SUMMARY OF SAFETY AND EFFECTIVENESS

I. General Information

Device Generic Name: Unicompartmental Mobile Bearing Knee

Device Trade Name: Oxford™ Meniscal Unicompartmental Knee System

Applicant's Name and Address:

Biomet Orthopedics, Inc.
P.O. Box 587
Airport Industrial Park
Warsaw, Indiana 46580

Date of Panel Recommendation: none

Premarket Approval (PMA) Number: P010014

Date of Notice of Approval to the Applicant: April 21, 2004

II. Indications for Use

The Oxford Meniscal Unicompartmental Knee System is intended for use in individuals with osteoarthritis or avascular necrosis limited to the medial compartment of the knee and is intended to be implanted with bone cement.

III. Contraindications

- Infection, sepsis, and osteomyelitis
- Use in the lateral compartment of the knee
- Rheumatoid arthritis or other forms of inflammatory joint disease
- Revision of a failed prosthesis, failed upper tibial osteotomy or post-traumatic arthritis after tibial plateau fracture
- Insufficiency of the collateral, anterior or posterior cruciate ligaments which would preclude stability of the device
- Disease or damage to the lateral compartment of the knee
- Uncooperative patient or patient with neurologic disorders who are incapable of following directions
- Osteoporosis
- Metabolic disorders which may impair bone formation
- Osteomalacia
- Distant foci of infections which may spread to the implant site
- Rapid joint destruction, marked bone loss or bone resorption apparent on roentgenogram
- Vascular insufficiency, muscular atrophy, neuromuscular disease
- Incomplete or deficient soft tissue surrounding the knee

- Charcot's disease
- A fixed varus deformity (not passively correctable) of greater than 15 degrees
- A flexion deformity greater than 15 degrees

IV. Warnings and Precautions

The warnings and precautions can be found in the Oxford Meniscal Unicompartmental Knee System physicians labeling (i.e., package insert).

V. Device Description

The Oxford Meniscal Unicompartmental Knee is a medial, unicompartmental knee prosthesis consisting of three components: a femoral component; a tibial component; and a tibial meniscal bearing.

Femoral Component

The femoral component is manufactured from cast cobalt chromium molybdenum (CoCrMo) alloy. The component has a highly polished, spherical, articular surface. The inner surface of the prosthesis is, for the most part, spherically concave and concentric with the articular surface. Posteriorly there is a small flattened surface, the plane of which lies parallel to the long axis of the femur and contains a cement pocket for enhanced cement fixation. A central peg lies parallel to the mechanical axis of the femur. The component is available in four sizes (small, medium, large, and extra large) which may be used on either the left or right knee. The four sizes have the following radii of curvature: 22.0 mm, 23.8 mm, 25.7 mm, and 27.5 mm, respectively.

In order to provide increased strength at the interface between the implant and the bone cement, the cemented surfaces of the femoral components have an Interlok® grit blasted finish.

Tibial Component

The tibial component is manufactured from cast CoCrMo alloy. The component is approximately semicircular in shape and extended anteriorly for anatomic bone coverage. The articular surface is flat and highly polished with a raised lip, or flange, running the length of the lateral edge. On the distal surface there is a keel to locate the component during insertion. The distal surface also contains a cement pocket for enhanced cement fixation.

There are six sizes of tibial components in left and right configurations. The sizes (in mm) are: 38 x 26, 41 x 26, 44 x 28, 47 x 30, 50 x 32, and 53 x 24.

In order to provide increased strength at the interface between the implant and the bone cement, the cemented surfaces of the tibial components have an Interlok® grit blasted finish.

Meniscal Bearing

The meniscal bearing component is made from compression molded ultra high molecular weight polyethylene (UHMWPe). The upper articular surface of the bearing

is spherically concave and of the same radius as the femoral component. The lower articular surface is flat to match the tibial component. There are eight thicknesses of meniscal bearings, varying from 3 mm to 9 mm (at the thinnest point) in 1 mm steps. The component contains an imbedded titanium wire and two tantalum balls to act as radiological markers.

Four sizes (small, medium, large, extra large) of bearings which may be used on either the left or right knee uniquely match the four sizes of femoral components.

VI. Alternate Practices and Procedures

- Non-surgical treatment (e.g., medications), or no treatment at all
- Fusion of the joint
- Realignment of the joint by osteotomy
- Fixed bearing unicompartmental replacement
- Total knee: prosthetic replacement

VII. Marketing History

The Oxford Meniscal Unicompartmental Knee Phase 2 device, the predecessor to the subject Phase 3 device, has been sold in the following countries for 15 years:

United Kingdom, South Africa, Australia, Austria, New Zealand, Hungary, Canada, Belgium, Netherlands, Denmark, Finland, France, Germany, Italy, Norway, Spain, Sweden, and Switzerland.

