



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 –
February 19, 2016**

Introduction:

The Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on February 19, 2016 to make recommendations and vote on information related to the Premarket Approval Application (PMA) for the DIAM™ Spinal Stabilization System sponsored by Medtronic.

The sponsor has proposed the following indications for use:

“The DIAM Spinal Stabilization System is indicated for skeletally mature patients that have moderate low back pain (with or without radicular pain) with current episode lasting less than one year in duration secondary to lumbar degenerative disc disease (DDD) at a single symptomatic level from L2-L5.”

Panel Deliberations/FDA Questions:

Panel Question 1:

Study Population

Based upon the observations described regarding the study population in Section 1.2 of the FDA Executive Summary, please address the following questions:

- a. Please comment on the adequacy of the study population in this IDE clinical trial to support the proposed indications for use.

The panel generally believed that the heterogeneity of the study population impacted the ability of the study data to support the proposed indications for use.

- b. Please comment on the impact of the observations (e.g., heterogeneity, ODI severity) described in Section 1.2 in interpreting the results of this IDE clinical trial in the context of the DIAM investigational device for its proposed target population.

The panel generally believed that the study observations impacted the ability to interpret the results of this clinical trial. To address this concern, a new clinical study was recommended.

- c. Please comment specifically on the heterogeneity of the study population, and whether the clinical data provided in support of this PMA are poolable for the purpose of evaluating the safety and effectiveness of the DIAM Spinal Stabilization System for the proposed indications for use. Please comment regarding whether this clinical data requires stratification and analysis according to specific types of spinal pathology (i.e., disc herniation, spinal stenosis, facet degeneration, degenerative spondylolisthesis, low back pain associated with degenerative changes limited to the anatomic components of the intervertebral disc) in order to permit a clinically meaningful interpretation of the results of this clinical trial. If you believe that stratification of the study data according to clinical subgroups is necessary, which specific subgroups are recommended and how should these subgroups be defined?

The panel generally believed that stratification should be performed in the new clinical trial. The subgroups identified in question 1.c. may be adequate. In addition, it was suggested that stratification could be done by back pain only, with or without neurogenic pain, limited to single level involvement.

Panel Question 2:

Nonoperative Control Group and Nonoperative Therapies

Based upon the observations related to the study control and nonoperative therapies described in Section 1.2 of the FDA Executive Summary, please comment on the adequacy of the nonoperative control group in this IDE clinical trial as a comparator.

The panel generally believed that the control group in this clinical trial was not adequate based upon the variability of care provided, individualization of the care provided, small size of the control group, and high number of crossover patients.

Panel Question 3:

Study Endpoint and Timepoint for Assessment

Please comment on the adequacy of the primary effectiveness endpoint and evaluation timepoint of overall success at 12 months, considering the factors described relating to the study endpoint and timepoint for assessment in Section 1.2 of the FDA Executive Summary.

The panel generally believed that the study endpoints were generally acceptable with the exception that the adverse event definitions in this clinical study were unclear. The panel also believed that a 12 month timepoint for a study involving an implant was too short; a minimum of 2 years was suggested, along with post market surveillance.

Panel Question 4:

Role of the DIAM as a Primary Therapy versus Adjunctive Therapy with Direct Spinal Decompression

The sponsor provided a summary of soft tissue (e.g., ligamentum flavum) and/or bone resections described in the operative reports related to the implantation of the DIAM investigational device (refer to Section 1.2 of the FDA Executive Summary). These reported observations suggests that indirect and/or direct spinal decompression was performed in conjunction with the implantation of the DIAM investigational device in a number of cases within this clinical trial. Please comment on the significance and effect of the soft tissue and/or bone resections performed at the time of implantation of the DIAM

device, both in terms of understanding if this technology should be considered a primary treatment or an adjunctive treatment with direct spinal decompression, and in terms of interpreting the safety and effectiveness results, and investigational device treatment effect, in this IDE clinical trial.

The panel generally believed that the DIAM was used as a primary treatment in this clinical study; however, without additional information, the panel generally did not believe it was possible to categorize the DIAM as a primary versus adjunctive treatment.

