SUMMARY OF SAFETY AND PROBABLE BENEFIT

I. General Information

Device generic name: Temporary total hip replacement prosthesis

Device trade name: PROSTALAC Hip Temporary Prosthesis System

Applicant name and address:
DePuy Orthopaedics, Inc.,
A Johnson & Johnson Company
700 Orthopaedic Drive
P.O. Box 988
Warsaw, IN 46580-0988

Humanitarian Device Exemption (HDE) Number: H000004

Date of Humanitarian Use Device Designation: July 29, 1997

Date of Panel recommendation: Not applicable (Refer to Section XII for discussion)

Date of Good Manufacturing Practices Inspection: December 5, 1999

Date of Notice of to the applicant: March 23, 2001

II. Indications for Use

PROSTALAC Hip Temporary Prosthesis System is indicated for use as a short-term total hip replacement (THR) in patients who need a two-stage procedure to treat a confirmed infection of their THR and where vancomycin and tobramycin are the most appropriate antibiotics for treatment of the infection based on the susceptibility pattern of the infecting microorganism(s).

III. Device Description

The PROSTALAC Hip is a total hip replacement prosthesis designed to function temporarily as a THR prosthesis, thereby providing a means for limited mobility of the patient following excision arthroplasty surgery. This device is also designed to function as a carrier device for antibiotic drugs for their local delivery within the periprosthetic space following surgery for the excision of an infected total hip replacement (THR) prosthesis. The PROSTALAC Hip is designed to remain *in situ* for approximately three (3) months after which a second surgery is performed for

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implantation of a permanent, cemented THR prosthesis. The design of this device requires that it be protected from the stresses associated with full weight bearing throughout the three-month implantation period.

The PROSTALAC Hip is comprised of a Co-Cr-Mo alloy core femoral component, a Co-Cr-Mo alloy modular femoral ball head, a one-piece ultrahigh molecular weight polyethylene (UHMWPe) acetabular component, a polymethylmethacrylate (PMMA) stem centering device, and antibiotic bone cement. The antibiotic bone cement is made of Endurance® Medium Viscosity Bone Cement, tobramycin sulfate (3.6 grams per 40 gram unit of cement) and vancomycin hydrochloride (1.0 grams per 40 gram unit of cement). The PROSTALAC Hip Temporary Prosthesis femoral component is constructed in the operating room.

The core femoral components are available in four (4) stem lengths. The three longer stem length components come in right and left configurations, whereas the shorter stem length components are a neutral configuration. Also, the shorter stem length components are available in either standard-offset or high-offset designs, whereas the longer stem length components have only one off-set design. The modular ball head has a 32 mm diameter and is available in five (5) neck lengths.

The various neck lengths and stem off-sets available provide the surgeon with options for the proper tensioning of soft tissues for improved muscle function and implant stability. Limb length can also be adjusted for improved mobility and patient comfort.

The one-piece UHMWPe acetabular component is available in one size having a 32 mm internal diameter and a 42 mm outer diameter. The acetabular component has a snap-fit design that captures the modular ball head of the PROSTALAC femoral prosthesis to resist distraction forces occurring between the femoral and acetabular prostheses.

The PMMA stem centering device is an optional implant component and is used at the surgeon's discretion to resist toggling of the femoral core implant after it is inserted into the mold instrument. The stem of the PMMA stem centering device is inserted into a corresponding hole at the distal tip of the femoral core implant. The PMMA stem centering device maintains the proper alignment of the core implant stem within the mold instrument while the polymerization of the surrounding PMMA bone cement occurs to facilitate a more uniform cement mantle thickness.

The charts below detail the sizes and dimensions of the component parts of the PROSTALAC Hip Temporary Prosthesis implants.

Femoral Core Components

Catalogue Number	Offset	Stem Length (mm)	Side
1541-01-000	Standard	120	R/L
1541-06-000	High	120	R/L
1541-13-000	Standard	150	Left

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1541-18-000	Standard	150	Right
1541-23-000	Standard	200	Left
1541-28-000	Standard	200	Right
1541-33-000	Standard	240	Left
1541-38-000	Standard	240	Right

Modular Heads

Catalogue Number	Diameter (mm)	Neck Length
1365-21-000	32	+1
1365-22-000	32	+5
1365-23-000	32	+9
1365-24-000	32	+13
1365-25-000	32	+17

Acetabular Cup

Catalog Number	Inner Diameter (mm)	Outer Diameter (mm)
1541-42-320	32	42

Endurance® Bone Cement

Catalog Number	Package Size
5450-50-000	40.0 gram unit

Generic Antibiotics (use antibiotic powder only)