The Oxford Meniscal Unicompartmental Knee Phase 3 device was introduced in November 1996.

Neither the Phase 2 nor Phase 3 devices have been withdrawn from any country due to issues related to safety or effectiveness.

VIII. Potential Adverse Effects of the Device on Health

The adverse events occurring in the clinical investigation of the Oxford Meniscal Unicompartmental Knee Phase 2 device, using a standard open surgical technique, range from intra-operatively to 12 years post-operatively. A time-course distribution of all adverse events reported in the clinical investigation of this device is provided in Table 1.

Table 1: Time-Course Distribution of Adverse Events reported in the clinical trial for the Oxford Meniscal Bearing Unicompartmental Knee* using a standard open surgical technique.

Adverse Events	Frequency							Percent of Population[1] (n=125)
Visit	IO	6 mo	1 yr	2 yr	3 yr	4 yr	≥5 yr	
Local – Operative Site								
Effusion			1					0.8 %
Deep Infection				**1**				0.8 %
Degeneration of contralateral condyle						**1**	**3**	3.2 %
Loose body and/or osteophyte removal		1		2			**1**	3.2 %
Soft tissue damage	2							1.6 %
Dislocation				**2**				1.6 %
Component mal-alignment		**1**						0.8 %
Patella dislocation				**1**				0.8 %
Component loosening					**1**	**2**	**3**	4.8 %
Post-operative bone fracture		**1**						0.8 %
Trauma		**1**						0.8 %
Mechanical symptoms			1					0.8 %
Instability							**1**	0.8 %
Persistent pain					**1**			0.8 %
Wear of bearing due to osteophyte					**1**			0.8%
Systemic								
Development of rheumatoid arthritis			**1**					0.8 %

*Phase 2 device design
IO = intraoperatively
[1]All percentages for adverse events are based the number of occurrences reported in a patient population of 125 knee cases. Those events listed in *italics* are considered device related events.
Boldface numbers represent revisions due to the given adverse event. One additional case was revised at 130 months post-operatively, cause unknown.

The following complications have also been reported in the clinical literature for unicompartmental and total knee replacement devices and could potentially occur with the Oxford Meniscal Unicompartmental Knee device.

- Major surgical risks associated with anesthetic including, brain damage, pneumonia, blood clots, heart attack, and death.
- Cardiovascular disorders including venous thrombosis, pulmonary embolism, and myocardial infarction.
- A sudden drop in blood pressure intraoperatively due to the use of bone cement.
- Damage to blood vessels, hematoma, delayed wound healing and/or infection.
- Temporary or permanent nerve damage may result in pain and numbness.
- Material sensitivity reactions.
- Particulate wear debris and discoloration from metallic and polyethylene components of joint implants may be present in adjacent tissue or fluid. It has

been reported that wear debris may initiate a cellular response resulting in osteolysis or osteolysis may be a result of loosening of the implant.

- Early or late postoperative, infection, and allergic reaction.
- Intraoperative bone perforation or fracture may occur, particularly in the presence of poor bone stock caused by osteoporosis, bone defects from previous surgery, bone resorption, or while inserting the device.
- Loosening or migration of the implants can occur due to loss of fixation, trauma, malalignment, bone resorption, excessive activity.
- Periarticular calcification or ossification, with or without impediment of joint mobility.
- Inadequate range of motion due to improper selection or positioning of components.
- Dislocation and subluxation due to inadequate fixation and improper positioning. Muscle and fibrous tissue laxity can also contribute to these conditions.
- Fatigue fracture of component can occur as a result of loss of fixation, strenuous activity, malalignment, trauma, non-union, or excessive weight.
- Fretting and crevice corrosion can occur at interfaces between components.
- Wear and/or deformation of articulating surfaces.
- Valgus-varus deformity.
- Transient peroneal palsy secondary to surgical manipulation and increased joint movement has been reported following knee arthroplasty in patients with severe flexion and valgus deformity.
- Patellar tendon rupture and ligamentous laxity.
- Persistent pain.

IX. Summary of Studies and Results

The Oxford Meniscal Unicompartmental Knee Phase 3 device, which is the subject of this PMA, contains modifications to the Oxford Meniscal Unicompartmental Knee Phase 2 device, which was the device evaluated in the non-clinical and clinical investigations used to support this application (except where noted). Testing on the Phase 2 device is believed to support the Phase 3 device design.

The following modifications to the Phase 2 device are reflected in the Phase 3 device:

- Additional sizes of femoral components
- Deeper posterior cement pocket on femoral components
- Change from 5 to 6 sizes of tibial components and addition of left and right configurations
- Diminishing tibial keel depth from 11 mm to 9 mm
- Redesign of the meniscal bearings
- Reduced the number of meniscal bearing thicknesses from 9 to 7
- Changed the x-ray markers from 2 titanium wires to 1 anterior wire and 2 tantalum balls posteriorly
- ArCom® polyethylene (compression molded in argon atmosphere)

A. Non-Clinical Studies:

Laboratory tests evaluated material properties while engineering analysis of range of motion, constraint, dislocation, and contact area were conducted. In addition, laboratory tests and retrieval studies evaluating polyethylene wear were also performed.

