

**SUMMARY MINUTES**

**MEETING OF THE ORTHOPEDIC AND REHABILITATION DEVICES  
ADVISORY PANEL**

**OPEN SESSION**

**DECEMBER 11, 2003**

**Gaithersburg Holiday Inn  
Gaithersburg, MD**

**Meeting of the Orthopedic and Rehabilitation Devices Advisory Panel**

**Attendees  
December 11, 2003**

*Chairperson*

Michael J. Yaszemski, M.D.

*Acting Executive Secretary*

Janet L. Scudiero, M.S.

*Voting Members*

Maureen A. Finnegan, M.D.

Richard J. Friedman, M.D.

Kinley Larntz, Ph.D.

Stephen Li, Ph.D.

Sanjiv H. Naidu, M.D., Ph.D.

*Consultants*

Edward Y. Cheng, M.D.

Fernando G. Diaz, M.D., Ph.D.

*Consumer Representative*

Crissy E. Wells, R.T., M.B.A., M.H.S.A.

*Industry Representative*

Sally Maher, Esq.

*FDA Representative*

Celia Witten, M.D., Ph.D.

## **CALL TO ORDER**

**Acting Executive Secretary Janet L. Scudiero, M.S.**, called the meeting to order at 8:59 a.m. She noted that tentative panel meetings are scheduled for the following dates in 2004: March 22 and 23, June 3 and 4, August 12 and 13, and December 2 and 3. She read the appointment to temporary voting status statement; panel consultants Edward Y. Cheng, M.D., and Fernando G. Diaz, M.D., Ph.D., have temporary voting status for the duration of the meeting. Ms. Scudiero then read the conflict of interest statement; a full waiver is granted to Kinley Lamtz, Ph.D., for his financial interests in firms at issue that could be affected by the panel's recommendations. The Agency took into consideration other matters involving Edward Y. Cheng, M.D., Maureen A. Finnegan, M.D., and Stephen Li, Ph.D., all of whom reported current or past interests involving firms at issue but in matters not related to the day's agenda, and determined that they can participate fully in the panel's deliberations. Ms. Scudiero then turned the meeting over to Panel Chair Michael Yaszemski, M.D., Ph.D.

**Dr. Yaszemski** noted for the record that the members present constitute a quorum. He stated that the purpose of the meeting was for the panel to consider an FDA-initiated reclassification of the intervertebral body fusion device (cage) for spinal fusion procedures in skeletally mature adults with degenerative disk disease (DDD) at 1 or 2 levels from C2–C7 and L2–S1 using autogenous bone graft. The proposed device identification does not include combination products. He then asked the panel members to introduce themselves.

**Barbara C. Zimmerman, Chief, Orthopedics Devices Branch**, reviewed actions from previous meetings and updated the panel on the status of pending actions. FDA has approved five PMAs reviewed by the panel since the last panel meeting: the Independence iBot 3000 Mobility System; the Ascension MCP; the Infuse Bone Graft/LT-Cage Lumbar Tapered Fusion

Device; the Encore Keramos Ceramic-on-Ceramic Hip System; and the Osteonics ABC System and the Trident System, a ceramic-on-ceramic hip system.

Ms. Zimmerman then updated the panel on reclassification and classification actions. A reclassification of the metal-on-polymer, porous-coated, uncemented patellofemoral knee joint prosthesis and unicompartmental, metal-on-polymer, uncemented femoraltibial knee joint prosthesis into class II was announced in the *Federal Register* on March 24, 2003, and a reclassification final rule for the metal-on-polymer constrained hip joint prosthesis in class II was published in the *Federal Register* on April 30, 2002. A final rule to classify the resorbable calcium salt bone void filler into class II was also published in the *Federal Register* on June 2, 2003. A reclassification petition for metal-on-metal total hip arthroplasty devices was denied in September 6, 2002. The Agency is reviewing a reclassification petition for mobile bearing knees.

Finally, the Agency cleared a 510(k) for the DePuy Delta Shoulder, which is designed with the “ball” of the articulation incorporated into the glenoid prosthesis and the “cup” of the articulation incorporated into the humeral prosthesis (i.e., a reverse prosthesis). The device is indicated for patients with rotator cuff-deficient shoulder joints.

