## SECTION IX.

## REGULATORY CONTROL OF RISKS

Preceding sections of this petition have shown that total hip arthroplasty incorporating the use of a metal/metal articulation as part of a total hip system is equivalent to the class II, semi-constrained, metal/polymer total hip prosthesis. Neither it nor any other surgical procedure is free of complications, but this petition demonstrates that the risks to health have been identified and the controls to minimize those risks are in place. The risks inherent in the metal-on-metal hip replacement procedure are similar to those for total hip replacement surgery utilizing a class II device.

Complications can be distinguished between those related to surgery in general, and those that are specific to the device. Broken components requiring revision surgery would be considered a failure of the device. Loosening may involve device design, but it also depends on surgical technique, as well as uncontrollable patient factors. Complications such as infection, pulmonary embolism, gastrointestinal and genitourinary problems are not generally device specific, but are risks associated with most major surgical procedures.

The primary difference between the metal-on-metal total hip prosthesis (class III) and the metal/polymer total hip prosthesis is the wear of articulating surfaces. The metal-on-metal articulating surfaces wear on both the metal ball and the acetabular cup, but at a much slower rate than metal/polymer articulating surfaces. The metal/polymer hip generally wears primarily in the polymer acetabular cup. The surfaces of the prosthetic components that are in apposition to bone (fixation surfaces) are the same in both the metal-on-metal and the metal/polymer devices. Moreover, the fixation methods to bone are the same for both devices.

Based upon the above considerations, this petition recommends that the approach to regulatory control of risks should be the same for a metal-on-metal hip prosthesis as for a metal/polymer hip prosthesis. Regulatory control of the device can be simple and straightforward. Device risks can be handled through material standards, with substantial equivalence determinations serving to control device design. Patient and surgical risks can be minimized through device labeling, and device quality through Good Manufacturing Practices (GMP) Quality System Regulation (QSR). FDA has authority through the 510(k) process, as well as its general authority over misbranding and adulteration, to impose controls along these lines. FDA guidance documents are available to provide specific guidance regarding materials, testing, and labeling. The risks defined by clinical experience are well suited to controls of these types, and this petition's specific recommendation of the appropriate controls follows in this section.

| RISKS AND CONTROLS FOR METAL ON METAL HIP ARTHROPLASTY | |
|---|---|
| **Risks/Complications Identified in this Petition** | **Means to Control/Minimize risks** |
| **Loosening/Migration of Components** | 510(k) Requirement – Sterility<br>Adulteration Authority – GMP,QSR Sterility<br>Misbranding Authority – Labeling<br>Indications/contraindications/warnings/precautions |
| **Revision of Components**<br>**Dislocation of the Hip prosthesis** | 510(k) Requirement – Substantially Equivalent Design<br>510(k) Requirement – Laboratory Testing<br>Wear/fatigue/liner torque-out/liner push-out/lever-out<br>510(k) Requirement – Conformance to Material Stds<br>Misbranding Authority – Labeling<br>Indications/contraindications/warnings/precautions |
| **Implant Failure**<br>**Fracture/Wear**<br>**Osteolysis**<br>**Sensitivity to Materials** | 510(k) Requirement – Substantially Equivalent Design<br>510(k) Requirement – Conformance to Material Stds.<br>510(k) Requirement – Conformance to FDA guidance for acetabular & hip femoral components<br>GMP/QSR – Design Controls/Quality Systems<br>Misbranding Authority – Labeling<br>Indications/contraindications/warnings/precautions |
| **Infection** | 510(k) Requirement – Sterility<br>Adulteration Authority – GMP/QSR Sterility<br>Misbranding Authority – Labeling<br>Indications/contraindications/warnings/precautions |
| **Nerve Impingement/ Damage**<br>**Pain**<br>**Vascular Disorders**<br>**Pulmonary Embolism**<br>**Gastrointestinal/Genito-urinary Complications** | Misbranding Authority – Labeling<br>Warnings/precautions/potential adverse effects |

Device related risks associated with metal-on-metal hips are similar to those reported in the reclassification petition for constrained hip prostheses, which the Panel recommended be classified into class II. Those risks, as these, are grouped into three major categories, as follows.