1. Material Properties:
   a. The following properties of cast CoCrMo alloy were provided in the PMA. Castings meet the requirements of ISO 5832-4 and ASTM F75 standards, including:
      - Composition of material
      - Minimum tensile strength
      - Yield strength
      - 2% proof stress
      - Minimum % elongation
      - Minimum reduction of area

   b. The ArCom compression molded UHMWPe conforms to ISO 5834 and ASTM F648 standards. The following properties and characterization of the material were included in the PMA and/or sponsor's Master File, including:
      - Tensile strength
      - Yield strength
      - Elastic modulus
      - Poisson's ratio
      - Ultimate elongation
      - Molecular weight
      - Density
      - Percent crystallinity
      - Transition temperature deformation
      - Hardness
      - Wear resistance
      - Extraneous matter
      - Particle size
      - Trace elements
      - Dynamic mechanical analysis
      - Fusion
      - Flexural testing
      - Fatigue crack growth
      - Impact testing
      - Differential scanning calorimeter testing
      - Effects of sterilization method

2. Microbiological, Immunological, Toxicity, and Biocompatibility Testing:
The Oxford Meniscal Unicompartmental Knee is manufactured from implant materials used in other marketed products with a long history of clinical use. Therefore, no additional microbiological, immunological, toxicological or biocompatibility testing was deemed necessary.

3. Fatigue Strength:
Testing of the tibial component demonstrated the device's ability to survive expected physiological loading: 10 million cycles at a 600 lb maximum - 60 lb minimum loading cycle, without visual sign of failure. Six 40 x 28 mm components were tested at 25 Hz and 75° F. Gross and microscopic examination revealed no sign of cracks or permanent deflection.

4. Wear:
Wear of the Oxford Mensical Unicompartmental Knee has been evaluated both in the laboratory as well as from explanted devices. The sponsor recovered 23 meniscal bearings from 18 failed bicompartmental Oxford Knee Phase 1 devices that had been implanted from one to nine years. Devices were implanted in Europe between February 1978 and March 1985. Fourteen bearings came from the lateral compartment, eight from the medial, and one was unknown. Compared to unused bearings, the mean penetration rate, calculated by two methods, was either 0.043 or 0.026 mm per year. In bearings retrieved from medial compartment replacements with no evidence of impingement against bone or cement, the mean penetration was 0.01 mm per year. This data has been shown to correlate well with laboratory wear testing.

   For a given size, the Phase 1, 2, and 3 devices have identical articulating surface geometries and contact areas. In addition, the ArCom UHMWPe utilized with the Phase 3 device has been shown to have an increased wear resistance over the traditionally manufactured UHMWPe previously used with Phase 1 and Phase 2 devices. Therefore, wear testing of the Phase 1 devices could be considered 'worst-case'. As a result, no wear testing was conducted on Phase 2 or Phase 3 components.

5. Shelf Life:
Sterility and package integrity results of old Oxford Phase 1 and 2 devices that had been kept on the shelf for 10-11 years, demonstrated that the components remained sterile. Performance (e.g. wear testing) of these components was not evaluated. Based on these results, the 10 year expiration date on the package labels of the CoCrMo femoral and tibial components is acceptable. The sponsor has chosen to limit the expiration date of the UHMWPe meniscal bearing components to 5 years, based upon evidence that UHMWPe components sterilized by gamma radiation in air begin to degrade due to oxidation after 5 years on the shelf, increasing their propensity for wear. It is noted that the sponsor sterilizes and packages

these components via gamma radiation in a stable atmosphere of argon gas, not air.

6. Other Test Results:
   a. Range of Motion
      The Oxford Meniscal Unicompartmental Knee is a prosthesis which relies for stability on the restoration of the normal length and tension to the ligamentous structures. Range of motion is both controlled and limited by the soft tissue structures around the knee. The device itself provides no limits to the range of motion in flexion or extension. The motion of a knee with a fully mobile meniscal bearing has been modeled and computer simulated.

   b. Constraint
      The Oxford Meniscal Unicompartmental Knee meniscal bearing is free to slide in any direction in the plane of the surface of the tibial tray component. However, the bearing has limited medial freedom (1 – 2 mm) as the raised flange along the medial side of the tibial component prevents excessive movement in the medial direction. The natural ligaments and muscles need to provide the constraint for this device. Therefore, insufficiency of the collateral, anterior and/or posterior cruciate ligaments is a contraindication for this device. The design of the device is such that the interface between the femoral component and meniscal bearing is highly conforming throughout the range of motion. As a result, translation and rotation at *this* interface is highly constrained.

