

The Proposed Amendment

Accordingly, pursuant to the authority delegated to me, the Federal Aviation Administration proposes to amend 14 CFR part 71 as follows:

PART 71—DESIGNATION OF CLASS A, CLASS B, CLASS C, CLASS D, AND CLASS E AIRSPACE AREAS; AIRWAYS; ROUTES; AND REPORTING POINTS

1. The authority citation for 14 CFR part 71 continues to read as follows:

Authority: 49 U.S.C. 106(g), 40103, 40113, 40120; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963 Comp., p. 389.

§ 71.1 [Amended]

2. The incorporation by reference in 14 CFR 71.1 of the Federal Aviation Administration Order 7400.9L, Airspace Designations and Reporting Points, dated September 2, 2003, and effective September 16, 2003, is amended as follows.

Paragraph 6005 Class E airspace areas extending upward from 700 feet or more above the surface of the earth.

* * * * *

ANM OR E5 Sunriver, OR (Revised)

Sunriver Airport, Sunriver, OR
(Lat. 43°52'35"N., long. 121°27'11"W.)
Deschutes VORTAC
(Lat. 43°51'10"N., long. 121°18'13"W.)

That airspace extending upward from 700 feet above the surface of the earth within a 6.1 mile radius of the Sunriver Airport and within 3.5 miles each side of the Deschutes VORTAC 196° radial extending from the 6.1 mile radius to 14 miles north of the airport.

* * * * *

Issued in Seattle, Washington, on February 18, 2004.

Raul C. Treviño,

*Acting Manager, Air Traffic Division,
Northwest Mountain Region.*

[FR Doc. 04–5033 Filed 3–4–04; 8:45 am]

BILLING CODE 4910–13–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 888

[Docket No. 2003N–0561]

Orthopedic Devices; Effective Date of Premarket Approval of the Hip Joint Metal/Polymer or Ceramic/Polymer Semiconstrained Resurfacing Cemented Prosthesis

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule; opportunity to request a change in classification.

SUMMARY: The Food and Drug Administration (FDA) is proposing to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis. The agency is summarizing its proposed findings regarding the degree of risk of illness or injury intended to be eliminated or reduced by requiring the device to meet the statute's approval requirements as well as the benefits to the public from the use of the device. The agency also is proposing to revise the name and identification of the device. In addition, FDA is announcing the opportunity for interested persons to request the agency to change the classification of the device based on new information. FDA is taking this action under the Federal Food, Drug, and Cosmetic Act (the act) as amended by the Medical Device Amendments of 1976 (the 1976 amendments), the Safe Medical Devices Act of 1990 (the SMDA), the Food and Drug Administration Modernization Act of 1997 (FDAMA), and the Medical Device User Fee and Modernization Act of 2002 (MDUFMA).

DATES: Submit written or electronic comments by June 3, 2004; submit written or electronic requests for a change in classification by March 22, 2004.

ADDRESSES: Submit written comments or requests for a change in classification to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>.

FOR FURTHER INFORMATION CONTACT: Pei Sung, Center for Devices and Radiological Health (HFZ–410), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–2036.

SUPPLEMENTARY INFORMATION:

I. Background

Section 513 of the act (21 U.S.C. 360(c)) requires FDA to classify medical devices into one of three regulatory categories (classes): Class I (general controls), class II (special controls), and class III (premarket approval). Generally, FDA has classified, or is classifying, devices that were on the market before May 28, 1976, the date of enactment of the 1976 amendments, and devices marketed on or after that date

that are substantially equivalent to such devices. For convenience, this preamble refers to the devices that were on the market before May 28, 1976, and the substantially equivalent devices that were marketed on or after that date as “preamendments devices.”

Section 515(b)(1) of the act (21 U.S.C. 360e(b)(1)) establishes the requirement that a preamendments device that FDA has classified into class III is subject to premarket approval. An applicant may commercially distribute a preamendments class III device without an approved PMA or a notice of completion of a PDP until 90 days after the effective date that FDA issues in a final rule requiring premarket approval for the device, or 30 months after final classification of the device under section 513 of the act, whichever is later. Also, an applicant may commercially distribute a preamendments device subject to the rulemaking procedure under section 515(b) without an approved investigational device exemption (IDE) part 812 (21 CFR part 812) until the date FDA identifies in the final rule requiring the submission of a PMA or PDP for the device. At that time, an applicant must submit an IDE if a PMA has not been submitted or a PDP has not been declared completed.