Tobramycin sulfate	3.6 grams/package of cement
Vancomycin hydrochloride	1.0 grams/package of cement

Endurance® Bone Cement Requirements (estimated):

Standard femoral stem, 120mm	1 package of cement
Long femoral stem, 150mm	1 package of cement
Long femoral stem, 200mm	1 package of cement
Long femoral stem, 240mm	1 package of cement
Acetabulum	1-2 packages (depending on individual patient anatomy)

IV. Contraindications, Warnings and Precautions

CONTRAINDICATIONS

The following conditions are contraindications for the use of the PROSTALAC Hip Temporary Prosthesis implant system:

1. Patient is immunocompromised, nutritionally deficient and/or is otherwise systemically compromised to the degree that a two-stage excision arthroplasty is contraindicated;
2. destruction of the proximal femur that precludes support of the PROSTALAC temporary femoral prosthesis;

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3. destruction of acetabulum that precludes support of the temporary acetabulum component;
4. loss of musculature, neuromuscular compromise or vascular deficiency in the affected limb rendering the procedure unjustified;
5. poor bone quality, such as osteoporosis, where, in the physician's opinion, there could be considerable migration of the prosthesis and/or a considerable chance of fracturing the femoral shaft;
6. insufficient bone stock to allow for a sound biomechanical reconstruction for a permanent total hip replacement prosthesis, i.e., resection arthroplasty or Girdlestone's procedure is required;
7. infection cannot be confirmed;
8. unable to remove all infected THR device components;
9. pathogens are resistant to antibiotics to be locally administered to treat the infection;
10. patient sensitivity to antibiotics to be locally administered to treat the infection;
11. systemic infection or a secondary remote infection is either confirmed or suspected; and/or
12. patient does not have a total hip replacement prosthesis, e.g., hip infection is secondary to septic arthritis, trauma, open reduction and internal fixation, osteotomy, arthrodesis, etc.

WARNINGS

The patient's wound drainage fluids during or following the PROSTALAC Hip Temporary Prosthesis surgery should not be re-infused. Wound drainage following PROSTALAC Hip Temporary Prosthesis surgery contains high levels of antibiotics eluted from the device and re-infusion of this fluid has the potential for the introduction of large quantities of antibiotics into the systemic circulation.

Peak and trough serum concentrations of tobramycin sulfate and vancomycin hydrochloride should be monitored periodically during intravenous administration of these antibiotics in the presence of the PROSTALAC Hip system to avoid potentially toxic levels. Tobramycin sulfate and/or vancomycin hydrochloride administered by the intravenous route have the potential for causing ototoxicity and nephrotoxicity. The PROSTALAC Hip system should be used with caution in patients who may be predisposed to tobramycin sulfate and vancomycin hydrochloride toxicity, since combined PROSTALAC and systemic administration of these antibiotics may result in higher than expected serum levels. Patients with the risk factors of advanced age, preexisting renal dysfunction, dehydration, receipt of large cumulative antibiotic doses, or concurrent or sequential use of other nephrotoxic and/or neurotoxic antibiotics are at increased risk of toxicity. Please consult the product labels for tobramycin sulfate and vancomycin hydrochloride for a complete list of adverse events, as well as for information regarding systemic administration.

The PROSTALAC Hip Temporary Prosthesis should not be re-implanted. Even though the implant may appear undamaged, it may be fatigued from previous stresses

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and may have developed microscopic imperfections, which may lead to implant failure.

PRECAUTIONS

Consult the product label for Endurance® Medium Viscosity Bone Cement, tobramycin sulfate, and vancomycin hydrochloride for specific Contraindications, Warnings, Precautions, and Instructions for Use for these components of the PROSTALAC Hip Temporary Prosthesis.

The patient must be informed as to the necessity of adherence to the physician's instructions regarding protected weight bearing throughout the implantation period and the need for additional surgery to explant the PROSTALAC Hip Temporary Prosthesis. The PROSTALAC Hip Temporary Prosthesis has been designed to withstand approximately three months of protected weight bearing for a person being treated for infection of his/her total hip joint replacement prosthesis and is not intended as a permanent hip prosthesis implant. The following conditions, singularly or concurrently, tend to impose severe loading on the affected extremity, thereby placing the patient at higher risk for failure of the PROSTALAC Hip Temporary Prosthesis:

1. Obesity
2. Heavy labor
3. Active sports participation
4. Likelihood of falls
5. Alcohol or drug addiction
6. Unprotected weight bearing

Keep prosthesis in the supplied protectors during sterilization cycle and until implantation. Do not allow contact of prosthesis with hard objects.

