible for ensuring that a humanitarian use device (HUD) under an approved HDE is administered only in facilities having institutional review board (IRB) oversight. In addition, approval by an IRB or an appropriate local committee is required before the HUD can be used at a facility, with the exception of emergency use. An HDE holder is also required to maintain records of the names and addresses of the facilities to which the HUD has been shipped, correspondence with reviewing IRBs as well as any other information requested by a reviewing IRB or FDA (21 CFR 814.126(b)(2)).

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below.

1. The Patient Specific Talus Spacer Registry PAS is a prospective post-approval US registry study to provide ongoing safety and probable benefit assessment of the Patient Specific Talus Spacer in treatment of avascular necrosis of the ankle. Based on the protocol summary received on February 2, 2021, it is planned for full enrollment of the subjects within 24 months, for a total of 50 subjects. Once enrolled, the subjects will be followed through 60-months from the time of each patient's index surgery, with interim visits at immediate post-operative up to 6-months, 12-months and annually thereafter.

   The primary safety endpoint is proportion of patients who undergo a secondary subsequent surgical intervention (SSSI). Secondary safety endpoints include assessment of adverse events (AEs), device- or procedure related AEs, and serious AEs.

   The primary probable benefit endpoint is improvement in Visual Analog Scale (VAS) pain at 5 years compared to baseline. Additional analyses will be performed to observe improvement at 5-years post-procedure compared to baseline on ankle range of motion (ROM) and foot and ankle outcome scores (FAOS – includes Pain, Symptom, Sport/Rec, Activities of Daily Living [ADL], and Quality of Life [QoL].

   The data will be collected at various timepoints:

   Collected at Baseline Only
   - Age
   - Gender
   - Body Mass Index
   - Smoking Status
   - Laterality of Index Ankle
   - Prior Index Ankle Surgeries
   - American Society of Anesthesiologists Class
   - Implant Volume
   - Implant Material

Collected at All Timepoints

- VAS Pain
- FAOS
- Ankle ROM
- SSSI
- Adverse Events

Collected at Pre-Op, 6 months, 12 months, and annually thereafter

- X-ray of index ankle

Descriptive statistics 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.

From the time of study protocol approval, you must meet the following timelines for:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months
- Submission of Final study report: 3 months from study completion (i.e. last subject, last follow-up date)

In addition, you must submit separate periodic reports on the progress of Patient Specific Talus Spacer Registry PAS as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports (i.e., every 3 months), in addition to your periodic (6-months) PAS Progress Reports, until FDA notifies you otherwise.

For all other condition of approval studies, you must submit separate PAS Progress Reports for each study, every six (6) months for the first two (years) and annually thereafter, unless otherwise specified by FDA.

Each PAS report should be submitted to the address below identified as an "HDE Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable HDE reference number.

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 814.118(a) and 21 CFR 814.126.

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 in accordance with 21 CFR 814.118(a)(6)-(7).

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).

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 an 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 a 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 post-marketing 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 post-marketing 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 post-marketing 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 8,000 Patient-Specific Talus Spacers. You must immediately notify the agency whenever the number of devices shipped or sold in a year exceeds the ADN; we recommend submitting this information in an HDE report (See section 520(m)(6)(A)(iii)). 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.

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 Home Page 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 Jay Kadakia at 301-796-2672 or Jay.Kadakia@fda.hhs.gov.

Sincerely,

Raquel A. Peat -S3

CAPT Raquel Peat, Ph.D., M.P.H., USPHS
Director
OHT6: Office of Orthopedic Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health