Section 515(b)(2)(A) of the act provides a proceeding to issue a final rule to require premarket approval. The agency must initiate the process by publishing a notice of proposed rulemaking in the **Federal Register**. The notice must contain: (1) The proposed rule, (2) the proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved PMA or a declared completed PDP and the benefit to the public from the use of the device, (3) an opportunity to submit comments on the proposed rule and the proposed findings, and (4) an opportunity to request reclassification of the device based on relevant new information.

If FDA receives a request to reclassify the device within 15 days of publication of the notice, section 515(b)(2)(B) of the act requires the agency to take the following action. Within 60 days of the publication of the notice, FDA must consult with the appropriate FDA advisory committee and publish a notice denying the requested reclassification or announcing the agency's intent to initiate a proceeding to reclassify the device under section 513(e) of the act. If FDA does not initiate such a proceeding, section 515(b)(3) of the act requires FDA, after the close of the comment period on the proposed

rule and consideration of any comments received, to: (1) Issue a final rule requiring premarket approval, or (2) publish a notice terminating the proceeding. If FDA terminates the proceeding, FDA must initiate reclassification of the device under section 513(e) of the act. FDA does not have to initiate reclassification of the device if the reason for termination is that the device is a banned device under section 516 of the act (21 U.S.C. 360f).

If a proposed rule to require premarket approval for a preamendments device becomes final, section 501(f)(2)(B) of the act (21 U.S.C. 351(f)(2)(B)) requires the applicant to file a PMA or notice of completion of a PDP for any such device no later than 90 days after the date that FDA identifies in the final rule, or 30 months after final classification of the device under section 513 of the act, whichever is later. If an applicant does not file a PMA or notice of completion of a PDP by the later of the two dates, commercial distribution of the device must cease. An applicant may distribute the device for investigational use, if the applicant complies with the IDE regulations. If the applicant does not file a PMA or notice of completion of a PDP by the later of the two dates, and no IDE is in effect, the device is deemed to be adulterated within the meaning of section 501(f)(1)(A) of the act. The device also is subject to seizure and condemnation under section 304 of the act (21 U.S.C. 334) if its distribution continues. Shipment of the device in interstate commerce is subject to an injunction under section 302 of the act (21 U.S.C. 332). The individuals responsible for such shipment are subject to prosecution under section 303 of the act (21 U.S.C. 333). In the past, FDA has requested manufacturers to take action to prevent the further use of devices that do not have a filed PMA. FDA may determine that such a request is appropriate for the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis.

If a proposed rule to require premarket approval for a preamendments device becomes final, the act does not permit the agency to extend the 90-day period after the rule's effective date for filing an application or a notice. The House Report on the amendments states "the thirty month 'grace period' afforded after classification of a device into class III * * * is sufficient time for manufacturers and importers to develop the data and conduct the investigations necessary to support an application for

premarket approval." (H. Rept. 94-853, 94th Cong., 2d Sess. 42 (1976).)

The SMDA added section 515(i) to the act requiring FDA to review the classification of preamendments class III devices that do not have a final rule issued requiring the submission of PMAs. After its review, FDA must determine whether or not each device should be reclassified into class I or class II or remain in class III. For devices remaining in class III, the SMDA directs FDA to develop a schedule for issuing regulations to require premarket approval. The SMDA does not prevent FDA from proceeding immediately to rulemaking under section 515(b) of the act on specific devices, in the interest of public health, independent of the procedures of section 515(i) of the act. Proceeding directly to rulemaking under section 515(b) of the act is consistent with Congress' objective in enacting section 515(i) of the act, i.e., that preamendments class III devices for which PMAs or notices of completed PDPs have not been required either be: (1) Reclassified to class I or II, or (2) subject to premarket approval requirements. In this proposal, interested persons have the opportunity to request reclassification of the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis.

