

## **FDA PROPOSAL FOR THE RECLASSIFICATION OF THE INTERVERTEBRAL BODY FUSION DEVICE**

### **Regulatory History of the Intervertebral Body Fusion Device (Cage):**

The intervertebral body fusion device (cage) was first marketed in the United States, after the Medical Device Amendments of 1976 (the 1976 Amendments) to the Food, Drug and Cosmetic Act (the Act) (21 USC 360C) as Class III, post-amendments devices requiring an approved Premarket Approval Application prior to marketing.

The 1976 Amendments as amended by the Safe Medical Device Act (SMDA) of 1990 and the FDA Modernization Act (FDAMA) of 1997 provide regulations for the classification and regulation of medical devices intended for human use. FDA may elect to reclassify a medical device, including the Class III medical devices into a lower regulatory class that can reasonably assure their safety and effectiveness for their intended use.

The Act established three categories (classes) of medical devices depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three classes are Class I (general controls), Class II (special controls), and Class III (pre-market approval). General controls are sufficient to provide reasonable assurance of the safety and effectiveness of Class I devices. General controls include the following: prohibition against adulterated or misbranded devices, premarket notification (510(k)), banned devices, the quality system regulation that includes design controls and good manufacturing processes (GMPs), registration of manufacturing facilities, listing of device types, record keeping, etc.

Class II devices are those that cannot be classified into Class I because general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of such devices. These devices are regulated using special controls and general controls. Special controls include guidelines (guidance documents), performance standards, postmarket surveillance, clinical data, labeling, tracking requirements, and other appropriate actions the Secretary of the Department of Health and Human Services deems necessary to provide such assurance.

Class III devices are those for which insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of the safety and effectiveness. These devices are life sustaining, life supporting, or substantially important in preventing impairment of human health, or they present unreasonable risk of illness or injury. Class III devices are regulated by using "valid scientific evidence" to establish the safety and effectiveness of the device. Valid scientific evidence includes well-controlled investigations, partially-controlled studies, uncontrolled studies, well-documented case histories, and reports of significant human experience.

When most devices were classified in the late 1970s and early 1980s, most Class I and Class II devices were cleared for marketing via the 510(k) process. Some Class I devices were also exempted from 510(k) clearance. Now many Class I devices and a few Class II devices are exempt from 510(k) clearance because their safety and effectiveness can be reasonably assured by other general controls, particularly by the quality system regulation general control.

FDA has regulated the intervertebral body fusion device as a Class III, Post-Amendments device. Presently, there is not a codified regulation number and device identification for this device. New devices require an premarket approval under section 515 of the act to allow commercial distribution.

Since 1996, CDRH has approved seven intervertebral body fusion device PMAs: six PMA devices using autograft and one PMA device as a combination product. Table 1 identifies intervertebral body fusion devices which have received PMA approval:

**Table 1: Intervertebral Body Fusion Devices with PMA Approval**

Product	Application Holder	Application Number	Characteristics	Indication	Approval Date
BAK-L BAK Proximity BAK Vista	Sulzer- Spinetech	P950002	<del>///</del> Hollow, threaded cylinder <del>///</del> Titanium Alloy (BAK-L, Proximity) or PEEK (BAK Vista) <del>///</del> UHMWPE Endcaps <del>///</del> 2 device/spinal level <del>///</del> Used with autograft	Lumbar	09-20-96
Ray TFC Ray TFC Unite	Stryker Howmedica Osteonics	P950019	<del>///</del> Hollow, threaded cylinder <del>///</del> Titanium body <del>///</del> UHMWPE Endcaps <del>///</del> 2 device/spinal level <del>///</del> Used with autograft	Lumbar	10-29-96
Lumbar I/F Cage	Depuy Acromed	P960025	<del>///</del> Parallel box <del>///</del> PEEK with carbon fiber <del>///</del> Inferior/superior teeth <del>///</del> 2 devices/spinal level <del>///</del> Used with autograft	Lumbar	02-02-99
Interfix Interfix RP LT-Cage	Medtronic Sofamor Danek	P970015	<del>///</del> Hollow threaded cylinder <del>///</del> Titanium <del>///</del> Endcaps <del>///</del> 2 devices/spinal level <del>///</del> Used with autograft	Lumbar	05-14-99
BAK-C	Sulzermedica	P980048	<del>///</del> Hollow, threaded cylinder <del>///</del> Titanium body <del>///</del> UHMWPE Endcaps <del>///</del> 2 device/spinal level <del>///</del> Used with autograft	Cervical	04-20-01
Affinity	Medtronic Sofamor Danek	P000028	<del>///</del> Hollow, threaded cylinder <del>///</del> Titanium body <del>///</del> UHMWPE Endcaps <del>///</del> 2 device/spinal level <del>///</del> Used with autograft	Cervical	06-13-02
Infuse	Medtronic Sofamor Danek	P000058	<del>///</del> Hollow, threaded cylinder <del>///</del> Titanium body <del>///</del> UHMWPE Endcaps <del>///</del> 2 device/spinal level <del>///</del> Used with rhBMP2 and collagen sponge	Lumbar	07-02-02

## Risks to Health

FDA regulates many other spinal devices manufactured from similar materials using autograft or allograft as Class III, Class II, and unclassified devices. For example, spinal plates and pedicle screw systems, manufactured from titanium or titanium alloy, are regulated as a Class II medical devices. The vertebral body replacement device (VBR), manufactured either from titanium alloy or from polymers (e.g., polyetheretherketone) using autograft or allograft is also regulated as Class II medical devices.

FDA is not including for consideration combination products such as the intervertebral body fusion device using bone morphogenic proteins and scaffolds because of the new questions of safety and effectiveness raised by these combination products and the current inability to identify special controls to address the risks associated with these products.

In order to summarize the potential risks associated with the use of the intervertebral body fusion device using autograft, we reviewed the adverse event reports submitted to the agency via the Medical Device Reporting (MDR) System. The MDRs for the intervertebral body fusion received by the Agency from 1996 to the present are summarized in Table 2.

**Table 2: Adverse Events Reported via MDR**

<b>Adverse Event</b>	<b>Number of MDRs</b>	<b>Percent Total MDRs</b>
<u>Device Related</u>		
Displacement	23	25.8
Displacement & Fracture	1	1.1
Drop through during surgery	5	5.6
Endcap separation	2	2.2
Extrusion	9	10.1
Fracture	20	22.5
Unknown	29	32.6
<u>Patient Related</u>		
Bleeding	2	2.2
Pain	18	20.2
Infection	1	1.1
Surgical time extended	7	7.9
Pseudoarthrosis	15	16.9
Secondary Surgery	51	57.3

Nine literature articles, published between 1997 and 2003, in the bibliography for this proposed reclassification are indicative of the published literature on the intervertebral body fusion device using autograft. They also describe some potential risks of using these devices.

These articles, as well as others, and intervertebral body fusion device labels were reviewed in order to compile the risks identified in Table 3. Tables 3 also identifies the methods that will be proposed to ameliorate these risks.

**Table 3: Table of Potential Risks and Controls**

Potential Risk	Control
<u>Vascular injuries</u> : injuries to the vena cava; iliac vein hypogastric vein; segmental vein bleeder; sacral vein injury; superficial bleeder	Surgeon training Product labeling
<u>Neurological injuries</u> : dural tear, footdrop; nerve root injuries; foraminal stenosis; reflex sympathetic dystrophy; numbness, warmth or burning of legs; dyesthesia; paresthesia; shooting pain in lower back, radiculopathy with tingling extremities; back and leg pain with other symptoms; de-nervated abductor magnus muscle	Surgeon training Product labeling
<u>Urological events</u> : retrograde ejaculation	Surgeon training Product labeling
<u>Other</u> : bleeding, pain, infection, adverse tissue reaction, donor site pain	Surgeon training Biocompatibility data Material standards Product labeling
<u>Spinal events</u> : non-union, bone-fracture, subsidence, disc space collapse, failure of biological fixation	Surgeon training Product labeling
<u>Device Related Events</u> : implant loosening, implant end-cap separation, implant extrusion/migration, mal-positioned implant, implant fracture, deformation or wear.	Surgeon training Product labeling Mechanical testing standards Guidance documents Product labeling