## **FDA PRESENTATION**

**Jodi N. Anderson, M.S., Orthopedics Devices Branch**, first described the medical device classification system devices pursuant to the 1976 amendments of the Food, Drug, and Cosmetic Act. She defined the three classes of medical devices and explained what general and special controls are. FDA can reclassify a medical device from class III into class II when the Agency can identify risks associated with the device and identify the manner in which those risks can be controlled by general and special controls. The Agency is required to follow the “least

burdensome” approach by classifying devices into the lowest class for which their safety and effectiveness can be reasonably assured.

Spinal cages are implanted, single- or multiple-component spinal devices that are intended to fill the intervertebral disc space. They are made from a variety of materials and come in a variety of shapes and sizes. They are intended for use in skeletally mature patients with degenerative disc disease (DDD), defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies and up to Grade I spondylolisthesis or retrolisthesis at the involved level. They are intended for use at one or two levels, between C2–C7 or L2–S1, with or without supplemental fixation. The devices are used with autogenous bone graft and are implanted through a laparoscopic, open posterior, or open anterior approach.

Spinal cages are class III postamendment devices. Since 1996, when they were first marketed, FDA has approved seven devices, six of which use autograft. One is a combination product that uses recombinant bone morphogenetic protein. Ms. Anderson listed the approved devices and their approval dates. These devices are well described in publicly available literature. Because a reclassification must rely only on publicly available information, only such information is referenced in the FDA presentation.

This publicly available data sufficiently identifies the device descriptions and specifications and provides a profile of device effectiveness and safety. A 2-year study of the Ray TFC found a 96 percent fusion rate at 2 years; a 4-year study of the BAK cage found a 95.1 percent fusion rate; and a 2-year study of the LT Cage achieved 93 percent successful fusion and 72 percent patient satisfaction. Other studies have been unable to duplicate those high success rates and have had high complication and revision rates. However, it is believed the failures may

be the result of technical difficulties and poor patient selection. The literature is clear that when studies are conducted in a rigorous and well-controlled fashion, the results are repeatable.

Device-related risks to health include loosening, end-cap separation, extrusion, migration, malpositioning, device fracture, deformation, and wear. Patient-related risks to health include vascular, neurological, and urological injury; infection; nonunion; vertebral fracture; subsidence; and end plate collapse.

FDA proposes reclassifying spinal cages from class III to class II. The Agency believes that the risks to health associated with the device can be controlled by general and special controls, and downclassification meets the FDA mandate to apply the least burdensome approach to device regulation. The proposal does not imply that FDA knows everything that there is to know about cages, only that the risks to health associated with the device can be controlled by general and special controls and no longer need to be controlled by a PMA.

FDA proposes the special control of a guidance document. The guidance would be modeled on existing guidance documents for spinal devices. The guidance document would provide information for manufacturers on the content and format of premarket notification (510(k)) submissions. It also would include sections on device description, labeling and training, and preclinical testing. FDA believes patient-related risks could be mitigated through the guidance document by providing requirements for surgeon training, product labeling, and materials biocompatibility. Device-related risks can be mitigated by surgeon training, product labeling, materials biocompatibility, and mechanical testing (static and dynamic compression; static and dynamic torsion; and subsidence) Prior to marketing a cage, a firm must submit a 510k which demonstrates their device meets the recommendations of the guidance document or provide equivalent assurances of safety and efficacy in an alternate way.

FDA proposes the following identification for the device: “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 disc space (e.g., hollow, threaded cylinder; mesh cylinder; fenestrated rectangular blocks; trapezoidal cubes; or wedge shaped solids). 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, through-holes intended to allow bony ingrowth, and end-caps. (Note that a device identification includes intended use). The intervertebral body 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. 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.”

Ms. Anderson then summarized the Agency’s questions for the panel’s deliberations.

### **Panel Questions for FDA**

The panel asked for clarification on the benefits of a guidance document versus developing a performance standard. FDA personnel noted that performance standards set forth criteria that all device sponsors must meet, whereas a guidance document permits *justifications*

for specific cases. It was noted that in the history of FDA, only one device performance standard has been issued.

Panel members also expressed concern that long-term data are not yet available for cages, but Agency staff noted that a guidance document functions not as a guarantee of efficacy but as a way to manage risks to health associated with devices. The Agency believes that the risks to health associated with cages can be managed through special controls. Part of the panel's charge is to evaluate whether that is possible. Panel members also discussed the merits of developing separate guidance documents for metallic and polymeric cages.

## **INDUSTRY PRESENTATION**

**Robert Zoletti, Director, Clinical and Regulatory Affairs, Cortek, Inc., representing OSMA**, stated that although OSMA supports the proposed reclassification, it is concerned that the scope of reclassification will be narrowed during the codification process in a manner that may not permit clearance of new devices under the 510(k) process.