A. Classification of the Hip Joint Metal/Polymer Semiconstrained Resurfacing Cemented Prosthesis

In the **Federal Register** of September 4, 1987 (52 FR 33686), FDA issued a final rule classifying the hip joint metal/polymer semiconstrained resurfacing cemented prosthesis into class III. The preamble to the proposed rule to classify this device (47 FR 29052, July 2, 1982) included the recommendation of the Orthopedic Device Classification Panel (the Panel), an FDA advisory committee, regarding the classification of the device. The Panel recommended that this device be classified into class II, and identified the following risks to health presented by the device: Loss or reduction of joint function, adverse tissue reaction, and infection. The Panel believed that controls to the design, material composition, and mechanical properties of the device, such as its flexibility, rigidity, strength, and surface finish, were necessary to address these risks to health. The Panel also believed that the labeling of the device should include information on the device's dimensions, kinematics, strength, and wear characteristics. The Panel believed that sufficient information existed to establish a performance standard to

provide reasonable assurance of the safety and effectiveness of the device.

FDA disagreed with the Panel's recommendation and proposed (47 FR 29052) that the hip joint metal/polymer semiconstrained resurfacing cemented prosthesis be classified into class III. FDA believed that general controls, either alone or in combination with performance standards applicable to class II devices, were insufficient to provide reasonable assurance of the safety and effectiveness of the device. FDA believed that there was insufficient information to establish a performance standard for the device and that the device presented unreasonable risks of illness or injury because there were not adequate data to ensure the safe and effective use of the device.

The preamble to the final rule (52 FR 33686) classifying the hip joint metal/polymer semiconstrained resurfacing cemented prosthesis into class III advised that the earliest date FDA could require PMAs or notices of completion of PDPs for the device would be 90 days after FDA issued a rule requiring premarket approval for the device. In the **Federal Register** of January 6, 1989 (54 FR 550), FDA published a notice of intent to initiate proceedings to require premarket approval of 31 preamendments class III devices. The notice described the factors FDA took into account in establishing priorities for proceedings under section 515(b) of the act for issuing final rules requiring that preamendments class III devices have approved PMAs or declared completed PDPs. In the **Federal Register** of May 6, 1994 (59 FR 23731), FDA announced the availability of its preamendments class III devices strategy document. The agency categorized the hip joint metal/polymer semiconstrained resurfacing cemented prosthesis as a high priority Group 3 device, a device the agency considered to have low probability of being reclassified into class I or class II. Subsequently, FDA determined that the ceramic/polymer semiconstrained resurfacing cemented prosthesis is substantially equivalent to the metal/polymer semiconstrained resurfacing cemented prosthesis. Accordingly, FDA is commencing a proceeding under section 515(b) of the act to require that the metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis have an approved PMA or declared completed PDP.

B. Dates New Requirements Apply

In accordance with section 515(b) of the act, FDA is proposing to require an applicant to file a PMA or notice of completion of a PDP with the agency for

the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis by no later than 90 days after FDA publishes a final rule based on this proposal. An applicant whose device was in commercial distribution before May 28, 1976, or whose device FDA has determined to be substantially equivalent to such a device, may continue to market the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis during FDA's review of the PMA or notice of completion of a PDP. FDA intends to review any PMA for the device within 180 days and any notice of completion of a PDP for the device within 90 days of the filing date. FDA cautions that under section 515(d)(1)(B)(I) of the act, the agency may not enter into an agreement to extend the review period for a PMA beyond 180 days unless the agency finds that “* * * the continued availability of the device is necessary for the public health.”

Under § 812.2(d), FDA intends that the preamble to any final rule based on this proposal will inform the applicant about limits on certain exemptions under the IDE regulations. No later than 90 days after FDA publishes a final rule requiring an applicant to file a PMA or notice of completion of a PDP, the exemptions in § 812.2(c)(1) and (c)(2) of the IDE regulations for preamendments class III devices will cease to apply to any hip joint metal/polymer or ceramic/polymer semiconstrained cemented prosthesis which is: (1) Not legally on the market on or before that date; or (2) legally on the market on or before that date but for which a PMA or notice of completion of a PDP is not filed by that date, or for which PMA approval has been denied or withdrawn.

If an applicant does not submit a PMA, notice of completion of a PDP, or an IDE application for the hip joint metal/polymer or ceramic/polymer semiconstrained cemented prosthesis by no later than 90 days after FDA publishes a final rule requiring premarket approval for the device, commercial distribution of the device must cease. FDA cautions that manufacturers not planning to submit a PMA or notice of completion of a PDP immediately, should submit IDE applications to FDA no later than 60 days after the final rule publishes. FDA considers investigations of the hip joint metal/polymer or ceramic/polymer semiconstrained cemented prosthesis to pose a significant risk as defined in the IDE regulation.

