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Subject: Review Memo for Reclassification Petition for Mobile Bearing Knees

To: The Record, Reclassification Petition for Mobile Bearing Knees

Summary:

This petition, sponsored by the Orthopedic Surgical Manufacturers Association (OSMA), was officially filed on June 13, 2003. An amendment to the petition, in response to the FDA deficiency letter of February 18, 2004, was dated March 31, 2004, and received April 1, 2004.

This petition seeks reclassification of mobile bearing knee prostheses from post-amendment Class III Pre-Market Approval (PMA) status to Class II Pre-Market Notification (510k) status. These mobile bearing knees are currently Class III PMA devices. This petition breaks the mobile bearing knee prostheses into two general groups: mobile bearing total knees and mobile bearing unicompartmental knees.

Presented in this petition are:

- ?? A brief introduction to the petition (see Section I).
- ?? General device information and proposed intended use (see Section II).
- ?? Proposed device descriptions for the Code of Federal Regulations (CFR) (see Section III).
- ?? The regulatory history of the devices considered for reclassification (see Section IV).
- ?? Basis for the petition (see Section V).
- ?? A summary of test results on wear, kinematics, and biomechanics from more than 45 articles published in peer-reviewed journals (see Sec. VI).
- ?? A summary of unpublished clinical data from seven on-going investigational device exemption (IDE) clinical studies and two large international clinical outcomes studies (see Section VII).
- ?? A summary of published clinical data from more than 50 articles published in peer-reviewed journals, together with a meta-analysis comparing clinical outcomes for different mobile bearing knees, and a meta-analysis comparing survivorship of mobile bearing knees versus fixed bearing knees (see Section VIII).
- ?? A listing of adverse events reported through the FDA's Medical Device Reporting (MDR) system (see Section IX).
- ?? A risk analysis, and suggested special controls to address the identified risks, such as labeling, preclinical tests and test methods (see Section X).
- ?? A list of mobile bearing knees currently or previously on the market, including 46 devices that are available internationally, five of which are also available in the U.S. (see Section XI).
- ?? Letters in support of the reclassification petition from orthopedic surgeons (see Appendix 1).

- ?? A summary of published literature from more than 40 articles published in peer-reviewed journals on the subject of ‘wear in total knee arthroplasty’ (see Appendix 1a of Amendment 1, Response to FDA letter of 2/18/04).
- ?? A description of the many different types of mobile bearing knee designs, their characteristics, biomechanical advantages/disadvantages, survival rates, risks, and proposed controls (for the identified risks) for each of the different device designs (see Appendix 1c, Amendment 1, Response to FDA letter of 2/18/04).
- ?? A summary comparing the clinical results for various mobile bearing knee device designs with fixed bearing devices (see Appendix 1d, Amendment 1, Response to FDA letter of 2/18/04).

Intended Use:

It is believed by FDA that patient indications for each device type (total knee and unicompartmental knee) are sufficiently different to warrant separation of the two devices.

Mobile Bearing Total Knee

The mobile bearing total knee is a device intended to be implanted to replace a knee joint. The device is indicated for:

- ?? Patients with knee pain and disability due to rheumatoid arthritis, osteoarthritis, traumatic arthritis, polyarthritis, collagen disorders and/or avascular necrosis of the femoral condyle
- ?? Post-traumatic loss of joint configuration (particularly when there is patellofemoral erosion, dysfunction, or prior patellectomy)
- ?? Moderate valgus, varus, or flexion deformities
- ?? The salvage of previously failed surgical attempts if the knee can be satisfactorily balanced and stabilized at the time of surgery.

The device may be used with or without bone cement.

No further device design specific indications were provided for the various types of mobile bearing total knees.