## RISKS TO HEALTH IDENTIFIED BY THE PETITIONER

(grouped into three major categories)

### 1. LOSS OR REDUCTION OF JOINT FUNCTION

Loosening, Revision of Components, Implant Failure/Fracture/Wear/Dislocation

**Special Controls to Minimize Risks**

**ASTM Material Standards** - F67, F75, F136, F1377, F1580, F1537
**ASTM Test Methods** – F1044, F1147, F1612, F1714, F1814, F1820, F1875, F1978
**ISO Test Method**-14242

**FDA Guidance Documents**

Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement. (Facts-on-Demand #827)

Guidance Document for Femoral Stem Prostheses (Facts-on-Demand #187)

Guidance Document for Testing Acetabular Cup Prostheses (Facts-on-Demand #453)

Guidance Document for Testing Non-Articulating, "Mechanically Locked" Modular Implant Components (Facts-on-Demand #916)

Draft Guidance Document for the Preparation of Premarket Notification 510(k) Applications for Orthopedic Devices – The Basic Elements (Facts-on-Demand #832)

Guidance for Industry on the Testing of Metallic Plasma Sprayed Coatings on Orthopedic Implants to Support Reconsideration of Postmarket Surveillance Requirements (Facts-on-Demand #946)

### 2. ADVERSE TISSUE REACTION

Osteolysis, Sensitivity to Metal Implants, Inflammatory Response, and Metal Toxicity

**ASTM Material Standards** - F67, F75, F136, F1377, F1580, F1537

**FDA Guidance Documents**

Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part I: Evaluation and Testing

## 3. INFECTION

**Special Controls to Minimize Risk**

510(k) Sterility Review Guidance

**Additional Risks**

Nerve Impingement/Damage, Pain, Vascular Disorders, Pulmonary Embolism, Gastrointestinal/Genitourinary Complications, Metal Ion Release, Carcinogenicity

These additional identified risks are associated with orthopedic surgery in general, and are not unique to constrained hip surgery.

The risk of tumors will be addressed in the labeling by adding the following statement to the Adverse Effect section: "Although there is no conclusive evidence of the relationship between orthopedic implants and malignant tumors, any condition that causes chronic damage to tissues may be oncogenic."

The risk of metal ion release and possible systemic effects is still under investigation and not well understood. The labeling under Precautions will state: "Patients with compromised kidney function or renal disease may not be candidates for metal on metal articulations."

A significant amount of research has been performed from human retrieval and in vitro studies to assess short and long-term biological effects of metal-on-metal total hip replacement. A report from Pat Campbell PhD, Joint Replacement Institute and J. Vernon Luck Orthopaedic Research Center Orthopaedic Hospital, Los Angeles, California is included and contains information on metal wear, particle identification, histology, and metal sensitivity (see Section VII, C. Published Biological Studies)

In terms of carcinogenicity, Howie et al[205] reported that particulate CoCr in animal models while associated with macrophages, had shown a doubtful link to tumor formation. Chromium in the $Cr^{+3}$ form, which is more stable at neutral pH, is unable to cross membranes as is the case with extremely toxic $Cr^{+6}$ ions. Studies to date have shown no formation of the $Cr^{+6}$ from solid implant materials.
Lewis et al[210] presented results of rats injected intraarticularly with wear particles 1.5 to 50 µm in size and examined over a two year period. CoCr particles were generated in a wear simulator. Positive (nickel subsulfide) and negative (manganese) controls were also used Those rats receiving CoCr particles had no local tumors. Particles were identified in the subsynovium with minimal fibrosis. The author offered that a significantly larger group (500 rats) would be needed to substantiate a 1% tumor incidence.

Swanson et al[218] pointed out that, although his wear and laboratory studies in rats tend to indicate CoCr particles constitute a risk for carcinogenesis, it is extremely small and not calculable. Additionally, the probable induction period is longer than the life expectation of many patients who could potentially benefit from such operations. As an interesting

comparison, Swanson noted that earlier rat studies on larger particle polyethylene generated this same conclusion (carcinogenesis).

Case et al[190-191] analyzed the genetic aberration (chromatid breaks, gaps, etc.) in the marrow samples of 71 revision arthroplasty patients and 30 primary arthroplasty patients. Revisions included 27 Charnley devices, 17 D-series, 5 Howse, 6 Thompson, 1 each of Harris-Galante, Wagner, Stanmore, and Exeter, 3 unknown, and 2 each of McKee-Farrar and Ring prostheses. Case found that aberration was higher (statistically significant) in marrow cells adjacent to stems in revision cases than in marrow of the iliac crest of the same patient or in patients undergoing primary arthroplasty. These findings are significant since the majority of the revision cases were "standard" arthroplasty devices and not metal/metal devices.

