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**DEPARTMENT OF HEALTH & HUMAN SERVICES  
Food and Drug Administration  
Center for Devices and Radiological Health**

**Public Health Service**

**Brief Summary of the Orthopaedic and Rehabilitation Devices Panel Meeting –  
April 20, 2016**

**Introduction:**

The Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on April 20, 2016, to make recommendations and vote on information related to the Premarket Approval Application (PMA) for the Cartiva<sup>®</sup> Synthetic Cartilage Implant.

The sponsor has proposed the following Indications for Use (IFU):

“The Cartiva<sup>®</sup> Synthetic Cartilage Implant is intended for use in the treatment of patients with degenerative or post-traumatic arthritis in the first metatarsophalangeal joint in the presence of good bone stock along with the following clinical conditions: hallux valgus or hallux limitus, hallux rigidus, and an unstable or painful metatarsophalangeal joint.”

**Panel Deliberations/FDA Questions:**

**Panel Question 1:**

Please comment on a 15% non-inferiority margin used for the Cartiva clinical study in terms of effectiveness, safety, and overall success. If a 15% margin for overall success is an appropriate margin for this study, please explain your rationale. If the Panel does not believe this margin to be appropriate or clinically meaningful, please recommend a non-inferiority margin that you believe to be appropriate and clinically meaningful for this study.

The Panel generally believed that a 15% margin appeared to be appropriate for this study.

**Panel Question 2:**

Both groups experienced pain reduction. However, the reduction from baseline pain scores was substantially lower for Cartiva subjects compared to Arthrodesis subjects at the pre-specified primary time point of 1 year. Similar results for comparisons of pain reduction occurred at every time point from 6 weeks to 2 years. Please discuss the clinical interpretation of these findings for the Cartiva device group and the Arthrodesis control group.

The Panel generally felt that the clinical results in both groups were similar.

### Panel Question 3:

Arthrodesis was substantially better for the pre-specified primary functional assessment, FAAM Sports at Month 12. In examining change from baseline FAAM ADL (FDA requested post-hoc) scores, Arthrodesis subjects performed better than Cartiva subjects at every time point from Month 3 to Month 24. A responder analysis showed non-inferiority, but to be a responder, the only requirement is to not worsen by 8 or 9 points in terms of function. In consideration of these assessment criteria, please discuss the clinical interpretation of these findings for the Cartiva device group, in which the device is intended to maintain motion over time, and the Arthrodesis control group.

The Panel generally believed that function was an important assessment parameter. Concerns were expressed regarding the choice of the assessment tools for functional ability, the Foot and Ankle Ability Measure (FAAM) ADL (Activities of Daily Living) or FAAM Sports subscore measures. Also, concerns were expressed regarding the adequacy of the success criterion utilized for these assessment tools (losses from baseline measurements of up to 8 or 9 points).

### Panel Question 4:

The rate of Subsequent Secondary Surgical Intervention (SSSI) events among randomized Cartiva subjects through 24 months was 10%. This does not include the 18% of roll-in subjects and does not include 4 SSSI events that occurred after 24 months. There is an element of subjectivity for determining the threshold for surgical intervention in either the Cartiva or Arthrodesis groups. Please comment on whether or not SSSI patients in the Cartiva and the reported procedures for device removal following successful Arthrodesis should be successes or failures. Please discuss the long term clinical interpretation of these findings for the Cartiva device group and the Arthrodesis control group.

The Panel generally believed that SSSI incidents of 10% for new technology would be acceptable provided this rate does not worsen with longer term follow-up. The Panel also generally believed that it may be preferable to characterize some of the more minor revisions in the arthrodesis group, such as screw removals, as anticipated adverse events rather than as failures. The Panel also felt that long term clinical data interpretation would depend on the duration of follow-up as well as the specific type of SSSI.

### Panel Question 5:

The two devices have different criteria for determining radiographic success or failure. Please discuss the clinical interpretation of these findings for the Cartiva group, in which the device is intended to maintain motion over time, and the Arthrodesis control group which is intended to eliminate motion.