V. Adverse Effects of the Device on Health

Adverse Effects Reported in the Retrospective Study

Adverse effects of the PROSTALAC Hip Temporary Prosthesis were determined from a single center, retrospective study of 135 PROSTALAC Hip cases. The frequencies of the complications reported for the intraoperative, interoperative and postoperative time intervals are provided in the following tables:

PROSTALAC Hip Surgery Intraoperative Complications (135 Cases)

Type	Frequency
Femoral Comp. Removal	16 (11.9%)
Femoral Fracture	8 (5.9%)
Difficult Bone Cement Removal	7 (5.2%)

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Acetabular Component Removal	4 (3.0%)
Vascular Damage	4 (3.0%)
Deficient Femoral/Acetabular Bone	3 (2.2%)
Acetabular Defect	2 (1.5%)
Femur Perforated	2 (1.5%)
Sinus Excision	2 (1.5%)

Other PROSTALAC Hip Surgery interoperative adverse events under one percent included: Bone cement retained; nerve damage; acetabular perforated; difficult insertion of acetabular component; cardiac arrest; fat embolism; difficult removal of antibiotic beads; trochanter avulsed; draining abscess; difficult dislocation of hip; tight cable grip; difficult screw removal (broke); cerclage wire removal; extended osteotomy of femur; fracture (type not specified); femoral prosthesis reinserted; allograft required; and antibiotic beads required.

Second Stage Surgery Intraoperative Complications
(118 Cases)

Type	Frequency
Femoral/Acetabulum Bone Grafts	7 (5.9%)
PROSTALAC Removal Difficult	5 (4.2%)
Femoral Fracture	3 (2.5%)
Acetabulum Fracture	2 (1.7%)
Acetabular Defect	2 (1.7%)
Heterotopic Bone	2 (1.7%)

Other Second Stage Surgery Intraoperative adverse events under one percent included: Femoral defect; femoral component retained; instability; and poor bone stock.

***Interoperative Operative Site Complications**
(118 Cases)

Type	Frequency
Recurrent or Persistent Infection	17 (14.4%)
PROSTALAC Reimplanted	8 (6.8%)
Dislocation/Subluxation	6 (5.1%)
Fracture	5 (4.2%)
†Wound Problem	5 (4.2%)
Pain	2 (1.7%)
Bone Cement Fracture	2 (1.7%)

Other Interoperative Operative Site adverse events under one percent included: Heterotopic ossification; acetabulum loosening; femoral loosening; skin reaction; nerve damage; patient fell; and wire removal.

*Defined as Time Interval Between PROSTALAC Hip and Second Stage Surgeries
†Categorized as Dehiscence, Necrosis and Superficial Infection.

***Interoperative Systemic Complications**
(118 Cases)

Type	Frequency
Cardiovascular	11 (9.3%)
Gastrointestinal	8 (6.8%)
Genitourinary	6 (5.1%)
Hematological	3 (2.5%)
Central Nervous System	3 (2.5%)

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Thrombosis/Thrombophlebitis	2 (1.7%)
Death	2 (1.7%)

Other Interoperative Systemic adverse events under one percent included: Endocrine/metabolic; swelling of leg; vasovagal episode; contralateral hip revision; optic neuropathy; psychosis; orbital fracture from fall; depression; knee infection; contralateral thigh abscess; skin rash; oral thrush; and respiratory.

*Defined as Time Interval Between PROSTALAC Hip and Second Stage Surgeries

****Postoperative Operative Site Complications (112 Cases)**

Type	Frequency
Dislocation/Subluxation	15 (13.4%)
Pain	11 (9.8%)
Persistent or Recurrent Infection	13 (11.6%)
†Wound Problem	9 (8.0%)
Partial or Complete Removal/Revision of Prosthesis	8 (7.1%)
Painful/Broken Cerclage Wires	5 (4.5%)
Fracture	4 (3.6%)
Patient Falls	4 (3.6%)
Trochanter Nonunion	4 (3.6%)
Hematoma	2 (1.8%)
Heterotopic Ossification	2 (1.8%)
Femoral Comp. Loosening	2 (1.8%)
Bone Cement Fractured	2 (1.8%)

Other Postoperative Operative Site adverse events under one percent included: Needle biopsy; bone cement extruded; bone screw failure; instability; and pain.

**Defined as Time Interval Following the Second Stage Surgeries
†Categorized as Dehiscence, Necrosis and Superficial Infection.