      Because the device provides no constraint in the plane of the tibial bearing/tray interface (except minimally in the medial direction), mechanical constraint testing was not performed. However, the movement of the meniscal bearing has been further characterized through a radiographic study of *in situ* Oxford Meniscal Unicompartmental Knees. The study showed that the meniscal bearing prosthesis follows the pattern of movement dictated by the retained ligaments and mimics the kinematics of a normal knee.

   c. Dislocation
      In the Oxford Meniscal Unicompartmental Knee, the meniscal bearing is held in place by engagement of the convex femoral component into the concavity of the meniscal bearing. Dislocation is restricted only by the tension of the ligaments and soft tissues of the knee. Therefore, mechanical testing is not relevant since the device itself has no means to resist dislocation.

   d. Contact Areas
      Contact area evaluations were performed on all 4 sizes of Phase 3 devices (small, medium, large, extra large). The articulating surface of

the femoral components has a single radius of curvature in both the sagittal and coronal planes and therefore articulates congruously with the mating meniscal bearings throughout the entire range of motion, both in flexion/extension movement and axial rotation. The congruency of the components provides for high contact areas and low contact stresses throughout the entire range of motion.

e. Interlok® Finish
The surfaces of the metal components have a 30 grit blast finish. A cast CoCrMo substrate with this surface treatment has been shown to have a fatigue strength of approximately 120,000 psi.

The Interlok® grit blasted finish has been shown to increase the bond between the implant surface and bone cement. Test results indicate the shear fatigue strength of bone cement against an Interlok® finish is almost twice that of a smooth finish.

B. Clinical Studies:

1. Study Design:
A prospective, multi-center, investigational clinical trial conducted under a common protocol with defined inclusion/exclusion criteria and study endpoints was conducted by the sponsor for the Oxford Meniscal Unicompartmental Knee Phase 2 device (a previous version of the current device), using a standard open surgical technique. Historical control groups were later selected from literature based on similarities in patient demographics, indications, length of follow-up and patient assessment methods, to the Oxford study group. Nine literature articles on 7 different unicompartmental knee devices were selected as controls.[1-9]

The clinical investigation involved an analysis of clinical effectiveness based on factors such as pain, function, and range of motion. Radiographic parameters such as inclination and radiolucency were also collected. The protocol stipulated patient follow-up pre-operatively, and at 6 months, 1 year, 2 years, 3 years, 4 years and 5 years post-operatively. A minimum 2 year follow-up was required for all patients. All general and operative site complications as well as device revision/removal events (also reported in terms of survivorship) were documented for analysis of safety. Clinical data collected under this study was pooled as a basis for comparison to the historical control groups.

2. Patient Selection:
Skeletally mature patients with a primary diagnosis of osteoarthritis, traumatic arthritis, correction of functional varus, valgus, or post-traumatic deformity and/or unsuccessful osteotomy were selected for the study. Patients were excluded from the clinical investigation if one or more of the following exclusion criteria were met: presence of infection; a primary diagnosis of rheumatoid arthritis or revision of a failed prosthesis; fixed varus or valgus deformity due to shortening of a collateral ligament; absence or damage to the anterior or posterior cruciate ligament

which would preclude stability of the device; uncooperative patient, predictably unable to get long-term follow-up; osteoporosis; metabolic disorders which may impair bone formation; vascular insufficiency, muscular atrophy, or neuromuscular disease in the affected limb; and, incomplete or deficient soft tissue surrounding the knee.

3. Patient Population:
A total of 125 unicompartmental Oxford Meniscal Unicompartmental Knee Phase 2 devices were implanted under the clinical investigation in 107 patients between June 26, 1989 and June 1, 1994 at 8 investigational sites. See Table 2 for a complete listing of investigators and the number of patients/knees enrolled into the study.

Table 2: Investigational Sites and Number of Knees/Patients Enrolled

Investigational Site	Investigator(s)	Number of Knees Enrolled	Number of Patients Enrolled
ClevelandClinic Cleveland, OH	Alan Wilde, MD	17	15
Horton Hospital Middletown, NY	Martin Altchek, MD	1	1
Kaiser Hospital Pasedena, CA	Dale Daniel, MD Donald Fithian, MD	20	15
Kendrick Memorial Hospital Mooresville, IN	Merrill Ritter, MD Philip Faris, MD E. Michael Keating, MD	17	14
Presbyterian Hospital of Dallas Dallas, TX	Roger Emerson, MD	60	52
St. John Medical Center Tulsa, OK	Arthur Murphy, MD	4	4
University of Iowa Hospital & Clinic Iowa City, IA	J. Lawrence Marsh, MD	2	2
Willis-Knighton Medical Center Shreveport, LA	David Waddell, MD	4	4
Total		**125**	**107**

The 9 selected control groups ranged in size from 28 to 128 knee cases, with average follow-up times ranging from 1 year to 7 years. Patient demographics such as age and indication were similar between the study and control groups. The Oxford study group did have a higher percentage of males when compared to several of the control groups, however separate analysis demonstrated no statistical difference between gender groups within the study data. Demographic information for the entire patient population is presented in Table 3.