The Panel generally felt that the differing radiographic criteria for the two treatment groups were, in general, acceptable and appropriate for each of the treatments. Panelists discussed some further refinements which could be made to these criteria such as the incorporation of radiographic observations such as radiolucency, implant fractures, osteolysis, and heterotopic ossification. Use of computed tomography (CT) and kinematics for assessment of gait was suggested as additional modalities for assessment of subjects in future studies.

### Panel Question 6

Prospective subjects will likely have the impression that increased mobility will allow for greater function in Cartiva as compared to Arthrodesis. However, the level of function for Cartiva appears to be the same or worse than Arthrodesis from 3 months to 2 years. Does the Panel have any suggestions regarding the education of prospective subjects so they are able to make informed decisions with regards to realistic expectations and goals regarding function following Cartiva or Arthrodesis procedures? Can the Panel provide a discussion on how best to objectively capture patient preferences with regards to either procedure?

The Panel generally was concerned that the allure of preserving motion was fairly high for patients, and that the expectations for this device needed to be clearly identified so that the device could be labeled appropriately. The Panel recommended that patients be informed that while range of motion may be preserved with the Cartiva device, the functional ability attained with this device may not be substantially different than the functional ability attained following a fusion procedure.

#### Panel Question 7

Please comment on the need for PAS (Post Approval Study(ies)) and what questions should be addressed by such study(ies), should FDA determine that this PMA application is approvable.

The Panel expressed various concerns about the safety and effectiveness of the Cartiva device, as well as concerns about persistent pain in patients treated with the device. Overall, the Panel generally felt these concerns were mitigated by the ability of the device to retain range of motion. Panel members questioned the inclusion of hallux valgus and unstable joints in the proposed indications for use for the device, and recommended exclusion of these conditions from final device labeling. It was also recommended that any explanted devices be analyzed in retrieval studies and tissue studies. Panel members also recommended that, if possible, advanced imaging studies such as computed tomography (CT) and magnetic resonance imaging (MRI) be used. In general, the Panel believed that the existing cohort should be followed-up for 5 years total. The Panel also recommended that if a new cohort is studied, it should also be studied for 5 years with the implementation of additional exclusion criteria including hallux valgus, unstable joints, and possibly Coughlin and Shurnas Classification Grade 2 hallux rigidus. The Panel also recommended the inclusion of additional functional endpoints as being potentially helpful.

#### Panel Vote

The Panel voted on the safety, effectiveness, and risk benefit ratio of the Cartiva® Synthetic Cartilage Implant.

1) Is there a reasonable assurance that the Cartiva Synthetic Cartilage Implant is safe for use in patients who meet the criteria specified in the proposed indications for use described above?

On Question 1, the Panel voted 10 (Yes), 0 (Abstain), 2 (No) that the data shows a reasonable assurance that the Cartiva Synthetic Cartilage Implant is safe for use in patients who meet the criteria specified in the proposed indications for use described above.

2) Is there a reasonable assurance that the Cartiva Synthetic Cartilage Implant is effective for use in patients who meet the criteria specified in the proposed indications for use described above?

On Question 2, the Panel voted 9 (Yes), 0 (Abstain), 3 (No) that there is a reasonable assurance that the Cartiva Synthetic Cartilage Implant is effective for use in patients who meet the criteria specified in the proposed indications for use described above.

3) Do the benefits of the Cartiva Synthetic Cartilage Implant outweigh the risks when used in patients who meet the criteria specified in the proposed indications for use described above?

On Question 3, the Panel voted 8 (Yes), 2 (Abstain), 2 (No) that the benefits the benefits of the Cartiva Synthetic Cartilage Implant outweigh the risks when used in patients who meet the criteria specified in the proposed indications for use described above.

### **Public Speakers**

The following Open Public Speakers attended the meeting: 1) Paul Voorhorst, Ph.D., Vice President of Clinical Research- DePuy Synthes Joint Reconstruction, Mitek and Power Tools, on behalf of the Orthopedic Surgical Manufacturers Association (OSMA) and the following patients: Gail Butt, Nancy Schmelter, John O'Meara, and Janet Geisberger.

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