****Postoperative Systemic Complications (112 Cases)**

Type	Frequency
Cardiovascular	9 (8.0%)
Genitourinary	8 (7.1%)
Pain (Shoulder, Knee, Contralateral hip)	6 (5.4)%
Death	4 (3.6%)
Revision/Removal of Contralateral Hip	4 (3.6%)
Musculoskeletal	3 (2.7%)
Respiratory	3 (2.7%)
Central Nervous System	2 (1.8%)
Tibia Fractured	2 (1.8%)
Femur Fractured (Contralateral)	2 (1.8%)
Contralateral Hip Replaced	2 (1.8%)
Gastrointestinal	2 (1.8%)

Other Postoperative Systemic adverse events under one percent included: Endocrine/metabolic; hematological; contralateral knee replaced; hardware removal of contralateral hip; prostate removed; unexplained fever; edema; delirium; cataracts; knee aspirated; cancer; trochanteric bursitis of contralateral; and infection from IV.

**Defined as Time Interval Following the Second Stage Surgeries

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Potential Adverse Effects

Many of the known or potential adverse effects or complications associated with single-stage exchange arthroplasty and two-stage excision arthroplasty for the treatment of infected THR prostheses are also associated with the PROSTALAC Hip temporary prosthesis implant system.

General Surgical Risks

Cardiovascular disorders, including venous thrombosis, pulmonary embolism, transitory hypotension, arrhythmias and myocardial infarction, and/or anesthesia-related adverse effects.

Device Risks

Local or systemic toxicity from the eluted antibiotics delivered to treat the infection; incomplete removal of necrotic and/or avascularized bone and other tissues, bone cement, previously implanted prosthetic components, fixation and/or reinforcement devices, e.g., cerclage wires, cement restrictor devices, etc., thereby increasing the likelihood for a recurrent or persistent hip infection; inability to eradicate the pathogen(s) due to resistance to, or ineffectiveness of, the vancomycin hydrochloride and tobramycin sulfate eluted from the PMMA; and/or the inability to regulate the dose or treatment duration of the locally administered antibiotics; and decreased mechanical strength of the PMMA due to the quantities of antibiotics contained within the PMMA.

Hip Joint Surgery Risks

Risks known or potentially associated with THR prosthesis surgery are also applicable to surgery with the PROSTALAC device. Adverse effects and complications that may result from this surgery include: Femoral and/or acetabular perforation; fractures of the femur or bones of the pelvis necessitating internal fixation; breakage of the prosthetic device components; damage to blood vessels; temporary or permanent nerve damage resulting in weakness, pain or numbness of the affected extremity; difficulty with insertion of the permanent hip prosthetic device components and/or difficulty with removal of the PROSTALAC Hip at the second stage surgery; subluxation and/or dislocation of the hip joint implant components; arthrofibrosis; limb-length discrepancy; phlebitis and thrombophlebitis; hematoma; delayed wound healing; wound problems (dehiscence, necrosis and superficial infection); and extensive blood loss.

VI. Alternative Treatments

There are four (4) modes of treatment that have been utilized for the treatment of infected THR prostheses: irrigation and debridement, single-stage exchange arthroplasty and two-stage and three-stage excision arthroplasty. All of these treatment regimes require the use of systemic (oral and/or parenteral) antibiotics as the primary pharmacotherapy for eradicating the pathogen(s).

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Irrigation and debridement involve the surgical exposure of the infected THR prosthesis followed by excision of all inflamed synovial tissue and any necrotic and/or avascularized tissue that may be present. Single-stage exchange arthroplasty involves the excision of the infected THR prosthesis and replacement with a permanent THR prosthesis during the same surgical intervention. Two-stage excision arthroplasty, and a variation of this technique, three-stage excision arthroplasty, involve the surgical removal of the infected THR prosthesis and reimplantation of a permanent THR prosthesis once eradication of the pathogen(s) has occurred. As an adjunct to the two stage (or three stage) treatment modality, it has become common orthopaedic practice, at the time of excision arthroplasty, to implant antibiotic impregnated beads or spacers into the void created by the excised prosthesis serving as a means of locally administered antibiotics. Currently, however, there are no antibiotic impregnated beads or spacers on the market intended for use in the treatment of infected total hip replacements.

Irrigation and debridement alone and three-stage excision arthroplasty have fallen into disfavor and are not currently considered to be viable as treatment modalities.

VII. Marketing History

The PROSTALAC Hip Temporary Prosthesis is not commercially available in the United States. It has been available in Canada since 1995 with approximately 147 PROSTALAC Hip Temporary Prostheses sold through 1999. The PROSTALAC Hip Temporary Prosthesis has not been withdrawn from any market for any reason relating to the safety and/or effectiveness of the device.

VIII. Summary of Studies

The primary objectives of the laboratory studies were to characterize the elution properties of the bone cement/antibiotics composite, determine the mechanical strength of the core stem component and the molded PROSTALAC femoral prosthesis.

