DT MedTech LLC
% Marcos Velez-Duran
President
M Squared Associates, Inc
575 8th Avenue
Suite 1212
New York, New York 10018

June 4, 2019

Re: P160036
Trade/Device Name: Hintermann Series H3™ Total Ankle Replacement System
Product Code: NTG
Filed: August 24, 2016
Amended: January 5, 2017, May 19, 2017, June 12, 2017, July 10, 2017, September 12, 2017, September 25, 2017, October 24, 2017, May 29, 2018, and December 6, 2018

Dear Marcos Velez-Duran:

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 Hintermann Series H3™ Total Ankle Replacement System. The Hintermann Series H3™ Total Ankle Replacement System is indicated for use as a non-cemented implant to replace a painful arthritic ankle joint due to primary osteoarthritis, post-traumatic osteoarthritis or arthritis secondary to inflammatory disease. The device system is for prescription use.

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. 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 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 5 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 the 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. This report, identified as "Annual Report" 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 PMA 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.

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 a "PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

1. The first post-approval study is designed to evaluate the long-term safety and effectiveness of the Hintermann Series H3™ TAR System among patients included in the Primary Safety and Effectiveness (PSE) Cohort. A prospective, single-center, single arm study design with hypothesis testing will be used to determine the 10-year survivorship and effectiveness of arthroplasty using the Hintermann Series H3™ TAR System in comparison to historical literature controls for a legally marketed mobile bearing ankle. If possible, Performance Goals (PGs) similar to the original study, should be constructed for the 10-year endpoint. The PGs used in the PMA study are based on a prospectively defined, systematic meta-analysis of available published literature and registry data for the control (a legally marketed mobile bearing ankle). The study population will consist of all living subjects who participated in the PSE cohort, regardless of whether or not the patient has had a revision/removal followed through the 10-year post-operation visit. A follow-up rate of 85% is expected at each timepoint. Specific attention will be given to patients with the smaller sized tibial implants (i.e. 1, 2, and 3), as the results appear to show a lower overall effectiveness for patients with the smaller sized implants. Patients will undergo clinical and radiographic evaluation postoperatively at 5 and 10 years. The 5 and 10-year data will be collected as in the PSE cohort during the PMA study. You have agreed to take reasonable measures to avoid loss to follow-up and statistically analyze impact of any missing data.

   You have agreed to collect information about any reoperation, revisions or removals of the Hintermann Ankle device components, and effectiveness endpoints, including the American Orthopaedic Foot and Ankle Society, the survivorship (absence of removal/revisions to include polyethylene revision), and the percentage of subjects with a serious device-related adverse event

other than a revision or removal. Again, special attention should be paid to the patients receiving the smaller sized (Size 1, 2 and 3) tibial implants in case the trend of lower effectiveness results still continues. You have also agreed to collect information about all adverse events reported for these patients, including details of the nature, onset, duration, severity, relationship to the device, and relationship to the operative procedure and outcome. Additionally, you have agreed to provide a detailed explant analysis of any explanted devices during the PAS.

Every six months for the first two years and then annually until the study is completed you are to submit a progress report to the FDA that includes, but is not limited to, the status of site enrollment, the status of patient enrollment, the status of patient follow-up, and other milestones as it compares to the stated goals in the protocol. Please provide all safety and effectiveness data collected during the reporting period and provide an explanation for any delay in meeting the stated goals in the protocol.

You must also update your patient and physician labeling (via a PMA supplement) to reflect the 10-year findings, as soon as these data are available, as well as any other timepoint deemed necessary by FDA if significant new information from this study becomes available.

Be advised that failure to comply with any post-approval requirement, including the requirements to meet the enrollment, treatment and completion dates outlined above, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c).

2. You have agreed to perform a second post-approval study to evaluate the trend in performance between each implant size and assess the outcomes of the primary surgeon of the study (accounting for approximately 80% of the registry) compared to other surgeons that are less familiar with the device. You agree to use a prospective, multicenter, single arm study design, and hypothesis testing to evaluate the performance of the different implant sizes of the Hintermann Series H3™ TAR System compared to the Hintermann Series H3™ TAR System performance in the PSE cohort. Multiple investigators should be recruited so that one surgeon does not conduct the majority of the cases. At the time of this approval, there are minimal data for several tibial sizes (Sizes 1, 2, 5, and 6), with size 1 and 6 having n =1 and n =3, respectively. Therefore, additional patients in each size are needed to demonstrate that the trend for overall lower success scores in smaller sizes is not an artifact due to the low sample size. Furthermore, approximately 80% of the clinical data in the primary safety and effectiveness cohort was conducted by one surgeon. Additional surgeons unfamiliar with the device should be recruited to evaluate the impact of experience on overall outcomes.

   You have agreed to enroll 220 new study subjects and follow these subjects for 5 years. We strongly encourage that the majority of these subjects be enrolled in the United States. Enough subjects should be enrolled in each tibial size to be able to evaluate the trend in performance between each size. Study subjects will undergo clinical and radiographic evaluation postoperatively at 6 weeks, 6 months, and yearly afterwards. You have agreed to take reasonable measures to avoid loss to follow-up. A follow-up rate of 85% is expected at each timepoint.

   You have agreed to collect information about safety, including any reoperation, revisions or removals of the Hintermann Ankle device, and effectiveness endpoints, including the American Orthopaedic Foot and Ankle Society at 2 years or more, the survivorship (absence of

removal/revisions to include polyethylene revision), the percentage of patients subjects with a serious device-related adverse event other than a revision or removal within 2 years, VAS score, patient satisfaction, and either SF-36 or PROMIS for general well-being. You will also collect information about all adverse events reported for these patients, including details of the nature, onset, duration, severity, relationship to the device, and relationship to the operative procedure and outcome. Additionally, you have agreed to provide a detailed explant analysis of any explanted devices during the PAS. Failure to obtain adequate study subject numbers for each size could potentially result in requirements to update labeling with advisory statements regarding the affected sizes, or the Agency taking action to remove approval of the affected sizes.

Be advised that failure to comply with any post-approval requirement, including the requirements to meet the enrollment, treatment and completion dates outlined above, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c).

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.

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 a PMA 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 a PMA supplement that includes complete protocols of your post-approval studies described above. Your PMA supplements should be clearly labeled as a "PMA Post-Approval Study Protocol" as noted above and submitted to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA 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). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). 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 effectiveness of the PMA 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" https://www.fda.gov/media/81431/download.

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.

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 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 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 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 PMA 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 Kevin Go at 240-402-5983 or Kevin.Go@fda.hhs.gov.

Sincerely,

Mark N. Melkerson -S

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