Visuri et al[221] reported on 433 cemented McKee-Farrar patients (511 devices) operated on from 1967 to 1973 representing 5729 person years. Average follow-up was 9.2 years for males and 9.8 years for females. Using the Finnish cancer registry, it was found that the risk of total cancer of THR patients did not increase. However, the incidence of site specific cancers did vary. A decreased risk of breast cancer was found. A slightly increased risk of leukemia and lymphoma was also found. The author cited other published reports supporting the fact that while cobalt has carcinogenic properties, there was inadequate evidence to show that it is a human carcinogen. Cobalt has reportedly been used for more than 20 years as an anemia treatment since it stimulates erythropoeisis; no cases of cancer have been reported. Longer term studies with more patients were recommended to allow further analysis.

As a follow-up to his prior work focusing on McKee-Farrar implants[221], Visuri[222] compared the incidence of cancer in both metal-on-metal and metal-on-polyethylene devices to that of the general population in Finland. Again using the registries available, a significant amount of follow-up (over 28,000 person years) over a long period of time (12.5 years for metal/polyethylene, 15.7 years for metal/metal) was assessed. Both groups were found to have significantly less occurrence of lung cancer and no variation in the rate of other cancers when compared to the general population. Metal-on-metal patients had an insignificantly (i.e., not statistically significant) increased risk of leukemia and lymphoma. No local sarcomas were noted in either group. The overall cancer rate for metal/metal patients was lower than that of the general population in all but the 12$^{th}$ year (examined over a 15 year period). Based on the information, it is suggested that factors other than the total hip arthroplasty played a major role in the origin of cancer. In a more recent study describing a longer follow-up, Visuri[220] was unable to confirm the previously described increased risk of leukemia and lymphoma. Furthermore, lung cancer and the risk for cancer mortality were reduced and the risk of local sarcoma was insignificant.

Tharani et al[219] concluded in their analysis that there was no causal link between total hip replacement and cancer, and that there was only one study in which there appeared to be an increased risk of cancer following metal/metal total hip replacement but that this was small in comparison with other studies. Their review also showed no increase in bilateral patients which is another observation against cancer induction by total hip arthroplasty.

Gillespie et al[197] presented results from an analysis of 1358 total hip patients (representing 14256 person years) in New Zealand from 1966 to 1973. Mean follow-up was 10.52 years

(6 months to 17 years). Similar to the works of Visuri[222], cancer and death registries were searched for this same time period; 164 cancers disease treatment or social/occupational factors (e.g., pesticides in agrarian New Zealand).

Mathiesen et al[211] presented an analysis of 10785 total hip patients in Sweden (representing 58437 patient years) implanted from 1974 to 1988. Use of the Swedish cancer registry and death registry allowed evaluation of tumor incidence. The overall actual incidence of malignancy (881) was lower than expected (917.7). Incidence of leukemia and lymphoma was slightly higher in the first year of follow-up but had a corresponding decrease the second year of follow-up. When year 1 and 2 are analyzed together, this incidence is not significant. Patients followed for greater than 10 years had a slightly higher incidence of total cancer, but a decreased risk of leukemia and lymphoma. Bilateral and revision patients were analyzed as a subset in order to evaluate potential for increased malignancy due to increased exposure. The overall cancer incidence in this subset was found to be less than expected for bilateral patients and slightly increased for revision cases; leukemias and lymphomas were less frequent than the entire series. Possible selection bias is cited as THR patients are generally more healthy with a longer life expectancy. The author notes that an association between THR and increased incidence of cancer during the first 10 postoperative years was unable to be made, possibly due to the long latency period for metal associated cancers.

In an extensive review article published in 2001[249], the authors referred to the Visuri studies cited above as the only ones assessing the risk of cancer after metal-on-metal total hip replacement. In that study, the relative risk of cancer was reported to be 0.95 (95% confidence interval, 0.79 to 1.13) suggesting that there is no apparent increased risk of cancer after metal-on-metal arthroplasty. In addition, the risk of sarcoma after metal-on-metal total hip replacement was found to be 0.00 (95% confidence interval, 0.00 to 6.59) However, these same authors found the relative risk of hemopoietic cancer to be 1.59 (95% confidence interval, 0.82 to 2.77) following metal on metal total hip replacement and 3.77 (95% confidence interval, 0.96 to 17.6) for leukemia when metal-on-metal implants were compared to metal-on-polyethylene implants. Again, the confidence intervals for these data are very broad and encompass unity, indicating that the risk is statistically neither increased or decreased. From an epidemiological perspective, these data are limited because of the small number of patients (579) who underwent metal-on-metal total hip replacement Because this number is small and the numbers of observed and expected cases are also small, the strength of the probability analysis is quite limited. In summary, the authors note that the available data do not support a causal link between total hip or knee arthroplasty and the development of cancer.