Table 3: Patient Demographics for the Oxford Clinical Study (Phase 2 Device)

Demographic Parameters	All Oxford Knees Enrolled
Total # Knees (# Patients)	125 (107)
Mean Age in years (range)	63±10.6 (29-85)
Sex	Males – 60 Females - 65
Indications	Osteoarthritis – 114 Post-Traumatic Arthritis – 10 Avascular Necrosis - 1
Side	Left – 56 Right – 69
Compartment	Medial – 119 Lateral – 6
Mean Height in Inches (range)	67.0±3.9 (59-77)
Mean Weight in pounds (range)	187±38.6 (105-256)

Table 4 provides an accounting for all cases enrolled into the study based on the number of cases with complete clinical follow-up (i.e., Hospital for Special Surgery (HSS) knee scores and radiographic data) and a cut-off date of when the last patient implanted reached their 2 year post-operative anniversary. One patient died and 8 were revised prior to reaching their 2 year post-operative evaluation. Complete 2 year clinical follow-up was available on 80 cases (69.0%). However, of the 116 cases expected for follow-up at 2 years post-operatively, 109 (94%) were known to have the device still in place.

Table 4: Device Accounting for the Oxford Clinical Study (Phase 2 Device) based on number of completed clinical follow-up examinations.

	6 Months	1 Year	2 Year	3 Year	4 Year	5 Year
[1]Theoretically Due	125	125	125	113	102	84
[2]Deaths	0	0	1	2	2	2
[3]Revisions	3	4	8	11	13	15
[4]Expected	122	121	116	100	87	67
[5]Clinical Follow-Up	100	110	80	83	69	51
[6]Percent Follow-Up	82.0%	90.9%	69.0%	83.0%	79.3%	76.1%

[1]Based on the cut-off date when the last patient enrolled reached their 2 year post-operative anniversary.
[2]Cumulative over time.
[3]Any component removed, cumulative over time.
[4]Theoretically Due – (Deaths + Revised).
[5]Cases with complete clinical data (i.e., HSS, radiographic), obtained at the specified time point.
[6]Clinical Follow-Up / Expected.

4. Patient Assessments:

Each patient was evaluated pre-operatively, and at the immediate and 6, 12, and 24 month post-operative intervals, and annually thereafter until the last patient enrolled had achieved their 24 month follow-up. At each follow-up visit an HSS knee score and anterior/posterior (A/P) and lateral radiographs were obtained. Radiographs were reviewed by the implanting surgeon with 10% randomly selected for review by an independent radiologist.

All operative and post-operative complications, whether device related or not, were noted for patients enrolled into the investigation.

A patient was defined as a success if they met each of the following 4 criteria:

- A Good/Excellent HSS score, i.e. > 70 points
- No radiolucent lines > 1 mm in width surrounding > 50% of the component after 1 year in-situ
- No progressive radiolucencies
- No revision/removal of any components

5. Effectiveness:
Clinical effectiveness was determined by the results for pain, function, range of motion and overall score by the use of the Hospital for Special Surgery (HSS) knee scoring system. Each clinical parameter is expressed in a number of categories with each category having a predetermined point value. Pain is divided into pain on walking and pain at rest, for a maximum of 30 points. Function is divided into evaluations of walking distance, stair climbing and transfer activity for a maximum of 22 points. Range of motion is recorded as the degrees of extension and flexion achievable by the knee for a maximum of 18 points. Evaluation of muscle strength, flexion deformity and varus/valgus instability contribute a maximum of 10 points each to a maximum score of 100 points. The score is further modified by subtracting up to 9 points for use of support, extension lag of 5° or more and varus or valgus deformity ≥ 5°. Based on the total numerical score achieved, the case can then be categorized as Excellent (85-100 points), Good (70-84 points), Fair (60-69 points), or Poor (< 60 points). Results recorded for the HSS scoring system were also converted to a modified HSS scoring system for further analysis.

Baseline pre-operative efficacy characteristics (i.e., HSS) of the entire study population are presented in Table 5.

Table 5: Baseline Characteristics for Oxford Study Patients

Pre-Operative	All Oxford Knees Enrolled
Number of Cases	125
HSS Score Distribution	Excellent - 0 Good – 23 (18.7%) Fair – 43 (35%) Poor – 57 (46.3%) Incomplete - 2
Mean HSS Score (range)	60.3 ± 10.86 (27.7 – 84.5)

Clinical effectiveness was based on the last available completed patient evaluation at or beyond 2 years post-operatively. The average length of follow-up for this group was 55 months (4.5 yrs), ranging from 21.5 months to 110 months (9 yrs). Over 50% of the cases (n=72) had 5 years follow-up or more.