C. Description of the Device

The hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis is an implanted device intended to replace a portion of the hip joint with minimal bone resection. FDA is proposing the following device identification for the hip joint metal or ceramic/polymer semiconstrained resurfacing cemented prosthesis to include ceramic/polymer semiconstrained resurfacing cemented hip joint prostheses that the agency has determined to be substantially equivalent (cleared) under § 888.3410 (21 CFR 888.3410):

A hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis is a two-part device intended to be implanted to replace the articulating surfaces of the hip while preserving the femoral head and neck. The device limits translation and rotation in one or more planes via the geometry of its articulating surfaces. It has no linkage across the joint. This generic type of device includes prostheses that consist of a femoral cap component made of a metal alloy, such as cobalt-chromium-molybdenum, or a ceramic material, that is placed over a surgically prepared femoral head, and an acetabular resurfacing polymer component. Both components are intended for use with bone cement (21 CFR 888.3027).

D. Proposed Findings With Respect to Risks and Benefits

As required by section 515(b) of the act, FDA is publishing its findings regarding: (1) The degree of risk of illness or injury designed to be eliminated or reduced by requiring an approved PMA or completed PDP for the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis, and (2) the benefits to the public from the use of the device.

E. Risk Factors

In the early 1950s, Townley (Ref. 1) designed a new type of hip joint prosthesis, the total articular resurfacing arthroplasty (TARA). The TARA is a type of hip surface replacement (HSR) prosthesis. A metallic component covers the articulating surface of the femoral head component of the device. The articulating surface of the acetabulum is resurfaced with a thin ultra-high molecular weight polyethylene (UHMWPE) shell. Because of the high failure rates of the TARA's acetabular component and the loosening of its femoral component, this device is no longer in use (Ref. 2). Since then, several slightly different HSR joint prosthesis designs have been marketed and investigated. These include metal-backed UHMWPE acetabular cups,

ceramic femoral resurfacing components, and porous-coated femoral and acetabular components.

Based on the published literature and other publicly available information, FDA has determined that the following risks to health are associated with the use of the hip joint metal/polymer semiconstrained resurfacing cemented prosthesis:

1. *Revision*—Due to mechanical aseptic failure, revision surgery is a major risk to health associated with implanting the metal/polymer or ceramic polymer semiconstrained resurfacing hip prosthesis. Revision surgery is a second major surgery to remove the device and replace it with a total hip replacement (THR).

Clinical investigations published before the device was classified in 1987 reported unacceptably high revision rates. These studies and studies published after the device was classified report revision rates up to 11.2 to 47.0 percent for followup periods ranging from 2 to 10 years for HSR arthroplasty with metal/polymer articulation (Refs. 3 to 9). With conventional THR, the 5- to 7-year failure rates range from 1.0 to 1.7 percent and 10-year failure rates are approximately 3 percent (Ref. 3).

In 1981, Head (Ref. 4) reported a 34 percent failure rate for the Wagner HSR prosthesis. The average time to failure of the device was 1½ years. He concluded that the causes of its high failure rate were: (1) A high susceptibility to avascular necrosis of the femoral head, (2) the younger ages of the patients, and (3) the device's biomechanical design.

In 1984, Head (Ref. 5) reported an overall anticipated failure rate for another HSR prosthesis. The rate was 34 percent (11.9 percent actual and 22 percent anticipated) after an average patient followup of 3.3 years. He predicted the “anticipated” device failure rate from radiographic evidence indicating device component failure in 15 patients who had experienced intermittent but not significant pain. Head believed that the radiographic evidence and pain were predictive of future failure and revision. He attributed the high incidence of component failure to: (1) The patients' high activity level, (2) poor cement distribution with resultant micro motion, and (3) increased frictional torque of the larger-diameter acetabular component.

Also in 1984, Capello et al. (Ref. 6) reported a 14.5 percent revision rate and a 10 percent loosening rate for the Indiana Conservative HSR prosthesis at 2 to 7 year's followup. They believed that this failure rate and non-traumatic loosening rate were unacceptable.