A. *In Vitro* Studies

Studies were performed to detect and quantify the extractable tobramycin sulfate and vancomycin hydrochloride from buffered saline extraction solutions of bone cement using high performance liquid chromatography (HPLC).

Test specimens consisted of 28mm x 20mm cylindrical disks with the antibiotics pre-blended into the bone cement powder prior to manufacture of the specimens. Three test specimens containing vancomycin hydrochloride, three containing tobramycin sulfate and three specimens with vancomycin hydrochloride and tobramycin sulfate combined were tested. The bone cement disks were extracted in 40 milliliters of buffered saline at 37 degrees centigrade at pre-determined time points for a period of

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35 days. Detection limits were validated for each antibiotic and the minimum quantifiable limit (MQL) was set at 10 μg/ml for vancomycin hydrochloride and 200 μg/ml for tobramycin sulfate.

For the test specimens containing a single antibiotic, the amount of vancomycin hydrochloride and tobramycin sulfate fell below the MQL after 1 hour. The test specimens containing the combination of these two antibiotics continued to elute amounts above the MQL for tobramycin sulfate for up to 6 hours and above the MQL for vancomycin hydrochloride for up to 14 hours. The antibiotic elution data is given in Attachment 1, Tables 1 and 2.

The amount of the antibiotics eluted from the disks was extrapolated to provide estimates of the total amount of antibiotic that will elute from a PROSTALAC Hip Temporary Prosthesis component. The surface area-to-weight ratio between the test samples and the small, medium, and large sizes of the femoral stem PROSTALAC constructs were calculated. Similarly, comparisons were made between the test samples and the 3 acetabular cup sizes. The extrapolations required calculations of weight/area of the test samples and the femoral or acetabular constructs. These values were used to calculate the expected antibiotic concentrations. The extrapolated concentrations of vancomycin and tobramycin are given in the Attachment 1, Tables 3 and 4. The elution studies demonstrate that when the cement contains only one antibiotic, the antibiotic levels are undetectable within 6 hours for both vancomycin and tobramycin. When the cement contains both antibiotics, the antibiotics are detectable for at least 6 hours (for tobramycin) and 14 hours (for vancomycin).

B. Mechanical Testing

Dynamic testing of the PROSTALAC core stem component was performed to determine its mechanical strength under cyclic loading. Two tests were conducted utilizing the modified Semlitsch hip stem test method. Five size 1 high-offset core implant stem components were used as the test specimens for each test. The first test was designed to test the stem mid-shaft region of the core stem component. The loading profile was compression-compression sine wave with R= 0.1. The load assigned for two specimens were 190 lbs. at 20 Hz and 15 Hz respectively; two specimens were assigned a 200 lb. load and the fifth specimen was loaded to 235 lb. All tests were conducted to 10 million cycles. No failures occurred.

The second test was designed to test the neck region of the core stem component. The distal stem portion of each test specimen was shortened to accommodate the test fixture. The proximal stem, immediately distal to the neck, was supported to maximize the applied load to the neck. Three specimens were loaded to 2300 lb, and two specimens loaded to 2000 lb. Tests were run at 15 Hz and 20 Hz to 10 million cycles. No failures occurred.

The design of the size 1 PROSTALAC high-offset core stem component was to determined to be satisfactory for its intended use.

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The PROSTALAC Hip composite femoral prosthesis (core femoral stem with the antibiotic cement mantle) was subjected to an *in vitro* cyclic fatigue test to determine the performance of the device under simulated loads found *in vivo*. Six test samples were subjected to cyclic loads ranging from 0.12-3.4 BW through 10^6 cycles at 8 Hz. The applied loads were increased to 0.44-4.4 BW and the test repeated. The samples were removed from the test apparatus for visual and radiographic evaluations of the cement mantle surrounding the core stems. There was no remarkable difference seen between the pre-test and post-test conditions of the core stem/cement mantle composite for any of the samples tested.

C. Clinical Studies

Methodology

Clinical evidence of the safety and probable benefit of the PROSTALAC Hip is based on a retrospective review of the source documents from a series of PROSTALAC Hip devices implanted at the University of British Columbia (UBC) Vancouver, British Columbia, Canada from a period between November 1989 and September 1998. The retrospective review was performed by the applicant and by an independent reviewer under the direction of the sponsor. Source documents included UBC hospital records and clinic records from the five orthopaedic surgeons who implanted the device for the purpose of eradication of a confirmed infection of the hip. All hospital records for each hospitalization, regardless of whether it was related to the PROSTALAC Hip surgery, were examined. Data were extracted from the source documents and recorded on case report forms developed specifically for this purpose. The recorded data were screened by the applicant and then compiled into an electronic database for tabulation and analysis. All subjects receiving any component of the PROSTALAC Hip were included in the retrospective study population. Data from subjects were included in the analyses for safety and probable benefit of the device only if predetermined criteria were met. Tabulated data from subjects not meeting the specified criteria were analyzed for safety concerns only.