At 2 years following surgery, 72 out of 80 patients (90%) experienced either mild or no pain with 50 of these patients (62%) experiencing no pain at

anytime. Also at 2 years after surgery, 74 out of 80 patients (92.5%) required no support when walking.

Post-operative HSS scores are included in Table 7. At the 2 year evaluation 96.3% (77/80) of cases reported good or excellent scores. At 3, 4, and 5 years post-operatively the percentage reporting good/excellent scores were 98.8% (82/83), 92.8% (64/69), and 98% (50/51), respectively. The average HSS score at 2 years post-operatively was 90.0 (n=80). At 3, 4, and 5 years post-operatively the average HSS scores were 90.6 (n=83), 90.7 (n=69), and 90.4 (n=51), respectively.

Effectiveness was also evaluated by the review of radiographs of 105 cases taken at 2 years or later, post-operatively. Over 50% of the cases evaluated (n=60) had their radiographs taken at 5 years follow-up or greater. Table 7 includes the number of cases that had observable radiolucencies ≥ 1 mm. There were no radiographic failures reported through 2 years. One radiographic failure (tibial) was noted at 4 years post-operatively due to progressive radiolucency and one radiographic failure (femoral) was reported at 5 years post-operatively due to a radiolucency >1 mm surrounding > 50% of the component.

As part of the determination of the clinical effectiveness of the Oxford Meniscal Unicompartmental Knee Phase 2 device, clinical evaluation results were compared to the literature-based control groups. Comparisons were made between data provided in each control article and the results from the Oxford study group and analyzed separately. A comparison was also made between the combined control groups and the Oxford study group. Analysis of knee scores and radiolucencies showed the Oxford Meniscal Unicompartmental Knee Phase 2 device achieved similar results as compared to the literature controls at the same follow-up time points.

6. Safety:
Safety was evaluated based on a comparison of complication rates and revision rates (also reported in terms of survivorship) with similar historical controls from the literature. Complications were categorized as systemic, operative-site, and/or device related. Revisions were categorized as device related (i.e. dislocation, fracture, loosening, pain) and non-device related (i.e. trauma, infection, progression of disease, surgical error).

One systemic complication (rheumatoid arthritis) was noted in the Oxford study. Occurrences of operative site and device related complications are presented in Table 1, in the Adverse Events section. Operative site and device related complications occurred at no greater frequency for the Oxford™ Meniscal Unicompartmental Knee Phase 2 devices of the study than for the literature based control groups.

There were a total of 23 revisions reported as of 6/1/03 for the Oxford study group (i.e., all patients ≥ 9 years post-operative), with 8 of these occurring

within 2 years post-operatively. Of the 8 revisions reported at 2 years, 2 were for tibial bearing dislocation, 1 for patellar dislocation, 1 for infection, 1 for component malalignment, 1 for recurrent arthritis due to trauma, 1 for onset rheumatoid arthritis, and 1 for femoral loosening and fracture at the bone-cement interface. In all but 1 case the knees were revised to a total knee prosthesis. The other case had the medial meniscal bearing replaced and another Oxford Meniscal Unicompartmental knee device placed into the lateral compartment of the knee.

For the remaining 15 revisions reported after 2 years, 6 were due to loosening, 4 to progression of osteoarthritis in the lateral compartment, 1 to persistent pain, 1 to instability, 1 to impingement on an osteophyte and subsequent wear of the tibial bearing, 1 to impingement of an osteophyte on the femur, and 1 failed to report a reason. Three of the revisions occurred at 2–3 years post-operatively, 3 at 3–4 years, 1 at 4–5 years, 2 at 6–7 years, 1 at 7–8 years, 2 at 8–9 years, 1 at 10–11 years, and 2 at 11–12 years post-operatively.

The survival rate at 2 years post-operatively for the Oxford Meniscal Unicompartmental Phase 2 device is 93.38%, based on the endpoint of revision/removal of any component. Table 6 displays the Kaplan-Meier life table for survivorship through 8 years post-operatively for the Oxford study group. Survivorship rates for the study group are comparable to those rates seen in the literature for other unicompartmental knee devices and the rates seen in other studies of the Oxford Phase 2 device.

Table 6: Survivorship for Oxford Clinical Study (Phase 2 Device)

Interval Since Operation (years)	Number in Beginning of Interval	Number of Revisions at End of Interval	%[1] Interval Survival	%[2] Cumulative Survival	95% Confidence Interval
0-1	125	4	96.75%	96.75%	(93.61 - 99.98)
1-2	117	4	96.52%	93.38%	(88.95 - 97.82)
2-3	109	3	97.16%	90.73%	(88.50 - 95.95)
3-4	99	2	97.91%	88.83%	(83.08 - 94.57)
4-5	90	2	97.74%	86.82%	(80.57 - 93.07)
5-6	85	0	100%	86.82%	(80.57 - 93.07)
6-7	65	3	94.92%	82.41%	(75.21 - 89.60)
7-8	50	1	97.87%	80.65%	(73.35 - 87.95)

[1] Percent survival for that interval only, taken at the end of the interval.
[2] Percent cumulative survival taken at the end of the interval.