The only mention of metal-on-metal implants in the discussion section of the Nationwide Study of Cancer Risk Among Hip Replacement Patients in Sweden, referred to an earlier report where the rate of kidney cancer was found to be statistically significantly elevated among hip implant recipients. This finding, however, was not confirmed in the newer cohort of patients who received implants during the period from 1984 to 1994. The authors stated that it is possible that hip implants from the earlier time period (more commonly metal-on-metal than polyethylene-on-metal) could influence renal cancer risk via properties that are not shared by newer implants. Also, hip implant patients are high consumers of analgesics, and the older cohort of patients had more opportunity to take phenacetin, an analgesic that was linked to both kidney failure and kidney cancer and, therefore

withdrawn from the Swedish market in the early 1970s. If one considers the number of associations examined in the analysis, it is also possible that the elevated Standardized Incidence Ratio (SIR) for kidney cancer in the 1965-1983 cohort was due to chance. This article referred to an earlier paper that found no excess of kidney cancer in a large cohort of Danish patients who had hip implant surgery during the period from 1977 through 1989 (SIR = 0.93; 95% confidence interval = 0.74 to 1.14).

In a 2005 publication[232] in the Journal of Athroplasty, the authors, Dumbleton and Manley, summarize the literature on metal-on-metal total hip replacement with focus on possible acquired hypersensitivity, mutagenicity and carcinogenicity. They note that reports of proven adverse effects are scant and that prospective, randomized trials with excess of 15 years will be needed to differentiate between the performance and effects of metal/metal and other bearing combinations. See reference 25 in appendix 3.

Jacobs et al[206-207] discussed the clinical relevance of increased concentrations of circulating metal degradation products derived from orthopaedic implants. According to the authors, this may have deleterious biological effects over the long term and warrant investigation Accurate monitoring of the concentration of metal in the serum and urine after total hip replacement can provide insights into the mechanism of ion release.

## Special Controls to Minimize Risks

### LIST OF SPECIAL CONTROLS

Following is a listing of special controls available to minimize the risks to health identified by the petitioner and by a previous panel. These special controls are in addition to the general controls applicable to all orthopedic implants. These special controls include 18 ASTM standards for materials and test methods, and 8 FDA Guidance Documents. In addition, the FDA may require certain mechanical testing as part of a 510(k) premarket notification. These tests could include wear testing of the articulating surfaces as described in this petition.

The ASTM standards define implant material specifications and testing methods applicable to the metal-on-metal hip prosthesis. Adherence to these standards and comparison of the results from these standard tests can control the risks to health of adverse tissue reaction, pain and/or loss of function, and revision by having the manufacturer use surgical implant quality materials, prudent design assurance and good manufacturing practices.

The ASTM standards are FDA recognized consensus standards. ASTM standards may be obtained from ASTM Customer Services, 100 Barr Harbor Dr., West Conshohocken, PA 19428 (Telephone 610-832-9585). ASTM has a site on the World Wide Web at http://www.astm.org/.