He stated that cages have a long history, and their use is growing. Hundreds of thousands have been implanted throughout the world. Fusion rates of 90 to 100 percent have been reported, but the device is not a cure for all patients. Fritzell et al. (2001) concluded that lumbar fusion in a well-informed and selected group of patients with severe and therapy-resistant chronic low back pain can diminish pain and improve function more efficiently than commonly used nonsurgical treatment.

Mr. Zoletti listed the published articles from cage studies and highlighted their results. He listed the product codes for spinal devices with class II classification and noted that several spinal devices with these product codes are currently cleared via 510(k).

Class II vertebral body replacement devices are similar in design and material to cages. They replace the vertebral body and disc, and fusion between vertebrae is often possible. They are cleared for thoracic and lumbar spine use. No clinical test data are required for these 510(k)s, but mechanical testing data for static compression or compression bending, dynamic compression or compression bending, dynamic torsion and expulsion must be submitted in a 510(k). Similar performance testing can be required for cages.

Analysis of MDR data on cage-related adverse events indicates that the combination of biocompatibility testing, materials standards, mechanical testing, and labeling can address the types of adverse events reported to date. The rates are very low compared with the number of implants used. The same standards used in the regulation of other class II spinal implants—ASTM F-136, F-2026, and F-2077 and ISO 10993—along with FDA guidance documents, can be applied. The summary of risks to health and special controls information demonstrates that a reasonable assurance that safety and efficacy can be established using class II special controls.

OSMA offered several recommendations regarding reclassification into class II for the panel's consideration: 1) The Agency should allow use of supplemental internal fixation systems with cages, allow the use of cages with allograft bone, and other approved bone substitutes; 2) FDA should permit post approval PMA studies to end now and should permit IDEs in progress to close; 3) Spinal levels should not be limited to C2–C7 and L2–S1; 4) Clinical data should be required only for new designs; and 5) Companies should not be required to conduct surgeon training courses because cage product technology is so mature.

OSMA member companies are reluctant to release their PMA data to the public due to possible use by competitors. The possible reclassification of only current designs will be

disadvantage to PMA holders. PMA holders are continuing to consider whether to release additional PMA data.

**Scott G. Tromanhauser, M.D., M.B.A., Boston Spine Group, L.L.C.**, noted that OSMA had paid his travel expenses to the meeting. He supports the reclassification proposal. He has 10 years of primary and revision surgery experience with cages. The risks are now well understood and are similar to those of other spinal implants that are already class II devices (e.g., pedicle screws, spinal plates, and vertebral body replacement devices). The level of surgical skill required to use cages is similar to that required for other class II spinal implants and is commonly taught at the residency and fellowship level. The success of cages can be defined in two ways: technical success (“Did it fuse?”) and clinical success (“Did the patient achieve improvement in function and pain?”). In reclassifying cages, he recommended that FDA should: 1) not limit use of supplemental fixation with cages; 2) allow use of allograft bone and other bone substitutes; 3) not limit use to specific spinal levels; 4) not limit the surgical approach unless a device cannot be used in any other way; and 5) let surgeons, not companies, train surgeons. He stated that company training is always disappointing, and surgeons have many other training opportunities.

**Michel Leroux, Vice President, Research and Development, Biorthex, Inc., Montreal, Quebec**, stated that his organization concurs with Dr. Zoletti’s recommendations. More than 500 patients have been treated with Biorthex’s Actipore nitinol lumbar and cervical devices, with excellent clinical outcomes. The company supports reclassifying of cages into class II; however, it strongly believes that the general reference to generic materials in the identification does not support the complete safety and efficacy of devices made from such materials. Identification of only two materials may induce some bias in the evaluation of new

devices. Nitinol meets the requirements for the device and should also be specified in the identification, if FDA includes examples of device materials. Mr. Leroux provided information on nitinol's compliance with material standards, biocompatibility, and mechanical testing requirements for cages.

To avoid potential bias, the company proposes changing the identification to "The intervertebral body fusion device is . . . made from a variety of materials that fulfill the requirements of general and special controls" or, if a generic material list must be included, to "The intervertebral body fusion device is . . . made from a variety of materials, including titanium alloys (e.g., Ti-6Al-4V), polymers (e.g., polyetheretherketone [PEEK]), or nitinol (e.g., TiNi)."