Panel Question 5:

Radiographic Outcomes

The sponsor provided the results and analyses of radiographic outcomes related to spinous process erosions, spinous process fractures, and sagittal plane angular motion and translational motion. Considering the observations described on radiographic outcomes in Section 1.2 of the FDA Executive Summary, please address the following:

- a. Please comment on the clinical significance of the reported spinous process erosions for a device that relies upon the spinous processes to exert its treatment effect, as well as on the adequacy of the outcome analysis performed by the sponsor to assess the significance of the observed spinous process erosions.

The panel generally believed that the observed erosions may mean something clinically that we don't fully understand, and suggested longer term follow-up. Additionally, there was some concern regarding the animal study results, and the inflammatory responses observed in the explant analyses.

- b. Please comment on the clinical significance of the reported spinous process fractures for a device that relies upon the spinous processes to exert its treatment effect, as well as on radiographic plan to detect and identify the incidence of these fractures.

The panel generally believed that the observed spinous process fractures are of lesser importance but could be important depending on the location of the fracture in relation to the implant. In addition, more information on the incidence of the fractures in the long term would be helpful.

- c. Please comment on the clinical significance of these results, given the proposed intended use of the DIAM investigational device to provide stability during flexion and extension motions, as well as to stabilize yet preserve motion.

The panel generally believed that there was not adequate information to provide a response.

Panel Question 6

Post-Approval Study (PAS)

Based on concerns with the premarket study design, including a heterogeneous patient population, and in view of concerns regarding confounding variables related to treatment non-uniformity in both the DIAM and Crossover groups, the Agency has concerns that the sponsor's proposed continued

enrollment (extended follow-up of the DIAM and Crossover groups) of the IDE study may not be adequate. Should the Panel determine that the premarket data reach the threshold for providing a reasonable assurance of safety and effectiveness, the Agency requests that the Panel discuss the following:

- a. Please discuss your assessment of the adequacy of the sponsor's proposed continued enrollment PAS.

The panel generally believes that the proposed PAS was inadequate as a stand alone study, but could be informative regarding long term results.

- b. Does the Panel believe a new enrollment PAS is necessary? If yes:
 - Please discuss the appropriate patient population(s) (e.g., specific spinal pathology subgroup(s)) for a new enrollment PAS.
 - Please discuss the appropriate control group(s) for the target population for a new enrollment PAS, if you believe that a control group(s) is necessary.

The panel generally believes that a new enrollment PAS is necessary.

- c. Based on the incidence of adverse events and radiographic findings (e.g., spinous process erosions and spinous process fractures) beyond the 12 month timepoint in the premarket study, and based on the concern for potentially diminished effectiveness long term, please discuss the appropriate duration of follow-up for a PAS for assessment of continued long term safety and effectiveness.

The panel responded that as previously stated a study should have a minimum of 24 months follow-up with provision for longer term follow-up depending upon the issues identified at the time of device approval.

- d. Please discuss what the Panel proposes as an appropriate PAS study design (e.g., two arm observation cohort study, randomized controlled trial, etc.)?

Predisposing that this device is found safe and effective, the PAS should have safety and effectiveness components, and consider the use of an operative control.

- e. Please discuss if there are additional postmarket concerns that should be addressed if the device is approved.

Long term explant and retrieval analysis were recommended by the panel, as well as longer term investigations of the bone implant interface.

Panel Vote

The panel voted on the safety, effectiveness, and risk benefit ratio of the DIAM Spinal Stabilization System.

- 1) Is there a reasonable assurance that the DIAM Spinal Stabilization System 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 4 (Yes), 0 (Abstain), 7 (No) that the data shows reasonable assurance that the DIAM Spinal Stabilization System 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 DIAM Spinal Stabilization System 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 2 (Yes), 1 (Abstain), 8 (No) that there is reasonable assurance that the DIAM Spinal Stabilization System 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 DIAM Spinal Stabilization System 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 0 (Yes), 4 (Abstain), 7 (No) that the benefits of the DIAM Spinal Stabilization System 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) Kevin Stevens- Associate Director of Regulatory Affairs- DePuy Synthes Spine on behalf of the Orthopedic Surgical Manufacturers Association (OSMA) 2) Tom VanLandingham, a DIAM patient.

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