Literature Reference Protocol

A review of the medical (English only) literature was performed for reports of patients treated with two-stage revision and/or resection arthroplasties for infections of their hips following total hip replacement implant surgery. The literature search covered the literature published in the years between 1960 to 1998. All available articles were screened for suitability based upon patient demographics, pathology, i.e., confirmed or suspected hip infections, treatment modalities, numbers of patients treated and length of follow-up. A total of 16 articles met the requirements for inclusion as control references from which the extracted data were pooled for comparison to the retrospective study population of PROSTALAC Hips. The control reference citations are provided in Section XV.

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The Study Population
The retrospective study population consisted of 135 PROSTALAC Hips implanted in 125 subjects with either confirmed or suspected infections of their hip replacement prostheses. There were 66 males and 69 females with a mean age of 65.8 years (range 27.2-87.7 yrs). All patients had at least one of the PROSTALAC Hip device components implanted during the course of their treatment. Tabular displays of the types and frequencies of index diagnoses and pathogens isolated for this cohort of 135 PROSTALAC Hip cases are provided in Attachment 2, Tables 1-2. The mean interoperative interval was 4.6 months (range 0.07 to 41.6 months) and the mean postoperative interval was 13.1 months. (range 0.5 to 61.7 months)

A variety of antibiotics were used in the construction of the PROSTALAC Hip Temporary Prosthesis device, including vancomycin, tobramycin, gentamicin, streptomycin, penicillin, ampicillin, cefuroxime, ceftizoxine, and cefamandol. Vancomycin or tobramycin was used in 110/135, or 81.5%, of the cases, and the vancomycin and tobramycin combination was used in 89/135, or 65.9%, of the cases.

The average time between the PROSTALAC Hip implantation procedure and the second-stage surgical procedure was 4.6 months (range = 0.1 - 41.6 months). The 7 cases that retained the PROSTALAC Hip implants or died prior to the second stage were not included in these figures. The mean postoperative follow-up was 13.1 months.

Probable Benefit
Probable benefit of the PROSTALAC Hip was determined from the numbers of patients who had successful treatments and successful clinical outcomes. In further support of device probable benefit, statistical comparisons were made between the infections reported at the interoperative, postoperative and combined postoperative and interoperative time intervals for PROSTALAC Hip study population and a literature based control population of patients undergoing two-stage revision arthroplasties for infections of their hip prostheses. Comparisons were also made between the proportions of PROSTALAC Hip patients and the literature control patients undergoing second stage total hip replacement.

Successful treatment outcomes were reported for 96 out of 116 cases eligible for an overall success rate of 83.0%. Successful clinical outcomes were reported for 89 of 97 cases having the minimum required one month follow-up information for their permanent hip replacement surgery for a successful clinical outcome of 91.7%. An analysis of infection results indicated that no statistically significant difference exists between recurrent and/or persistent infection rates reported for the PROSTALAC Hip cases and those reported for the combined results of the literature controls. The higher proportion of PROSTALAC Hip patients versus control patients proceeding to second stage THA was statistically significant. A two-tailed Fisher's Exact test (α=.05) was used in each instance.

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Safety
Safety was determined through the statistical comparisons between the frequencies of device removals, complication and mortality rates reported for the PROSTALAC Hip and the literature controls. Patient deaths were further examined for causes that may have been attributable to the device.

The lower rate of second stage removals among cases treated with the PROSTALAC Hip implant is statistically significant compared to controls. No difference in death rate is evident between patients treated with the PROSTALAC Hip and control patients. Complication rates were significantly greater for the PROSTALAC Hip for dislocation/subluxation, wound problem, pain and complications categorized as "other." However, these complications are not expected in patients treated with excision arthroplasty alone. No differences between complication rates were found for fracture, loosening, trochanter nonunion, osteomyelitis, nerve palsy, heterotopic bone formation and hematoma. A two-tailed Fisher's Exact test (α=.05) was used in each instance.