In 1986, Ritter and Gioe (Ref. 7) compared the Indiana Conservative HSR prosthesis and the Trapezoidal 28 (T-28) conventional THR implanted in the same patient. After an average patient followup of 5.4 years, failure rates were six times greater in patients implanted with the resurfacing design hip joint prosthesis (26 percent) than in patients implanted with the T-28 THR (4 percent). The complications of the resurfacing hip joint prosthesis group included femoral and acetabular loosening and femoral neck fracture.

In 1987, Kim et al. (Ref. 8) reported a comparison between the THARIES hip joint prosthesis, a type of HSR prosthesis, and two conventional THRs, the Biomet Charnley and the T-28 hip joint prostheses, in patients younger than 40 years old. Patient followup was up to 8.5 years. Kaplan-Meier failure rates were calculated at 3 and 5 years. In the highest risk patients, the younger non-rheumatoid arthritis (non-RA) and non-juvenile rheumatoid arthritis (non-JRA) patients, the conventional THR patients had significantly better hip functions than the patients with the THARIES prosthesis. In the lowest risk RA or JRA patients, the THARIES prosthesis appeared to perform as well as conventional THR. Kim et al. predicted that all acrylic-fixed hip joint prostheses, THARIES or THRs, would undergo early mechanical loosening in non-RA, non-JRA patients younger than 30 years old. They advised against the use of acrylic cement fixation of THARIES prostheses in patients younger than 30.

In 1990, Faris et al. (Ref. 9) reported on 64 Indiana Conservative HSR prostheses implanted in 61 patients with an average followup of 6.8 years. There was a 47 percent failure rate. Acetabular failure occurred in 20 patients, femoral failure occurred in 18 patients, and both acetabular and femoral failure occurred in 13 patients. Faris et al. concluded, "There seems to be little or no place for this design in contemporary hip joint arthroplasty."

In 1994, Mesko et al. (Ref. 3) reported a 13.2 percent revision rate for the TARA prosthesis at a mean patient followup of 8 years. The revised patients were an average of 7 years younger than the non-revised patients. The cemented TARA prosthesis had better intermediate to long-term success than other cemented resurfaced hip joint prostheses. However, the TARA prosthesis did not compare favorably to the conventional THR's lower 5- to 7-year failure rates of 1.0 to 1.7 percent and 10-year failure rates of 3 percent.

HSR was developed as an alternative to conventional THRs because of its

minimal requirements for bone removal. However, the failure rates of the HSRs reported in section E.1. of this document (Refs. 3 to 9) are significantly higher compared to the failure rates of conventional THRs. In addition, due to the inadequate UHMWPE thickness of some early HSR designs, biomechanical analyses indicated that device loosening is the predominate reason for the high failure rates of the HSR prosthesis compared to conventional THRs.

Potential etiologies for the high loosening rates cited previously include the following (Refs. 10 to 16): (1) Inadequate device design—impingement between the rim of the acetabular cup and the femoral neck, increased friction torque of the larger acetabular component, and inadequate implant-cement and/or cement-bone interfaces, (2) UHMWPE wear debris associated with macrophage response, cellular membrane development, granuloma formation and/or bone resorption, (3) surgical technique error such as inadequate cementing technique or cement distribution, inadequate bone strength beneath the components, various placement positions of the device, i.e., varus or valgus positions that cause toggling within the femoral intramedullary canal, and (4) higher physical activity levels of younger patients.

2. Loss or Reduction of Hip Joint Function—Improper design or inadequate mechanical properties of the device, such as lack of strength and resistance to wear, may result in a loss or reduction of hip joint function due to excessive wear, fracture, dislocation and/or deformation of the device components.

3. Adverse Tissue Reaction—Inadequate biological or mechanical properties of the device, such as lack of biocompatibility and resistance to wear, may result in an adverse tissue reaction. This reaction is due to dissolution or erosion of the device's articulating surfaces and release of debris to surrounding tissues and the systemic circulation.

4. Infection—The presence of an implanted device within the body may lead to an increased risk of infection.

FDA notes that loss or reduction of hip joint function, adverse tissue reaction, and infection are risks to health common to all implanted hip joint prostheses.

F. Benefits of the Device

The hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis is an implanted device intended to replace a portion of the hip joint with minimal

bone resection. The potential benefits intended from implantation of the device are relief of intense, disabling pain and restoration of hip joint function. This would result in a return to daily activities and an improved quality of life, especially in young patients.

