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

July 1, 2016

Cartiva, Incorporated
Ms. Deborah Moore
Vice President, Regulatory, Clinical, and Quality Affairs
6120 Windward Parkway, Suite 220
Alpharetta, Georgia 30005

Re: P150017
Trade/Device Name: Cartiva Synthetic Cartilage Implant
Filed: May 1, 2015
Amended: May 1, June 15, August 31, November 23, 2015; January 19, February 11, May 18, 2016 and May 19, 2016
Product Code: PNW

Dear Ms. Moore:

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 Cartiva Synthetic Cartilage Implant. This device is indicated for use in the treatment of patients with painful degenerative or post-traumatic arthritis (hallux limitus or hallux rigidus) in the first metatarsophalangeal joint with or without the presence of mild hallux valgus. 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 2 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 from the date of approval of the original PMA. Two copies of 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. This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final 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. For more information on these requirements, please see the UDI website, http://www.fda.gov/udi.

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.

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. Two (2) copies of each report, identified as an "ODE Lead 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.

ODE Lead PMA Post-Approval Study – Metatarsophalangeal Joint Osteoarthritis as Compared to a Control: Long-Term Follow-up (MOTION Extend Study): The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The MOTION Extend Study is as follows:

Based on the study plan received on May 16, 2016 and amended on June 23, 2016, you will perform a PAS to extend the duration of follow-up to 60 months of patients treated with the Cartiva Synthetic Cartilage Implant (SCI) device in the original MOTION study. The study will evaluate the long-term safety and effectiveness of the Cartiva SCI device by following all available Cartiva patients from the pivotal study conducted in Canada and the United Kingdom. The sample size will include 135 Cartiva subjects (119 randomized and 16 roll-in) eligible for study participation. Assuming a 15% lost to follow-up rate, you estimate that 115 subjects will have 5-year device status determined. The post-approval study duration will be approximately 36 months as all the patients have reached 24 months prior to the start of this study.

You will collect data to assess the following primary and secondary study endpoints:

Primary Study Endpoints

The primary endpoint will evaluate the long-term safety of the Cartiva implant by demonstrating the following:

1. Durability of the implant over the longer term.

2. Assessment of no unanticipated safety concerns that arise after Month 24 up to 5 years. Addressed by:

    a. determining the incidence of serious device-related adverse events per year and overall from Month 24 to Year 5; and

    b. summarizing device-related radiographic major complications[1] over time from Month 24 to Year 5.

Secondary Study Endpoints

1. Evaluation of maintenance of range of motion;

2. Wear characteristics or device degradation for any Cartiva implant removed;

3. Pain and function over time (Visual Analog Scale [VAS] pain scores, Foot and Ankle Ability Measure [FAAM] Activities of Daily Living [ADL] function scores and FAAM Sports function scores); and

4. Evaluation of radiographic findings (radiolucency, bony reactions, and heterotopic ossification) looking at presence or progression from 24 months to 5+ years as well as correlation with the 5+ years clinical outcomes (effectiveness and safety).

The primary hypothesis of this extended follow-up post approval study is that the performance of the Cartiva SCI device implant removal rate at 5 years post-op is non-inferior to the rate expected assuming the same exponential removal rate observed during the first 24 months of follow up. The hypothesis test will be performed based on the 2-5 year data collected in this

[1] Major complications are radiographic findings assessed by an independent radiographic reviewer. These include absence of device displacement, device fragmentation, and avascular necrosis in the Cartiva group.

post-approval study, with expected cumulative event rate from 2 to 5 based on exponential survival equal to 13.5%. The hypothesis stated is:

H_0: $\pi_A > \pi_0 + \delta$
H_A: $\pi_A \leq \pi_0 + \delta$

where π_A is the true proportion of subjects expected to have revision in the 2-5 year period, π_0 is exponential removal rate from 2 to 5 years estimated based on the 24 month data, ($\pi_0 = 0.135$), and a non-inferiority $\delta = 0.10$.

In addition, the rates of Cartiva SCI device removal and conversion to arthrodesis over time will be computed and presented to assess device survivorship.

FDA will expect at least 85% follow-up at the 60-month time point to provide sufficient data to evaluate safety and effectiveness as well as the sensitivity analyses to address missing data.

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. 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" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm).

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" http://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 http://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 http://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 http://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 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 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
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If you have any questions concerning this approval order, please contact Jemin J. Dedania, MS, RAC at 301-769-6949 or jemin.dedania@fda.hhs.gov.

Sincerely,

William H. Maisel -S

William H. Maisel, MD, MPH
Deputy Center Director for Science
Center for Devices and Radiological Health