FDA PANEL QUESTIONS

Note: Please refer to Section 1.2 in the FDA Executive Summary for background information related to the FDA Panel Questions.

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Panel Non-Voting 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.

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.

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?

Panel Non-Voting 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.

Panel Non-Voting 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.

Panel Non-Voting 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.

Panel Non-Voting 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.

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.

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.

Reminder

- The discussion of a PAS prior to FDA determination of product approvability should not be interpreted to mean that FDA is suggesting that the product is safe and effective.

- The plan to conduct a PAS does not decrease the threshold of evidence required by FDA for product approval.

- The premarket data submitted to the Agency and discussed today must stand on its own in demonstrating a reasonable assurance of safety and effectiveness and an appropriate risk/benefit balance.

Panel Non-Voting 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.

a. 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.

Panel Non-Voting Question 6 (cont'd)

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.

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

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

Panel Voting Questions

The proposed target population for the DIAM Spinal Stabilization System consists of patients with moderate low back pain secondary to single level symptomatic lumbar degenerative disc disease (DDD). For the purpose of this study, the following definitions were utilized:

Low back pain is defined as persistent back pain, with or without radicular pain, with current episode less than one year in duration.

Degenerative disc disease is confirmed by patient history, physical examination, and radiographic studies with one or more of the following factors (as measured radiologically by MRI scans or x-rays):

- decreased disc height > 2 mm, compared to the disc space at the next adjacent (superior or inferior, whichever had the greatest height) spinal level
- scarring/thickening of the ligamentum flavum, annulus fibrosis, or facet joint capsule
- herniated nucleus pulposus

Panel Voting Question 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?

Panel Voting Question 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?

Panel Voting Question 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?

Thank You!