Conclusions
The records for 135 cases from a single center treated with the PROSTALAC Hip Temporary Prosthesis were examined by the applicant adhering to strict eligibility criteria for inclusion into a retrospective study population for comparison to a literature based control population of patients undergoing standard treatments for infections of their hip replacement prostheses. No differences were seen in the mortality rates between the PROSTALAC Hip treatment group and the comparative controls. Infection rates following treatment with the PROSTALAC Hip were not significantly different from those reported in the literature. The proportion of cases proceeding to second stage surgery for implantation of a total hip prosthesis was significantly greater than that reported in the literature. One adverse event of a systemic reaction to the antibiotic eluted from the PROSTALAC Hip was reported.

IX. Conclusions Drawn from the Studies

Dynamic and static tests of the PROSTALAC Hip Temporary Prosthesis were conducted and the results from those tests demonstrate that the device has sufficient strength and durability for its intended use. *In vitro* elution studies quantified the amount of antibiotics delivered from the bone cement. Results reported from the clinical use of the PROSTALAC Hip from a single center were tabulated and compared to a literature based control population of patients undergoing generally accepted standards of treatment for their hip infections following total hip joint replacement surgery. Based upon comparisons between the results from the single center study and those reported in the medical literature, the PROSTALAC Hip Temporary Prosthesis is a safe and probably effective adjunctive therapy for the treatment of patients with infections of their hips following total hip joint replacement surgery.

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X. Risk/Benefit Analysis

The use of the PROSTALAC Hip Temporary Prosthesis in a two-stage procedure to treat infected total hip replacements provides for the delivery of vancomycin hydrochloride and tobramycin sulfate antibiotics locally to the infected hip joint region and maintains the soft tissue envelope. In addition, the device allows the patient hip range of motion and limited ambulation. The alternative treatment, excision of the infected total hip prosthesis without replacement, leads to significant scarring of the soft tissues, limb shortening, and significant difficulties in the second stage surgery. In addition, it does not provide any hip joint stability and requires the patient to remain bedridden for the duration of the systemic antibiotic treatment. The potential benefit of improving the rate of successful treatment of the hip joint infection due to the antibiotics eluted from the device has not been demonstrated.

XII. Panel Recommendation

This HDE was not taken to a meeting of the Orthopedics and Rehabilitation Devices Panel because other marketing applications for antibiotic bone cement devices for similar indications and total hip replacement devices similar in design have been reviewed by the Panel. It was determined, therefore, that the clinical issues raised by this HDE are similar to those previously reviewed by this Panel.

XIII. CDRH Decision

CDRH has determined that, based on the data submitted in the HDE, the PROSTALAC Hip Temporary Prosthesis will not expose patients with infected total hip replacements to an unreasonable or significant risk of illness or injury, and the probable benefit to health from using the device outweighs the risks of illness or injury, and issued an approval order on March 23, 2001.

XIV. Approval Specifications

Directions for use: See the "Surgical Technique" manual.

Indications for use: See Section II above.

Hazards to health from the use of the device: See Warnings, Precautions, and Adverse Effects sections.

XV. Publications and Other Outside Information

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CONTROL GROUP REFERENCES FOR THE RETROSPECTIVE STUDY

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Attachment 1

Table 1
Time/Concentration of Eluted Vancomycin HCl

Vancomycin HCl (ug\mL in 40 ml extract)			
Sample	1 hour	6 hour	14 hour
Endurance (vancomycin only) #1	35.5	ND	ND
Endurance (vancomycin only) #2	26.9	ND	ND
Endurance (vancomycin only) #3	32.9	ND	ND
Palacos R (vancomycin only) #1	40.3	ND	ND
Palacos R (vancomycin only) #2	40.4	ND	ND
Palacos R (vancomycin only) #3	53.8	ND	ND
Endurance (vancomycin and tobramycin) #1	23	15.9	10.8
Endurance (vancomycin and tobramycin) #2	19.6	15.8	10.4
Endurance (vancomycin and tobramycin) #3	17.3	10.7	10.5
Palacos R (vancomycin and tobramycin) #1	39.4	14.9	ND
Palacos R (vancomycin and tobramycin) #2	49.8	12.9	ND
Palacos R (vancomycin and tobramycin) #3	36.3	11.5	ND
Note: Detection limit was 10ug\ml			

ND= Not Detectable

Table 2
Time/Concentration of Eluted Tobramycin Sulfate

Tobramycin Sulfate (ug/mL in 40 mL extract)		
Sample	1 hour	6 hour
Endurance (tobramycin only) #1	329	ND
Endurance (tobramycin only) #2	322	ND
Endurance (tobramycin only) #3	328	ND
Palacos R (tobramycin only) #1	320	ND
Palacos R (tobramycin only) #2	337	ND
Palacos R (tobramycin only) #3	334	ND
Endurance (vancomycin and tobramycin) #1	212	209
Endurance (vancomycin and tobramycin) #2	209	207
Endurance (vancomycin and tobramycin) #3	206	219
Palacos R (vancomycin and tobramycin) #1	255	ND
Palacos R (vancomycin and tobramycin) #2	251	ND
Palacos R (vancomycin and tobramycin) #3	253	ND
Note: Detection limit was 200ug\ml		