Mobile Bearing Unicompartmental Knee

The mobile bearing unicompartmental knee is a device intended to be implanted to replace part (one compartment) of a knee joint. The device is indicated for:

- ?? Patients with knee pain and disability due to osteoarthritis or traumatic arthritis
- ?? Previous tibial condyle or plateau fractures with loss of anatomy or function
- ?? Varus or valgus deformities
- ?? Use with an intact anterior cruciate ligament (ACL)
- ?? Revision of previous unicompartmental arthroplasty procedures

The device may be used with or without bone cement.

Device Description/Principle of Operation:

The sponsor has proposed the following classification description for mobile bearing total knees and mobile bearing unicompartmental knees:

Mobile Bearing Total Knee

‘Knee joint patellofemorotibial metal/polymer mobile bearing cemented or porous coated uncemented prosthesis’.

A knee joint patellofemorotibial metal/polymer mobile bearing cemented or porous coated uncemented

prosthesis is a device intended to be implanted to replace a knee joint. The device permits either unconstrained or constrained rotation of the articular surface in the transverse plane and may or may not permit limited anteroposterior and/or mediolateral movement of the articular surface upon the tibial component. It has not linkage across the joint. The device may use affixed structural porous metal in place of the porous coating. This generic type of device is designed for use with bone cement and/or to achieve biological fixation to bone without the use of bone cement.

Mobile Bearing Unicompartmental Knee

‘Knee joint femorotibial (unicompartmental) metal/polymer mobile bearing cemented or porous coated uncemented prosthesis’.

A knee joint femorotibial (unicompartmental) metal/polymer mobile bearing cemented or porous coated uncemented prosthesis is a device intended to be implanted to replace part of a knee joint. The device permits either unconstrained or constrained rotation of the articular surface in the transverse plane and may or may not permit limited anteroposterior and/or mediolateral movement of the articular surface upon the tibial component. It has not linkage across the joint. The device may use affixed structural porous metal in place of the porous coating. This generic type of device is designed for use with bone cement and/or to achieve biological fixation to bone without the use of bone cement.

Risk to Health /Special Controls

The sponsor performed a search of the MDR reporting information on FDA’s MAUDE website database which yielded 385 reports. The dates searched ranged from November 15, 1993 to December 31, 2002. All hits were from the DePuy LCS Mobile Bearing Knee System, the only approved mobile bearing knee system on the market in the U.S. during this time. The 385 reports contained 365 adverse events, of which 333 were reported as injuries, 29 as malfunctions, 2 were other/no answer, and 1 report was submitted as a death. The event descriptions are included in Section IX. The greatest number of adverse events were reported for pain (with effusion, hemarthrosis, or swelling), fractured bearings, and loosening, respectively.

The risks to health presented in this petition have been grouped into three general categories: infection, adverse tissue reaction, and loss or reduction of joint function/revision (see Section X). These risks are evaluated in two tables using a common engineering tool, a Failure Modes and Effects Analysis (FMEA). Table 5 (in Section X) contains the hazards common to both fixed and mobile bearing knees, while Table 6 contains hazards deemed specific to mobile bearing knees, exclusively. Each hazard (risk) is identified along with ways they can be controlled to reduce the potential risk to the patient. Finally, special controls are identified for each of the hazards. Many of the common risks can be mitigated by material standards, proper device design, labeling, Good Manufacturing Practices (GMP) and Quality System Regulations (QSR). As noted in Table 5, most risks identified are common to both fixed and mobile bearing knees. Only two hazards were identified as unique to mobile bearing knees, and they are related to ‘loss of reduction of joint function/revision’. Specifically, the potential for the mobile bearing to rotate beyond design objectives and the potential for greater wear due to additional articulating surfaces were the hazards cited as uniquely related to the design of mobile bearing knees.

The sponsor believes that risks associated with mobile bearing knees are known, and can be mitigated to acceptable levels with the general and special controls available to the FDA for other class II knee devices (e.g., FDA guidance documents, ASTM/ISO standards, labeling restrictions - indications/contraindications/warnings, etc.) to provide reasonable assurance of safety and efficacy. In

addition, suggested tests and test methods for mobile bearing knees are provided. In the original submission none of the suggested testing differed from what is currently required by FDA for evaluating fixed bearing knee devices.