7. Patient Success:
Table 7 provides overall clinical results for the patients enrolled in the Oxford clinical study. Patient success rates (percent of cases successful) include both efficacy (HSS and radiographic) and safety (device revision/removal) endpoints as noted above.

Table 7 - Oxford Clinical Study Results* (Phase 2 Device) using a standard open surgical technique.

Clinical Parameters	Pre-Op	1 Year	2 Year	3 Year	4 Year	5 Year
Cases with complete HSS		110	80	83	69	51
Average HSS Score	59.5	89.3	90.0	90.6	90.7	90.4
[1]Cases Rated as Good-Excellent HSS	20/123 (16.3%)	105/110 (95.5%)	77/80 (96.3%)	82/83 (98.8%)	64/69 (92.8%)	50/51 (98.0%)
Femoral Lucencies ≥ 1mm		6/108 (5.5%)	2/80 (2.4%)	2/83 (2.4%)	2/68 (2.9%)	2/51 (2.9%)
Tibial Lucencies ≥ 1mm		5/108 (4.6%)	6/80 (7.5%)	8/83 (9.6%)	7/68 (10.3%)	3/51 (5.9%)
Number of G/E cases with radiolucent lines >1mm around >50% of component		0	0	0	0	1 femoral
Number of G/E cases with progressive radiolucencies		0	0	0	1 tibial	0
[2]Revisions		4	8	11	13	15
[3]Cumulative Survivorship		96.75%	93.38%	90.73%	88.83%	86.82%
[4]Successful Cases		105	77	82	63	49
[5]Percent Successful		92.5% 105/114	87.5% (77/88)	87.2% (82/94)	76.8% (63/82)	74.2% (49/66)

*Based on the cut-off date when the last patient enrolled reached their 2 year post-operative anniversary.
[1]Hospital for Special Surgery score > 70.
[2]Number of components removed at specified time point.
[3]Kaplan-Meier Life Table results.
[4]A successful case required a Good-Excellent HSS score, no revision/removal of any component, no radiolucent lines > 1 mm in width surrounding > 50% of the component, *and* no progressive radiolucencies.
[5]Denominator includes cases with complete HSS and radiographic data, *and* revisions.

8. Clinical Information for Phase 3 Devices:
In addition to the minor design changes noted in the Summaries of Studies and Results (Section IX), the surgical technique and some of the surgical instruments for the Phase 3 device have been modified to accommodate a more minimally invasive, and more technically demanding, surgical procedure. The technique is performed through a small parapatellar incision and does not require dislocation of the patella, thus preserving the quadriceps mechanism without altering the general principles of the method.

At FDA's request the sponsor provided additional clinical data for the Oxford™ Meniscal Unicompartmental Knee Phase 3 devices implanted through a small minimally invasive incision. The sponsor described results from consecutive case series of the Phase 3 device at 3 centers in Europe. Data was provided from 208 knees at the Nuffield Orthopaedic Center (NOC) in the U.K. (two surgeons experienced in implanting the Phase 2 device), 40 knees from Macclesfield Hospital in the U.K. (one surgeon experienced in implanting the Phase 2 device), and 80 knees from Groningen in Holland (3 surgeons with no prior experience in Oxford unicompartmental knee replacement). The follow-

up is reportedly prospective and is at least 2 years for all of these knees. The investigators in these studies used the Knee Society Score (KSS) knee score rather than the HSS score used in the Oxford clinical study.

Of the 328 Phase 3 cases implanted, 11 patients died and 10 patients were lost to follow-up prior to their 2 year evaluation. Two-year results were available on 307 of the 328 cases (93.6%). Of these, 5 knees were revised within 2 years post-operatively (1.6%). The modifications to the Phase 3 device, surgical instrumentation, and surgical technique, were not expected to negatively impact the clinical results of the Oxford Knee System. This was further demonstrated by the results of the 2 year survivorship and KSS knee score results on the approximately 300 Phase 3 cases. The Phase 3 devices demonstrated short term (2 year) survivorship results (98.4%) similar to the historical literature controls and Phase 2 devices studied in the Oxford clinical study.

Table 8 summarizes the 2 year HSS data (efficacy) and revision results (safety) by site and as a combined group for the 3 sites implanting the Phase 3 device, with the Oxford clinical study data (Phase 2) included for comparison.

Table 8: Results at 2 Years for Phase 2 Device using open surgical technique and Phase 3 Device using minimally invasive surgical technique.