ND= Not Detectable

Table 3

Extrapolated Concentration of Eluted Vancomycin HCl and Tobramycin Sulfate

Extrapolated Tobramycin and Vancomycin Levels (μg/ml) (From cement that contains one antibiotic)			
		Endurance Cement	Palacos Cement
		1 hour	1 hour
Size 1 femoral	Tobra	349.3	353.3
	Vanco	34.0	48.0
Size 5 femoral	Tobra	610	617.7
	Vanco	59.4	83.8
Long stem femoral	Tobra	783.3	793
	Vanco	76.3	107.6
Acetabular	Tobra	270.7	274.3
	Vanco	26.4	37.2

ND= Not Detectable

Table 4

Extrapolated Concentration of Eluted Vancomycin HCl and Tobramycin Sulfate

Extrapolated Tobramycin and Vancomycin Levels (μg/ml) (From cement that contains both antibiotics)							
		Endurance			Palacos		
Size	Antibiotic	1 hour	6 hours	14 hours	1 hour	6 hours	14 hours
Size 1 femoral	Tobra	223.7	226.7	-	271	ND	-
	Vanco	21.4	15.1	11.3	44.8	14.0	ND
Size 5 femoral	Tobra	390.7	211.7	-	473	ND	-
	Vanco	36.4	26.4	19.7	78.2	24.5	ND
Long stem femoral	Tobra	501.7	508.3	-	607	ND	-
	Vanco	47.9	33.9	25.4	100.4	31.5	ND
Acetabular	Tobra	173.3	175.7	-	210	ND	-
	Vanco	16.6	11.7	8.9	34.7	10.9	ND

ND= Not Detectable

Attachment 2

Table 1

Diagnoses at Index Surgeries N=135		
CATEGORY	Frequency	Percent
OSTEOARTHRITIS	55	40.7
FRACTURE	20	14.8
UNKNOWN	16	11.9
FAILED PROSTALAC	10	7.4
POST-TRAUMATIC ARTHRITIS	9	6.7
AVASCULAR NECROSIS	6	4.4
RHEUMATOID ARTHRITIS	6	4.4
CONGENITAL HIP DYSPLASIA	4	3.0
SEPTIC ARTHRITIS	4	3.0
ANKYLOSING SPONDYLITIS	1	0.7
LEG-CALVE-PERTHES	1	0.7
OTHER	1	0.7
PSORIATIC ARTHRITIS	1	0.7
SUBCAPITAL FRACTURE	1	0.7

Table 2

Pathogens Confirmed at or Prior to PROSTALAC Hip Surgery N=231		
Pathogen	Frequency	Percent
S. AUREUS	62	26.8
S. EPIDERMIS	57	24.7
STAPHYLOCOCCUS	27	11.7
ENTEROCOCCUS	11	4.8
OCCULT GRAM-POS. COCCI	8	3.5
S. VIRIDANS	8	3.5
E. COLI	6	2.6
STREPTOCOCCUS	6	2.6
B-HEMOLYTIC STREP.	5	2.2
BACTEROIDES FRAGILIS	3	1.3
DIPTHEROIDS	3	1.3
ENTEROBACTER	3	1.3
ENTEROCOCCUS FAECALIS	3	1.3
STAPH. LUGDUNESIS	3	1.3
ENTEROBACTER CLOACAE	2	0.9
GRAM-NEG. COCCUS	2	0.9
KLEBSIELLA PNEUMONIAE	2	0.9
PROTEUS MIRABILIS	2	0.9
PSEUDOMONAS AERUGINOSA	2	0.9
BACILLUS SPECIES	1	0.4
BACTERIUM JEIKIUM	1	0.4
CANDIDA ALBICANS	1	0.4
CANDIDA PARAPSILOSIS	1	0.4
CORYNE BACTERIUM	1	0.4
ERYSIPELOID	1	0.4
MIXED FLORA	1	0.4
PEPTO. ASACCHARALYTICUS	1	0.4
PEPTOSTREPTOCOCCI	1	0.4
PNEUMOCOCCUS	1	0.4
PROPIONIC BACTERIA	1	0.4
STAPH ALBUS	1	0.4
STREP. PNUEMONIAE	1	0.4
TUBERCULOSIS	1	0.4
XANTHOMAS MALTOPHILIA	1	0.4
YERSINIA ENTEROLITICA	1	0.4