November 17, 2023

restor3d, Inc.
Brianna Prindle
Head of Regulatory
311 W Corporation St
Durham, North Carolina 27701

Re: H230003
HUD Number: 21-0464
Trade/Device Name: restor3d Total Talus Replacement
Product Code: QNN QYQ
Filed: June 5, 2023
Amended: September 12, 2023

Dear Brianna Prindle:

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 restor3d Total Talus Replacement. The restor3d Total Talus Replacement Implant is indicated for:

- avascular necrosis of the talus
- avascular necrosis of the talus in addition to talar collapse, cysts or non-union
- large, uncontained, unstable, or cystic talar osteochondral defects with risk of collapse or talar osteochondral defects not responsive to traditional treatments
- non-union following talar fracture or talar extrusion, unresponsive to more conservative treatments

The implant is patient specific and is designed from computed tomography (CT) scan. The anatomical landmarks necessary for the design and creation of the restor3d total talus replacement implant must be present and identifiable on CT scan.

Based upon the information submitted, 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 available 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 all other applicable requirements, including those governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 6 months from the day that 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 must 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)).

You must obtain approval of your post-approval study (PAS) protocol within 60 days from the date of this order. 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 below. Your HDE supplement should be clearly labeled as an "HDE Post-Approval Study Protocol" as noted below 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.

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

Total Talus Replacement (TTR) PAS-You will perform a multicenter, single-arm, 5-year prospective study for patients who received the restor3d TTR device to evaluate the continued safety and probable benefit of the restor3d TTR device in commercial use in adults (≥22 years of age) for treatment of:

- Avascular necrosis of the talus
- Avascular necrosis of the talus in addition to talar collapse, cysts or non-union
- Large, uncontained, unstable, or cystic talar osteochondral defects with risk of collapse or talar osteochondral defects not responsive to traditional treatments
- Non-union following talar fracture or talar extrusion, unresponsive to more conservative treatments

It is planned for full enrollment of the subjects within 24 months, for a total of 50 subjects. This study will include a minimum of 5 U.S. centers, with a maximum of 20 patients at any one site that meets the selection criteria. The sample size should be adequate to allow for inclusion of a diverse patient population with

respect to age, sex, ethnicity, and race. Depending on the population enrolled for the study, oversampling may be necessary to ensure that the population enrolled is sufficiently representative of the US population. Once enrolled, subjects will be followed through 60 months from the time of each patient's index surgery, with interim visits at 3 months, 6 months, 12 months and annually thereafter.

The primary endpoint for this PAS is a composite of safety and probable benefit, which is the proportion of participants who pass safety and probable benefit outcomes at 5 years post-implantation. The safety endpoint is defined by the absence of a device-related serious adverse event (SAE) and a subsequent secondary surgical intervention (SSSI) on the affected joints. The probable benefit endpoint is defined by joint salvage with the restor3d implant in place.

Secondary safety endpoints include assessment of procedure-related SAEs, and device- or procedure-related adverse events (AEs). Secondary probable benefit endpoints include assessment of pain using the 11-point Pain Numeric Rating Scale (NRS), ankle Range of Motion (ROM), Foot and Ankle Outcome Scores (FAOS) Composite score, and FAOS Subscales (Pain subscale, Symptoms subscale, Sports/Recreation subscale, Quality of Life [QOL] subscale, and Activities of Daily Living [ADL] subscale).

Exploratory endpoints include x-ray assessments to evaluate the presence of AEs, tibiotalar alignment, talar tilt angle, Boehler's angle, talar declination angle and Meary's angle, patient preference questions (e.g., if the patient would choose to undergo this procedure again if given the option), and use of soft tissue attachment sites and any relationship to AEs or SAEs.

The data will be collected at various timepoints:

Collected at Baseline Only:

- Age
- Sex
- Race/Ethnicity
- CT Scan
- Indication for Use
- Surgical History
- Laterality of Index Ankle
- Implant Volume
- Use of Soft Tissue Attachment Site

Collected Annually Starting at 12 months:

- Preference Questions

Collected at All Timepoints (Baseline, 3 months, 6 months, 12 months and annually thereafter):

- BMI
- Smoking Status
- Working Status
- Ambulatory Status
- Comorbid Conditions
- 11-point Pain NRS

- FAOS Composite score, and FAOS Subscales (Pain subscale, Symptoms subscale, Sports/Recreation subscale, QOL subscale, and ADL subscale)
- Ankle ROM
- Safety Events: AEs, SAEs, SSSIs
- X-Ray (including intraoperative scan)

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

From the date of study protocol approval, you must meet the following timelines for the Total Talus Replacement (TTR) PAS:

- 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

In addition, you must submit separate periodic reports on the progress of the Total Talus Replacement (TTR) PAS as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the HDE approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports every 3 months in addition to your periodic (6-month) PAS Progress Reports, until FDA notifies you otherwise.
- Submit the Final PAS Report three (3) months from study completion (i.e., last subject's last follow-up date).

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 Studies Program Database Webpage, available at 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. Under 21 CFR 814.108, 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 Premarket Approval Application 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 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 Part 830 Subpart E). For more information on these requirements, please see the UDI website available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production and process controls (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 post-marketing safety reporting (21 CFR Part 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

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 Part 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.

This device may not be sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device. See section 520(m)(3) of the Federal Food, Drug, and Cosmetic 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 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 Zhijiang He at 301-796-2982 or Zhijiang.He@fda.hhs.gov.

Sincerely,

Jiping Chen -S

Jiping Chen, MD, PhD, MPH
Director
DHT6A: Division of Joint Arthroplasty Devices
OHT6: Office of Orthopedic Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health