In 1984, Amstutz et al. (Ref. 17) reported on the THARIES TARA prosthesis and T-28 THR for the treatment of primary hip osteoarthritis after a 6-year followup period. They concluded that the THARIES prosthesis appeared to be an acceptable alternative to THR after intermediate followup for 38 months. They stated that HSR could become a preferred treatment for primary osteoarthritis, "if these results are maintained after longer follow-up or are improved using better technique and a metal backing."

In 1987, Kim et al. reported that for low risk non-RA, non-JRA patients younger than 40 years old, the THARIES prosthesis appeared to perform as well as conventional THR after 3 to 5 years of followup (Ref. 8).

FDA has determined from review of the literature that the major causes of device loosening and subsequent device failure necessitating revision appear to be: (1) UHMWPE or metal particulate wear debris-induced bone resorption, and (2) high patient activity levels. Both cause increased wear and subsequent device failure necessitating revision.

Based on its evaluation of the benefits and risks described previously, FDA has concluded that the safety and effectiveness of the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis have not been established by valid scientific evidence as defined in 21 CFR 860.7.

II. PMA Requirements

A PMA for the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis must include the information required by section 515(c)(1) of the act and § 814.20 (21 CFR 814.20) of the PMA regulations. The PMA should include a detailed discussion of risks as well as a discussion of the effectiveness of the device for which premarket approval is sought. In addition, a PMA should include all data and information on: (1) Any risks known, or that should be reasonably known to the applicant that were not identified in this proposed rule; (2) the effectiveness of the specific hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis that is the subject of the submission; and (3) full reports of all device preclinical and clinical

information from the safety and effectiveness investigations for which premarket approval is sought.

A PMA should include valid scientific evidence as defined in 21 CFR 860.7, obtained from well-controlled clinical studies or another form of valid scientific evidence. In addition to the basic requirements for a PMA described in § 814.20(b)(6)(ii), the agency recommends that studies use a protocol that meet the criteria described further in section II of this document.

An applicant should submit the PMA in accordance with FDA's "Premarket Approval Manual," which is available on the Internet at <http://www.fda.gov/cdrh/devadvice>.

A. Preclinical Testing

FDA recommends the following types of preclinical testing to establish reasonable assurance of the safety and effectiveness of the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis:

1. *Materials Information*—This information should include, but is not limited to, chemistry; impurities identification and quantification; physical, chemical, and mechanical properties; and manufacturing process description. If the acetabular component is modular, you should include locking mechanism characterization. (See the FDA guidance document entitled "Guidance Document for Testing Non-Articulating, 'Mechanically Locked' Modular Implant Components," which is available on the Internet at <http://fda.gov/cdrh/devadvice> (Facts-on-Demand No. 916).

2. *Device Characteristics*—These characteristics should include, but are not limited to: Wear rates; debris size, geometry, and distribution; wear mechanism and wear markings; frictional torque measurement, axial and shear loading characteristics per American Society for Testing and Materials consensus standards and impingement latitude; implant-cement and cement-bone interfacial bonding strength, e.g., shear and tensile strengths; and UHMWPE thickness.

3. *Biocompatibility Information*—Biocompatibility information for finished devices made of a new hip-resurfacing material should be in accordance with ISO-10993 standards, "Biological Evaluation of Medical Devices," 21 CFR parts 1 to 16.

B. Clinical Testing

FDA believes that clinical testing is necessary to establish the reasonable assurance of the safety and effectiveness of the hip joint metal/polymer or

ceramic/polymer semiconstrained resurfacing cemented prosthesis. The clinical study should distinguish between the intended function of the device and the clinical benefit to the patient. The study also should demonstrate both statistical significance and clinical utility.

FDA recommends that device specific considerations include the following:

1. *Primary and Secondary Endpoints*—The applicant should identify the primary endpoints, such as reduced pain, improved function, and radiographic confirmation of device placement and secondary endpoints, such as improved quality of life and return to activities.

2. *Patient Evaluation*—Validated patient evaluation system(s) should be capable of demonstrating both patient improvement and deterioration. After enrolling patients, you should obtain baseline measurements. Subsequently, at each patient followup interval, you should measure the variables using the same patient evaluation method(s) and the same radiographic evaluation showing the position of the prosthesis in the skeleton and the condition of the surrounding bone.