### **Panel Questions for Industry Presenters**

Panel members noted the low rates of reporting to the MDR system and pointed out that the number of adverse events could be much [higher](#) than the actual number of events reported. They asked for data on the number of revision procedures performed with cages, the composition of vertebral body replacements, and use of the devices at other spinal levels. Dr. Zoletti did not have the data available but indicated that individual manufacturers might have it. Dr. Tromanhauser noted that most revisions are the result of surgeon failures due to various factors, such as inexperience and inappropriate device placement.

Panel members also expressed concern that even though the devices depend on fusion for success, no performance test for fusion potential exists; they wanted to be sure that the current standards for testing will work for devices of different shapes and materials. In addition, no tests for fusion or fracture are currently required. Panel members discussed methods for assessing

stability and fusion in the long-term and the difficulty of determining success. Even with the best imaging methods, evaluation is difficult.

Panel members also raised concerns about surgeon training, noting that surgeons not based at research centers are at a disadvantage. Other topics of concern included the effects of wear debris from polymeric cages and the need for a patient-selection algorithm, given the role of patient selection in success of the cages.

## **OPEN PUBLIC HEARING**

No comments were made.

## **PANEL DELIBERATIONS**

Dr. Witten clarified that FDA's proposal is to reclassify all of the existing PMA devices except for the combination device. The guidance document may need to specify "with or without external fixation." The Agency can only reclassify devices it has already approved. New devices are evaluated for substantial equivalence; FDA might require additional information as part of the review process. Downclassification leaves the door open for different types of devices, as long as the manufacturer demonstrates substantial equivalence.

**Panel Discussant Fernando Diaz, M.D., Ph.D.**, discussed the importance of patient selection. Spine surgeons have to make specific decisions, based on the device indications, to choose the right tool for a given patient to achieve the appropriate outcome. In the wrong person, even the best tool will fail. If a patient has comorbidities, the device may fail through no fault of the device or the surgeon. Cages come in variety of shapes, sizes, and materials. Those

characteristics affect the success and failure of the procedure, and the decisions of the surgeon consequently play a critical role.

Dr. Diaz said that clinical success is the most important consideration: Are the patient's pain and neurological problems resolved? If so, device performance is not a concern, and the outcome is considered satisfactory. The reverse situation is more common: The patient has outstanding mechanical success and fusion, but the pain and neurological problems continue. The cage devices are comparable to vertebral body replacement devices in many ways, and those devices are already in class II.

Panel members discussed how the issue of surgical approach could be addressed in a guidance document. Dr. Witten replied that the Agency proposes to reclassify the devices generically. Products do not have generic instructions for use: Device sponsors will submit specific instructions for each device, and the Agency will determine whether the device is substantially equivalent to what is on the market. It was noted that the likelihood of fusion is lower with a posterior approach because the procedure destroys the *facet* creating an unstable spine.

The panel also discussed whether both metal and polymer devices could be reclassified with a single guidance document special control. PEEK devices may need different special control requirements due to breakage and wear debris; moreover, tiny changes in the polymer formulation can affect device performance. The panel was divided as to whether to consider the devices separately. Although the devices appear to be safe and effective, MDR data are not the best indication of device performance once a device is on the market. Cervical devices will not necessarily work in the lumbar region, although lumbar devices may work in the cervical region.

FDA staff noted that any change to a polymeric material would be considered a new material and would be reviewed.

The panel was concerned that fracture testing was not a requirement. Dr. Li clarified the differences between fracture, fatigue, and static testing.

Panel members raised the issue of adjacent segment disease, but it was pointed out that the devices, by immobilizing a spine segment, increase the load above and below. The device itself plays little role in additional disease. The probability of fusion is increased with PEEK devices because they are more load sharing than load bearing.

**Question 1: Please discuss the descriptive information and intended use presented in the proposed reclassification identification.**

The panel discussed the descriptive information and intended use separately. Panel members had a wide spectrum of opinions. The main disagreement concerned whether one guidance document can adequately address both metal and polymeric devices or two guidance documents should be issued. Several panel members believed that metal and polymeric devices should be treated separately. Panel members were concerned about the lack of testing for fracture toughness and possible long-term problems with wear particles. Dr. Witten clarified that one classification could cover the range of materials and that a guidance document could be written to cover a range of materials. The panel concurred that the intended use provided in the device identification is satisfactory.