## ASTM Standards

1. ***ASTM F67-95 Standard Specification for Unalloyed Titanium for Surgical Implant Applications.*** This specification covers the chemical, mechanical, and metallurgical requirements for four grades of unalloyed titanium used for the manufacture of surgical implants.
2. ***ASTM F75-98 Standard Specification for Cobalt-28 Chromium-6 Molybdenum Casting Alloy and Cast Products for Surgical Implants (UNS R30075).*** This specification covers the requirements for Cast cobalt-chromium molybdenum alloy shot, bar, or ingot for surgical implant applications.
3. ***ASTM F86-91 Standard Practice for Surface Preparation and Marking of Metallic Surgical Implants***
4. ***ASTM F136-98 Standard Specification for Wrought Titanium-6 Aluminum-4 Vanadium ELI (Extra Low Interstitial) Alloy (R56401) for Surgical Implant Applications.*** This specification covers the chemical, mechanical, and metallurgical requirements for wrought annealed Titanium-6 Aluminum-4 Vanadium ELI (extra low interstitual alloy (R56401) to be used in the manufacture of surgical implants.
5. ***ASTM F648-98 Standard Specification for Ultra-High-Molecular-Weight Polyethylene Powder and Fabricated Form for Surgical Implants.*** This specification covers ultra-high-molecular-weight polyethylene powder (UHMWPE) intended for use in surgical implants.
6. ***ASTM F983-86 Standard Practice for Permanent Marking of Orthopaedic Implant Components.*** The purpose of this standard is to (1) recommend that orthopedic implants be permanently marked, and (2) recommend practical amounts of information that should be included in the marking.
7. ***ASTM F1044-99 Standard Test Method for Shear Testing of Calcium Phosphate and Metal Coatings.*** This test method covers "lap shear" testing of porous and non-porous coatings adhering to dense metal substrates.
8. ***ASTM F1147-99 Standard Test Method for Tension Testing of Calcium Phosphate Porous Metal Coatings.*** This test method covers tension testing of porous and nonporous metal
   coatings adhering to dense metal substrates at ambient temperatures and determination of the degree of adhesion of coatings to substrates, or the internal cohesion of a coating in tension normal to the surface plane.
9. ***ASTM F1377-98a Standard Specification for Cobalt-28 Chromium-6 Molybdenum Powder for Coating of Orthopedic Implants (UNS-R30075).*** This specification covers requirements for cobalt-chromium-molybdenum alloy powders for use in fabricating coatings on cobalt-chromium-molybdenum alloy orthopedic implants.
10. ***ASTM F1472-99 Standard Specification for Wrought Titanium-6Aluminum-4Vanadium Alloy for Surgical Implant Applications (UNS R56400).***
11. ***ASTM F1612-95 Standard Practice for Cyclic Fatigue Testing of Metallic Stemmed Hip Arthroplasty Femoral Components with Torsion.*** This practice covers a method for the fatigue testing for evaluation in comparisons of various designs and materials used for stemmed femoral components.
12. ***ASTM F1636-95e1 Standard Specification for Bores and Cones for Modular Femoral Heads.*** This specification covers the functional dimensions and tolerances for tapered cones of proximal femoral stems and the bores of mating ceramic and metal heads.

13. ***ASTM F1714- 96 Standard Guide for Gravimetric Wear Assessment of Prosthetic Hip-Designs in Simulator Devices.*** This guide describes a laboratory method using weight-loss technique for evaluating the wear properties of materials or devices, or both, which are being considered for use as bearing surfaces of human-hip-joint replacement prostheses. The hip prostheses are evaluated in a device intended to simulate the tribological conditions encountered in the human hip joint, for example, use of a fluid such as bovine serum, or equivalent pseudosynovial fluid shown to simulate wear mechanisms and debris generation as found in vivo, and test frequencies of 1 Hz or less.
14. ***ASTM F1814-97a Standard Guide for Evaluating Modular Hip and Knee Joint Components.*** This guide covers a procedure to assist the developer of a modular joint replacement implant in the choice of appropriate tests and evaluations to determine device safety.
15. ***ASTM F1820-97 Standard Test Method for Determining the Axial Disassembly force of a Modular Acetabular Device.*** This test method covers a standard methodology by which to measure the attachment strength between the modular acetabular shell and liner. Although the methodology described does not replicate physiological loading conditions, it has been described as means of comparing integrity of various locking mechanisms.
16. ***ASTM F1875-98 Standard Practice for Fretting Corrosion Testing of Modular Implant Interfaces: Hip Femoral Head-Bore and Cone Taper Interface.*** This practice describes the testing, analytical, and characterization methods for evaluating the mechanical stability of the bore and cone interface of the head and stem junction of modular hip implants subjected to cyclic loading by measurements of fretting corrosion.
17. ***ASTM F1978-99 Standard Test Method for Measuring Abrasion Resistance of Metallic Thermal Spray Coatings by Using the Taber™ Abraser.*** This test method quantifies the abrasion resistance of metallic coatings produced by thermao spray processes on flat metallic surfaces. It is intended as a means of characterizing coatings used on surgical implants.
18. ***ASTM F1537 Standard Specification for Wrought Cobalt 28 Chromium 6 Molybdenum Alloy for Surgical Implants.*** This specification describes the chemical composition and mechanical requirements for wrought cobalt chromium molybdenum alloys for surgical implants.