3. *Patient Evaluation Systems*—These systems should include patient demographics (osteoarthritis or rheumatoid arthritis disease severity classification, comorbidities, medications, allergies, prior surgery, smoking, etc.); Harris Hip Score Evaluation or Western Ontario and McMaster University (WOMAC) Osteoarthritis Index; radiographic evaluation for subsidence and fracture; and quality of life evaluation, such as the SF-36 or SF-12 Health Survey.

4. *Patient Evaluation Schedule*—Patient evaluations should occur at regular intervals, such as baseline preoperative, intraoperative, and postoperative at 6 weeks, 3 months, 6 months, 12 months, and 24 months.

FDA recommends that the general clinical study considerations include the following:

1-1. *Study Design*—The applicant should evaluate the device in a prospective, randomized, clinical trial that uses adequate controls or other form of valid scientific evidence. The trial should answer all safety and effectiveness questions concerning the device, including its risk to benefit ratio. These questions should relate to the pathophysiologic effects that the device produces, as well as the primary and secondary endpoints used to analyze safety and effectiveness. You should define study endpoints and success. The study should have objectively measurable endpoints. The study design

should include an appropriate rationale, supported by background literature, and a clear study hypothesis statement.

The study should obtain statistical and clinical significance for the primary and secondary endpoints. For example, for each primary endpoint, you should use an alpha level of 0.05 and a beta level of 0.2. However, under certain restricted circumstances, a clinically significant result may be documented without statistical significance.

FDA recommends that the applicant conduct the study in three phases: enrollment, baseline measurement, and followup. A preferred method for subject enrollment is randomization by a central monitor.

The study should have a well-defined patient population. The patient population should be as homogenous as possible to minimize selection bias and reduce variability. Sample size justification should show that enough patients are enrolled to attain statistically and clinically meaningful results. You should carefully define inclusion and exclusion criteria. Inclusion criteria should include the patient's potential for benefit, the ability to detect a benefit in the patient, the absence of contraindications and competing risk, and assurance of patient compliance.

In a heterogeneous sample, stratification of patient groups participating in a multicenter clinical trial may be necessary to analyze homogeneous subgroups and minimize potential bias. FDA recommends that the applicant include a sufficient number of patients from each subgroup analysis to allow for stratification by pertinent demographic characteristics. Initial patient screening according to the inclusion and exclusion criteria and compliance of the patient population is recommended to minimize dropout. Patient exclusion due to dropout or loss more than 15 percent may invalidate the study due to bias potential. You should account for all missing data, such as dropouts. In the data analysis, you should document circumstances and procedures used to ensure patient compliance.

FDA recommends that the applicant evaluate and minimize potential sources of error, including selection bias, information bias, disease misclassification bias, comparison bias, or any other potential bias. The validity of these measurement scales should ensure that the treatment effect being measured reflects the intended use.

The applicant should measure baseline variables, e.g., age, gender, activity level, and other variables at the time of treatment. You should measure

other variables during the study as needed to completely characterize the particular device's safety and effectiveness. Also, throughout the study, you should record and evaluate adverse effects, complications, failure, revisions, and deaths.

FDA recommends rigorous monitoring to assure that the study data are collected in accordance with the study protocol. Attentive, unbiased monitors contribute prominently to a successful study.

For any other testing needed to assure a well-controlled study and meaningful results, you should describe the testing sufficiently to demonstrate its utility and adequacy. This is dependent on what the applicant intends to measure or what the expected treatment effect is based on each device's intended use.

The agency recommends the involvement of a biostatistician to provide proper guidance in the planning, design, conduct, and analysis of a clinical study.

1–2. *Data Analysis*—The agency recommends analyzing the following types of data: Effectiveness primary endpoints measured by patient evaluation systems and radiography; effectiveness secondary endpoints; safety endpoints, including adverse events, complications, device failures, revisions, and deaths; survival analyses (time to event or revision; and patient satisfaction). The analyses should include actual patient data.

There should be sufficient description and documentation of the statistical analysis methods, their appropriateness, and the test results. This should include complete descriptions of the methods, comparison group selection, sample size justification, stated hypothesis test(s), underlying assumptions, population demographics, study site pooling justification, clear data presentation, and clear discussion of the conclusions. The data analysis should relate to the medical claims. It should evaluate the comparability between treatment groups and control groups, including historical controls. The analysis should also account for all enrolled patients, including those lost to followup for any reason and a discussion of the impact of their loss. This should include both the evaluable population and the intent to treat population. The applicant should report actual patient data used to determine the result.

