

FDA Draft Questions

May 22, 2013 Meeting of the Orthopaedic and Rehabilitation Devices Panel of Medical Devices Advisory Committee

Pedicle Screw Spinal Systems (for certain indications)

Please refer to the Regulatory Reference Sheet for additional information regarding classification procedures and definitions.

1. FDA has identified the following risks to health for traditional, rigid pedicle screw spinal systems based upon the input of the original classification panel, review of industry responses to the 2009 515(i) Order, the Manufacturer and User facility Device Experience (MAUDE) database, and FDA's review of the medical literature:
 - Malposition
 - Implant Loosening
 - Device Breakage
 - Device Malfunction
 - Disassembly
 - Bone Fracture
 - Graft Settling/Displacement
 - Loss of Correction
 - Pseudoarthrosis
 - Bleeding/Vascular Injury
 - Neurologic Injury
 - Back/Leg Pain
 - Dural Injury/CSF Leak
 - Wound Problems
 - Infection/Sepsis
 - Skin Irritation
 - Cardiac
 - Respiratory
 - Gastrointestinal
 - Revision Surgery
 - Death

Is this a complete and accurate list of the risks to health presented by traditional rigid pedicle screw spinal systems? Please comment on whether you disagree with inclusion of any of these risks, or whether you believe that any other risks should be included in the overall risk assessment of pedicle screw spinal systems. Risks associated with dynamic stabilization systems for fusion will be discussed below in Question 4.

2. According to 21 CFR 860.7(d)(1), "there is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence use to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness

or injury association with the use of the device for its intended uses and conditions of use.” In addition, according to 21 CFR 860.7(e)(1), “there is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.”

FDA believes that the available scientific evidence supports a reasonable assurance of safety and effectiveness of traditional, rigid pedicle screw spinal systems when intended to provide immobilization and stabilization of spinal segments as an adjunct to fusion in the thoracic, lumbar, and sacral spine as an adjunct to fusion in the treatment of degenerative disc disease (DDD), and spondylolisthesis other than either severe spondylolisthesis (grades 3 and 4) at L5-S1, or degenerative spondylolisthesis with objective evidence of neurologic impairment.

- a) Do you agree that the available scientific evidence is adequate to support the safety and effectiveness of traditional, rigid pedicle screw spinal systems for these indications for use?
 - b) Do the probable benefits to health from use of traditional, rigid pedicle screw spinal systems for these indications for use outweigh the probable risks to health?
3. FDA believes that the special controls (labeling, biocompatibility, sterility, and mechanical testing) can adequately mitigate the risks to health for traditional, rigid pedicle screw spinal systems when intended to provide immobilization and stabilization of spinal segments as an adjunct to fusion in the thoracic, lumbar, and sacral spine as an adjunct to fusion in the treatment of degenerative disc disease (DDD), and spondylolisthesis other than either severe spondylolisthesis (grades 3 and 4) at L5-S1, or degenerative spondylolisthesis with objective evidence of neurologic impairment. FDA believes the special controls also provide sufficient evidence of safety and effectiveness.

Do you agree that these special controls are adequate to mitigate the risks to health for traditional, rigid pedicle screw spinal systems for these indications for use? Please comment on whether you disagree with the inclusion of any of these special controls, or whether you believe any other special controls are necessary.

4. FDA believes that the safety and effectiveness of dynamic stabilization systems (DSSs), a subtype of pedicle screw spinal systems when intended as an adjunct to fusion, is not well established. FDA bases this determination on the lack of valid scientific evidence to support the safety and effectiveness for these uses. The potential risks to health associated with DSSs may not be the same as those identified for traditional, rigid pedicle screw spinal systems. Therefore, FDA does not believe that there is sufficient information to determine whether special controls can be established to assure the safety and effectiveness of DSSs intended as an adjunct to fusion. Please address the following questions:
- a) DSSs have different design features that allow bending or rotation while still facilitating fusion. Components used to achieve this flexibility include polymer cords, moveable screw heads, and springs. Please discuss the technological features that fall under the scope of DSS.

- b) Please state whether there are any differences in the risks to health for DSSs, as compared to traditional, rigid pedicle screw systems, and specifically identify any risks to health that have not been discussed in response to Question 1.
- c) Do you agree that the available valid scientific evidence is not adequate to support the safety and effectiveness of DSSs intended as an adjunct to fusion? If you do not agree, please explain by identifying and discussing the following:
 - i) the valid scientific evidence available in support of a reasonable assurance of safety and effectiveness of DSSs when intended as an adjunct to fusion; and
 - ii) special controls that you believe would be sufficient to mitigate the risks to health and provide a reasonable assurance of safety and effectiveness of DSSs intended as an adjunct to fusion.

5. Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:

I: Insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness or that application of special controls would provide such assurance, AND

II: If, in addition, the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

- a) The FDA believes that traditional rigid pedicle screw spinal systems could be eligible for classification as a Class III device, because they are permanent implants. However, the FDA believes that sufficient information exists to develop special controls that would provide reasonable assurance of safety and effectiveness.