However, as noted in the tables in appendix 1c of the March 31, 2004, amendment, there are numerous 'sub-categories' of the two types of mobile bearing knees identified above. These include devices with multidirectional platforms, rotating platforms, meniscal bearings, tricompartmental (mobile bearing patella), bicompartamental (femorotibial – total), unicompartamental, cone-in-cone, tibial tray post, longitudinal curved tracks, with and without rotational stops, and all with varying levels of femorotibial congruency. In Section XI of the original submission the sponsor provides a listing of 46 mobile bearing devices that are currently, or were, on the market either in the U.S. or overseas. They represent a wide variety of design approaches to mobile bearing knees, as noted above. In the U.S., only the DePuy LCS Rotating Platform, LCS Meniscal Bearing, LCS Unicompartamental Knee, P.F.C. Sigma Rotating Platform, P.F.C. Sigma Stabilized Rotating Platform, and Biomet's Oxford Meniscal Unicompartamental Knee have been approved for use.

Due to the unique risks that may exist within each of the various designs it may only be possible to evaluate these designs on a case by case basis. One set of special controls may not be appropriate to encompass the whole range of mobile bearing knees. These concerns were addressed to OSMA in the FDA letter of February 18, 2004. Their March 31 amendment attempts to address these concerns.

In response to the FDA questions posed in the 2/18/04 letter, the sponsor did identify additional risks unique to mobile bearing knees. These included 'spinout' of the tibial bearing insert, disassociation of the insert from the tibial tray, and insert deformation due to overhang. The sponsor also provided specifics on preclinical testing (special controls) to address these risks. In appendix 1c of the March 31, 2004, amendment, descriptions of preclinical testing to evaluate characteristics unique to mobile bearing knees were provided. In particular, standardized wear test methods originally developed for fixed bearing knees (ASTM F-1715 "Standard Guide for Wear Assessment of Prosthetic Knee Designs in Simulator Devices, and ISO 14243-1, "Implants for Surgery – Wear of total knee joint prostheses – Part 1: Loading and displacement parameters for wear-testing with load control and corresponding environmental conditions for test") were noted along with two potential methods for evaluating backside wear (wear between the tibial tray and tibial insert). It was also suggested that particulate analysis (size/morphology/quantity) of wear particles be performed and compared with that seen from a clinically successful predicate control to determine if there is an increased risk of osteolysis due to the mobile bearing design (i.e., dual articulating surfaces). 'Spinout' was noted as a risk unique to mobile bearing knees. 'Spinout' is defined as, "excessive rotation of the tibial insert resulting from at least one femoral condyle riding up and over the lip of the insert such that the femoral condyle disassociates from the inserts articular surface". The sponsor states this should be evaluated to limit or eliminate the potential for bearing spinout. They suggest it may be assessed using modified constraint testing standard ASTM F-1223 (Standard Test Method for Determination of Total Knee Replacement Constraint) after adapting for physiologic compressive loads, rotary torques, and varus moments that are deemed to be causative of insert spinout.

The risks of disassociation of the insert from the tibial tray or increased impingement of the insert against other portions of the device due to design (e.g. sliding tracks, captured tibial tray posts, etc.) have also been identified. The sponsor states that this should be evaluated to determine that there is not an increased risk of occurrence, and that a successful result (insert does not bind or disassociate under

physiological loads) would provide reasonable assurance that it will not occur during normal use.

Overhang deformation of the polyethylene tibial insert is another risk unique to mobile bearing knees that was identified in the petition. Overhang refers to any portion of the tibial insert that is not directly supported by the tibial tray. Mobile bearing knees should be designed to limit overhang and/or tested to determine if any overhang presents a new failure mechanism by restricting rotation due to deformation or increasing wear due to deformation. Although there is no standard for this evaluation, the sponsor suggests this can be assessed during knee simulator wear testing.