**FDA Guidance Documents**

1. Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement. (Facts-on-Demand #827)
2. Guidance Document for Femoral Stem Prostheses (Facts-on-Demand #187)
3. Guidance Document for Testing Acetabular Cup Prostheses (Facts-on-Demand #453)
4. Guidance Document for Testing Non-Articulating, "Mechanically Locked" Modular Implant Components (Facts-on-Demand #916)
5. Draft Guidance Document for the Preparation of Premarket Notification 510(k) Applications for Orthopedic Devices – The Basic Elements (Facts-on-Demand #832)
6. Guidance for Industry on the Testing of Metallic Plasma Sprayed Coatings on Orthopedic Implants to Support Reconsideration of Postmarket Surveillance Requirements (Facts-on-Demand #946)

7. Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part I: Evaluation and Testing (Facts-on-Demand #361)
8. 510(k) Sterility Review Guidance...and Revisions of 11/18/94 and ORDB 7/3/97 (K90-1) (Facts-on-Demand #361)

FDA guidance documents provide guidance on how to meet general orthopedic device premarket notification (510(k)) requirements, including biocompatibility testing, sterility testing, mechanical testing, and physician and patient labeling. Use of the preclinical section of the FDA guidance documents can control the risks to health of adverse tissue reaction, infection, pain, and/or loss of function, and revision by having manufacturers use surgical quality implant materials, adequately test and sterilize their devices, and provide adequate directions for use, including recommended surgical techniques and patient information.

Guidance documents can be received via fax machine by telephoning the Center for Devices and Radiological Health's (CDRH) CDRH Facts-on-Demand system at 800-399-0381, or 301-827-0111 from a touch tone telephone. At the first voice prompt, press 1 to access the Division of Small Manufacturers Assistance FAX, at the second voice prompt, press 2, and then enter the document number followed by the pound sign (#). Then follow the remaining voice prompts to complete the request. The guidance documents are also available from CDRH World Wide Web address at http://www.fda.gov/cdrh.

## LABELING

The following indications for use, relative contraindications, warnings, and precautions were identified by a previous panel for the devices to be reclassified.

### Indications For Use

The metal on metal total hip replacement prothesis is indicated for use in patients requiring hip replacement due to the following conditions:

a) Non-inflammatory, degenerative joint disease including avascular necrosis, diastrophic variant, fracture of the pelvis, fused hip, Legg-Calve-Perthes disease, osteoarthritis, slipped capital epiphysis, subcapital fractures, and traumatic arthritis.
b) Rheumatoid arthritis
c) Correction of functional deformity
d) Treatment of non-union, femoral neck fracture, and trochanteric fractures of the proximal femur with head involvement, unmanageable using other techniques.
e) Failed previous surgery including: Joint reconstruction, internal fixation, arthrodesis, surface replacement arthroplasty, hemi-arthroplasty or previous total hip replacement

### Relative Contraindications

1. Bone or musculature compromised by disease, prior infection, or prior implantation that cannot provide adequate support or fixation for the prosthesis.
2. Any active or suspected infection in or about the hip
3. Skeletal immaturity

Warnings

1. Patients should be warned on the impact of excessive loading that can result if the patient is involved in an occupation or activity that includes substantial walking, running, lifting, or excessive muscle loading due to patient weight causing extreme demands on the hip that can result in the failure of the device. Extreme demands on the device may also cause loosening of the prosthetic components.Bending, contouring, or modifying the device may adversely affect the implant potentially leading to early implant failure.
2. Do not combine components from different manufacturers. This may lead to premature wear or failure of the device.

Precautions

Patients with kidney disease or compromised renal function may not be candidates for implantation with a metal-on-metal articulation.

Potential Adverse Effects

1. Infection
2. Pain
3. Loosening, wear, or mechanical failure of prosthetic components
4. Dislocation of the hip prosthesis requiring additional surgery
5. Localized progressive bone resorption (osteolysis)
6. Nerve impingement or damage, vascular disorders (including thrombus)
7. Heterotopic bone formation
8. †Sensitivity to implant materials
9. Gastrointestinal and/or genitourinary complications
10. Pulmonary embolism
11. Death
12. Myocardial infarction
13. Effusion
14. Bursitis
15. Special Note: Although there is no conclusive evidence of the relationship between orthopedic implants and malignant tumors, any condition that causes chronic damage to tissues may be oncogenic.

†A low incidence of metal hypersensitivity has been reported with failed metal-on-metal implants. The clinical relevance of these findings is unclear, and it is not known whether metal hypersensitivity causes implant failure.