Do you recommend Class II or Class III for traditional, rigid pedicle screw spinal systems as an adjunct to fusion for the treatment of degenerative disc disease (DDD) and spondylolisthesis other than either severe spondylolisthesis (grades 3 and 4) at L5-S1 or degenerative spondylolisthesis with objective evidence of neurologic impairment? Please provide a rationale for your final classification recommendation, taking into account the available scientific evidence, the special controls proposed in Question 3, and the criteria listed above for placing a device into Class III.

- b) Similarly, the FDA believes that DSSs could be eligible for classification as a Class III device, because they are permanent implants. In addition, the FDA believes that insufficient information exists to determine if general controls and special controls would provide reasonable assurance of safety and effectiveness.

Do you recommend Class II or Class III for DSSs when intended as an adjunct to fusion for any indication? Please provide a rationale for your final classification recommendation, taking into account the available scientific evidence, special controls you proposed in Question 4 (if any), and the criteria listed above for placing a device into Class III.

6. Following this panel meeting, FDA will work to update the existing pedicle screw spinal system regulation, 21 CFR 888.3070, based on the panel's recommendations for classification.
- a) The current regulation describes pedicle screw spinal systems used as an adjunct to fusion as intended for "skeletally mature patients" for the Class II indications for use (21 CFR 888.3070(b)(1)), while the regulation is silent with respect to skeletal maturity in the Class III indications for use (21 CFR 888.3070(b)(2)). However, FDA has cleared numerous pedicle screw spinal systems dating back to 1998 for general pediatric use (e.g., "pediatric patients"), as well as for specific pediatric indications for use (e.g., "adolescent idiopathic scoliosis," "spondylolisthesis/spondylolysis and fractures caused by tumor and/or trauma"), that incorporate the skeletally immature patient population. Consequently, FDA proposes to remove the "skeletally mature" terminology from the indications for use for this device type for either the Class II or current/existing Class III indications for use. Please comment on whether you agree with this proposal, or whether you believe that other terminology should be used in lieu of "skeletally mature," if any.
- b) There are various interpretations and definitions in the medical community related to degenerative disc disease (DDD).
- i) FDA's "Guidance Document for the Preparation of IDEs for Spinal Systems," issued on January 13, 2000, defines lumbar DDD as "back and/or radicular pain with degeneration of the disc as confirmed by patient history, physical examination, and radiographic studies with 1 or more of the following factors (as measured radiographically, either by CT, MRI, plain film, myelography, discography, etc.):
- instability as defined by 3mm translation or 5° angulation;
 - osteophyte formation of facet joints or vertebral endplates;
 - decreased disc height, on average by >2mm, but dependent upon the spinal level;
 - scarring/thickening of ligamentum flavum, annulus fibrosis, or facet joint capsule;
 - herniated nucleus pulposus;
 - facet joint degeneration/changes; and/or
 - vacuum phenomenon.

In addition, FDA-approved PMAs were based on IDE studies that enrolled patient populations that were primarily diagnosed with DDD but also included patients with grade 1 degenerative spondylolisthesis (PMA P050010) and subjects with a history of prior spinal procedures including discectomy, laminotomy, laminectomy, or nucleolysis at the target spinal level (PMA P040006).

As the regulatory definitions of DDD described above include posterior elements beyond the spinal disc that resides in the anterior column of the spine, would degenerative spine pathology (DSP) more aptly describe these findings? Please comment on whether you agree with this new terminology, whether DDD is adequate to describe the conditions above, or whether you believe that other terminology would be more appropriate.

- ii) Related to the question above, FDA's "Guidance Document for Industry and FDA Staff: Spinal Systems 510(k)s," issued on May 3, 2004, defines DDD as neck (cervical systems) or back (non-cervical systems) pain "of discogenic origin with degeneration of the disc confirmed by history and radiographic studies." Please comment on the adequacy of this regulatory definition, or whether you believe that additional details not captured in this definition should be described to define DDD, such as the need to distinguish between symptomatic (e.g., pain) and asymptomatic (e.g., spinal imaging findings) spinal degeneration, as well as the need to identify clinically relevant subgroups in the DDD or DSP population.

- c) 21 CFR 888.3070(b)(1) currently contains the requirement for a warning and a precaution in the labeling for the Class II indications.
 - i) 21 CFR 888.3070(b)(1) currently requires the following warning: "Warning: The safety and effectiveness of pedicle screw spinal systems have been established only for spinal conditions with significant mechanical instability or deformity requiring fusion with instrumentation. These conditions are significant mechanical instability or deformity of the thoracic, lumbar, and sacral spine secondary to severe spondylolisthesis (grades 3 and 4) of the L5-S1 vertebra, degenerative spondylolisthesis with objective evidence of neurologic impairment, fracture, dislocation, scoliosis, kyphosis, spinal tumor, and failed previous fusion (pseudoarthrosis). The safety and effectiveness of these devices for any other conditions are unknown." Given the findings presented to this Panel, FDA believes this warning is no longer relevant.

Please comment on whether or not removal of the warning is warranted, given that there is additional clinical data available since the creation of the original pedicle screw classification regulation.

- ii) 21 CFR 888.3070(b)(1) currently requires the following precaution: "Precaution: The implantation of pedicle screw spinal systems should be performed only by experienced spinal surgeons with specific training in the use of this pedicle screw spinal system because this is a technically demanding procedure presenting a risk of serious injury to the patient."

Please comment on whether inclusion, revision or removal of the precaution is appropriate.