**Question 2: Please discuss any specific preclinical testing criteria you believe are needed to characterize the intervertebral body fusion device.**

The panel concurred that the existing testing is appropriate; the testing should be the same as that specified for intervertebral body replacement devices, with the addition of fracture toughness testing. If a device fractures during testing, then wear debris testing might be

appropriate. Devices should meet the specifications for use in the lumbar region, even if they are intended primarily for use in the cervical region, because of the possibility of off-label use.

**Question 3: Please discuss the risks to health for the intervertebral body fusion device.**

The panel agreed that the individual surgeon is an important factor in risks to patient health because of the importance of patient selection and technique. Attention should be paid to training surgeons in use of the devices. Additional concerns were raised about adjacent segment disease; however, that is not affected by the properties of the device used to achieve fusion. The panel concurred that some manner of company contribution to training is appropriate until use of cages are considered a regular part of spinal surgery training. Companies can work with professional groups to provide training.

**Question 4: Please discuss any other risks to health for these devices that have not been presented.**

Ms. Anderson noted that the panel had answered the question in its earlier discussion.

Panel members had no additional comments.

**Question 5: Do you believe special controls can be developed to adequately control the risks associated with this device?**

The panel agreed that special controls can adequately control the risks associated with the device. Separate guidance documents might be necessary for different types of devices. The panel expressed concerns about long-term follow-up. Some members believed that device tracking was appropriate in light of the lack of long-term data on issues such as effects of wear particles and cord problems. Although some panel members expressed concern that the current preclinical testing is unable to determine which cages will fail, panel members pointed out that

the fusion process itself is the result of osteoconductive tissue placed in the device and the ability of the body itself to complete fusion.

Ms. Maher noted that most patients do not want to be tracked and that tracking should be done only if there is a serious risk to patient health. Other fusion devices on the market are in class II and raise similar issues as the intervertebral body fusion devices under consideration. In addition, vertebral body replacements are made of PEEK and are not raising the issues the panel discussed. Finally, FDA continually deals with 510(k)s and is skilled at distinguishing between types of changes in device design. 510(k) review is appropriate for some kinds of design changes while significant design changes would require a PMA.

#### **CLASSIFICATION QUESTIONNAIRE AND SUPPLEMENTAL DATA SHEET**

The panel completed the General Device Classification Questionnaire and Supplemental Data Sheet with the assistance of **Marjorie Shulman, Premarket Notification Staff**. The panel reached consensus that the intervertebral body fusion device could be classified into Class II. The panel recommended that the special control for the device be a guidance document that would include requirements for clinical data; device tracking limited to the length of time required to achieve fusion; and testing guidelines, including analysis of retrieved specimens and fracture toughness testing along with the existing standards.

The panel was divided on the need for device tracking; some panel members believed that it would be holding class II devices to a standard higher than class III devices, would be difficult and costly to implement, and would be an undue burden on the industry. However, it was pointed out that long-term data are not yet available, and examples abound of problems arising with devices after they reach the market. The oncological potential of a device is not

realized after just one or two years. The panel agreed to limit tracking to the time required to accomplish fusion. Members decided against requiring performance standards, because of the long time needed for their implementation and their immutability.

In completing the Supplemental Data Sheet, the panel referenced its earlier discussions. It recommended that the proposed reclassification into class II have high priority. They believed that general and special controls can control the risks to health associated with use of the device, as discussed during the meeting. They noted that the special control guidance document could reference existing FDA guidance documents and consensus standards applicable to the device, including ASTM and ISO standards for fracture toughness, fatigue, and material properties, as discussed during in the meeting.

#### **VOTE**

The panel voted unanimously (6-0) to recommend reclassification of cage devices from class III to class II, pursuant to the panel's responses to the General Device Questionnaire and Supplemental Data Sheet.

#### **POLL**

When asked to state the rationale for their vote, panel members stated that with the special controls recommended, reasonable assurance of safety and effectiveness can be provided. One panel member suggested that surgical approaches should be deleted from the device identification and that addition of allografts should be considered. Several panel members expressed confidence in the devices and suggested that they should be allowed at multiple points along the spinal column.

## ADJOURNMENT

Dr. Yaszemski thanked the participants and adjourned the panel at 2:12 p.m.

I certify that I attended this meeting of the  
Orthopedic and Rehabilitation Devices  
Advisory Panel on December 11, 2003, and that  
these minutes accurately reflect what transpired.

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Janet L. Scudiero, M.S.  
Acting Executive Secretary

I approve the minutes of the December 11, 2003,  
meeting as recorded in this summary.

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Michael J. Yaszemski, M.D.  
Chairperson

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