Clinical Parameters	Oxford Study Phase 2 N = 125 knees	Combined European Data* Phase 3 N = 328 knees	European Site 1 Phase 3 N = 208 knees	European Site 2 Phase 3 N = 40 knees	European Site 3 Phase 3 N = 80 knees
Revision Rate[1]	**6.8%** (8/117)	**1.6%** (5/307)	**2.0%** (4/196)	**2.7%** (1/37)	**0%** (0/74)
Percent with a Good or Excellent Knee Score[2]	N = 80 **96.3%**[3] (77/80)	N = 271 **83.0%**[4] (225/271)	N = 160 **83.1%**[4] (133/160)	N = 37 **86.5%**[4] (32/37)	N = 74 **81.0%**[4] (60/74)

*Combined data from European Site 1, Site 2, and Site 3.
European Site 1 = Nuffield Orthopaedic Centre (U.K.), Site 2 = Macclesfield Hospital (U.K.), and Site 3 = Groningen Hospital (Holland).
[1]Revision rate (%) at 2 years = cumulative number of revisions / (N – # deaths - # lost to follow up).
[2]Percent with Good or Excellent HSS or KSS knee score at 2 years.
[3]Based on HSS knee scoring system.
[4]Based on KSS knee scoring system.

9. Additional Clinical Information:
For unicompartmental arthroplasty with the Oxford™ Meniscal Unicompartmental Knees (Phase 1 and Phase 2), the long-term results (i.e., revision rates) are related to the number of procedures performed by the center. Using data obtained from the Swedish Knee Arthroplasty Registry for unicompartmental knees implanted during a 10 year period from 1986 to 1995, Robertsson et al.[10] showed that hospitals implanting an average of more than 23 Oxford™ Meniscal Unicompartmental Knees per year achieve significantly better results, with a 6.67% cumulative

revision rate at 8 years, compared to those centers that implant less than an average of 23 per year and showed a cumulative revision rate of 20% at 7.5 years.

X. Conclusions Drawn from the Studies:

Preclinical laboratory tests, engineering analyses, and retrieval studies, evaluating and characterizing the materials and device design/performance/kinematics were performed on the Oxford™ Meniscal Unicompartmental Knee (Phase 1, Phase 2, and Phase 3 devices). Preclinical test results indicate the Phase 3 device should perform as intended when used in the target population in accordance with the directions for use.

Effectiveness was demonstrated through the compilation of data exhibiting pain relief, function, and range of motion (HSS knee scores), and radiographic analysis of the affected joint, which was collected during the course of this prospective multicenter trial. The HHS knee scores and radiographic failure rates compared favorably to those reported for other commercially available knee components, i.e., historical literature controls.

Safety was established through the collection of adverse events and component removal events. The adverse events occurring in the clinical investigation of the Oxford™ Meniscal Unicompartmental Knee Phase 2 device, using a standard open surgical technique, were similar to those reported in the literature controls that used the same surgical approach. Other than the risks generally associated with unicompartmental knee arthroplasty no additional risks were identified for the Oxford Meniscal Unicompartmental Knee.

The overall failure rates for the Oxford™ Meniscal Unicompartmental Knee Phase 2 device compared favorably to the literature controls.

The Phase 3 device has evolved from the 15 year clinical experience with the Phase 2 device. The differences between the Phase 3 and Phase 2 devices have been identified and evaluated. Based on these evaluations the modifications should not impact (negatively) the clinical performance of the device. The Phase 3 device is expected to perform as well as the Phase 2 device.

The preclinical and clinical data provides reasonable assurance that the Oxford™ Meniscal Unicompartmental Knee Phase 3 (to be marketed as the Oxford™ Meniscal Unicompartmental Knee) is safe and effective for unicompartmental knee replacement in patients diagnosed with osteoarthritis or avascular necrosis limited to the medial compartment of the knee, when implanted with bone cement.

XI. Panel Recommendation:

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA application was not referred to the Orthopedic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CDRH Decision:

The sponsor has adequately responded to the FDA's questions and comments on their PMA application. As a condition of approval, the sponsor will be required to conduct a post-approval study to further evaluate the long-term performance of the subject device. Details of the post-approval study protocol, including number of patients, duration of follow-up, and type of data collected, should be submitted by the sponsor in a supplement to the PMA. Also, as a condition of approval, the sponsor must ensure that physicians receive training prior to using this device, due to the more technically demanding minimally invasive surgical procedure.

Therefore, FDA finds in favor of approval of the Oxford™ Meniscal Unicompartmental Knee. The sponsor's manufacturing facilities were inspected and determined to be in compliance with the Quality System Regulation (21 CFR Part 820).

FDA issued an approval letter to the sponsor on April 21, 2004.

XIII. Approval Specifications:

Directions for Use: See the Device Labeling

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the label

Post-Approval Requirements and Restrictions: See Approval Order

XIV. References:

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