**Special Controls:**

The special control used to ameliorate risks associated with the intervertebral body fusion device will be a guidance document entitled “Class II Special Controls Guidance: Intervertebral Body Fusion Device.” This guidance, will describe compliance with the following:

- ?? material standards (e.g. ASTM F-136-02: Standard Specification for Wrought Titanium-6Alumnum-4Vanadium ELI Alloy for Surgical Implant Applications; ASTM F-2026-02 Standard Specification for Polyetheretherketone (PEEK) Polymers for Surgical Implant Applications);
- ?? mechanical testing standards (e.g., F2077-03 Test Methods For Intervertebral Body Fusion Devices;
- ?? biocompatibility standards (e.g., ISO 10993 – Biological Evaluation of Medical Devices); and
- ?? labeling.

### **Proposed Reclassification:**

The Agency is proposing that the intervertebral body fusion device using autograft may be reclassified to a lower classification (Class II, special controls). Devices of this generic type have been regulated by CDRH since 1996. During this time the agency believes a sufficiently large body of clinical and preclinical data has become available that indicate that these generic devices when used in accordance with their approved labeling demonstrate relative safety and effectiveness. The information in the literature and MDRs have identified the greatest potential risks to health associated with intervertebral body device use. These risks to health are identified in Table 2. The Agency believes that all of these potential risks can be addressed via special controls in the form of a guidance document.

The applications affected by this reclassification would include all of those listed in Table 1. The products within this category are currently manufactured from the following materials:

- ?? Titanium alloy (Ti-6Al-4V) conforming to American Society Testing and Materials (ASTM) Standard F136
- ?? Polyetheretherketone (PEEK) reinforced with carbon fiber.

### **PROPOSED CFR LISTING for the Intervertebral Body Fusion Device**

(a) Intervertebral body fusion device—

(1) Identification. The intervertebral body fusion device is an implanted single or multiple component spinal device made from a variety of materials, including titanium alloys (e.g. Ti-6Al-4V) and polymers (e.g., polyetheretherketone (PEEK)). Such a spinal implant assembly consists of a construct intended to fill the intervertebral body space (e.g., hollow, threaded cylinder; mesh cylinder; fenestrated rectangular blocks; trapezoidal cubes; or wedge shaped solids). These constructs may contain end-caps. The implant is available in a range of sizes and may be angled to fit the patient's anatomical and physiological requirements. The implant may have a variety of features, some of which include spiked teeth on the inferior and superior surfaces of the implant and through-holes intended to allow bony ingrowth. The interbody fusion device is intended for spinal fusion procedures in skeletally mature patients with degenerative disc disease (DDD) at one or two levels from C2-C7 and L2-S1. DDD is defined as discogenic neck/back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients may also have up to Grade I spondylolisthesis or retrolisthesis at the involved level. The implant is intended to be used with autogenous bone graft and implanted via a laparoscopic, an open posterior approach, or an open anterior approach.

(2) Classification. Class II (special controls). The special control for the device is the guidance document entitled "Class II Special Controls Guidance: Intervertebral Body Fusion Device."

**Questions for the Panel:**

1. Please discuss the descriptive information and intended use presented in the reclassification identification.
2. Please discuss any specific pre-clinical testing criteria you believe are needed to characterize the intervertebral body fusion device.
3. Please discuss the risks to health for the intervertebral body fusion device.
4. Please discuss any other risks to health for these devices that have not been presented.
5. Please discuss any additional special controls needed to adequately control the risks associated with this device.