The sponsor also states that those mobile bearing knees that utilize a mechanical stop to limit or eliminate rotation, spinout, or sliding movements should be evaluated for polyethylene wear/fracture caused by contact with the stop. Again, modified wear simulator testing is suggested as the method of evaluation.

In summary, most of the preclinical testing identified for the mobile bearing knees is the same type of testing currently asked by FDA for fixed bearing knee devices (tibial tray fatigue, contact area/stress, constraint, etc.). For risks unique to mobile bearing knees most of the 'new' testing suggested revolves around some sort of modified wear simulator testing to evaluate a specific characteristic (i.e., particulate analysis, overhang deformation, mechanical stop impingement, disassociation, etc.). The hard part is going to be actually defining what these modified tests are, and trying to determine whether they are truly predictive from one mobile bearing design to another. Can reasonable assurance of safety and efficacy for myriad device designs be made based on modifications to existing test methods (e.g., knee simulator wear testing)? That is, are the proposed special controls (or others) adequate to address the inherent risks of the mobile bearing knee designs (or some subset of these knee designs) identified in this petition, and to provide reasonable assurance of safety and effectiveness?

Although labeling has been identified as a special control with which to address the above risks to health, the proposed labeling requirements are consistent with those generally found in current fixed bearing total and unicompartmental knee package labeling. No specific labeling requirements were identified for any of the mobile bearing specific risks.

Known Potential Benefits

No specific benefits of mobile bearing knee prostheses were stated in this petition, however, evidence has been provided to show that available long term data suggests that mobile bearing devices are equally safe and effective as compared with fixed bearing devices in total or unicompartmental knee arthroplasty.

Dual surface articulation between a polyethylene insert and metallic femoral and tibial tray components are a consequence of mobile bearing knee designs. Their advantage may lay in the maximization of femoral-tibial contact area which results in the attenuation of peak stresses, minimizing the potential for UHMWPE damage. Additionally, the mobility of the tibial insert allows for reduction of implant-bone interface torque contributing to in-vivo component fixation longevity. An increasing number of these designs are being utilized globally in total knee reconstruction, particularly among younger age groups with degenerative joint pathology.

Potential benefits for both fixed and mobile bearing knees include a decrease or cessation of pain, and increased mobility and function post-operatively as compared to pre-operatively.

Summary of Clinical Data

Please see Dr. Buch's review memo for a complete evaluation of the clinical data presented in this petition. Selected series of 48 studies have been summarized in Table 7, 8, and 9 of appendix 3 of the original submission. Data presented includes available demographics, study design, safety, effectiveness, and survivorship data. Included in these tables are 4 studies for multidirectional mobile bearing knees, 4 for rotating bearing knees, 8 for meniscal bearing knees, 11 for combination rotating platform and meniscal bearing in same study, and 21 for unicompartmental devices. Minimum follow-ups ranged from roughly 2 years to 12 years. These experiences underscore the strong influence of the technical performance of the operation on the long-term success of a knee device. Properly aligned knee arthroplasties that have restored ligament balance (medial and lateral, flexion and extension) appear to have survival rates of ten years or greater, irrespective of bearing mobility. These data indicate that when provided with medial-lateral stabilization, mobile bearing knees provide equivalent results as fixed bearing knees.

Bibliography and References

An extensive bibliography containing 193 citations was provided in the original petition, which included case studies, well controlled investigations, studies without matched controls, non-clinical bench studies, and retrieval studies. In addition, unpublished data from 7 ongoing IDE studies was provided. An additional 43 articles on wear were provided in the March 31, 2004, amendment.

Comments

A number of orthopedic surgeons have provided letters expressing their desire to include mobile bearing knees in their list of treatment options, particularly for younger patients (appendix 1 of original submission).