1–3. *Data Presentation*—The applicant should present effectiveness clinical findings in a series of tables that include complete patient accounting. FDA recommends using a table for each followup time point. Each table should show the number of patients in each

treatment group, the number of patients actually evaluated, the number of patients with missing data, and reasons for the missing data.

If the evaluation uses subcategories of rating specific clinical observations, (e.g., the pain, function, motion, subcategories of the Harris Hip Scoring System), you should include the number of patients in each disease rating category.

Similarly, FDA recommends that you present safety data in a series of tables for each time point, including the number of patients expected at that time point and the number of patients with adverse effects, complications, device failures, and revisions. You should include the types of adverse events, complications, device failures, and revisions.

Use of Kaplan Meier life tables to present actuarial survivorship data for the acetabular component and femoral component and the complete device is recommended. You should include the actual patient data used to generate the presentation.

The applicant should analyze and explain the reasons for missing data and the impact of the missing data.

C. Labeling

The applicant should provide copies of all proposed labeling for the device. You should include any information, literature, or advertising that constitutes labeling under section 201(m) of the act (21 U.S.C. 321(m)). The general labeling requirements for medical devices are in 21 CFR part 801. Information in the PMA should completely support the intended use statement in the labeling, including specific indications for use, specific patient populations, and directions for use. This information should include a detailed step-by-step illustrated surgical technique manual.

III. PDP Requirements

An applicant may submit a PDP for the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis in lieu of a PMA. A PDP must follow the procedures outlined in section 515(f) of the act and should include the following: A description of the device, preclinical trial information, clinical trial information, a description of the manufacturing and processing of the device, labeling of the device, all relevant information about the device, progress reports, and records of the trials conducted under the protocol on the safety and effectiveness of the device for which the completed PDP is sought.

FDA's Device Advice Web site has comprehensive updated information on PDP approval, including the guidance document entitled "Contents of a Product Development Protocol" issued on July 27, 1998, on the Internet at <http://www.fda.gov/cdrh/devadvice>. The guidance document is also available from CDRH's Facts on Demand at 1–800–899–0381 or 301–827–0111. Specify number 473 when prompted for the document shelf number.

IV. Opportunity to Request Reclassification

Before requiring the filing of a PMA or a notice of completion of a PDP for a device, section 515(b)(2)(A)(i) through (b)(2)(A)(iv) of the act and 21 CFR 860.132 require FDA to provide an opportunity for interested persons to request reclassification of the device based on new information. Any proceeding to reclassify the device is under the authority of section 513(e) of the act.

You may submit a reclassification request for the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis in a reclassification petition that contains the information required under § 860.123 (21 CFR 860.123). This includes any new information relevant to the reclassification of the device.

To ensure timely filing of a reclassification petition, submit your petition to the Division of Dockets Management (see **ADDRESSES**) and not to the address provided in § 860.123(b)(1). If you submit a timely reclassification petition for the hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis, FDA will: (1) Consult with the Orthopedic and Rehabilitation Devices Advisory Panel about reclassifying the device, and (2) publish an order in the **Federal Register** either denying the request or announcing the agency's intent to reclassify the device in accordance with section 513(e) of the act and 21 CFR 860.130 of the regulations.

V. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 5 p.m., Monday through Friday.

1. Townley, C.O., "Hemi and Total Articular Replacement Arthroplasty of the Hip With the Fixed Femoral Cup," *Orthopedic Clinics of North America*, 13: 869–894, 1982.

2. Mont, M.A., A.D. Rajadhyaksha, and D.S. Hungerford, "Outcomes of Limited Femoral Resurfacing

Arthroplasty Compared With Total Hip Arthroplasty for Osteonecrosis of the Femoral Head," *Journal of Arthroplasty*, 16 suppl. 1: 134–139, 2001.

3. Mesko, J.W., F.G. Goodman, and S. Stanescu, "Total Articular Replacement Arthroplasty: A Three- to Ten-Year Case-Controlled Study," *Clinical Orthopaedics and Related Research*, No. 300: 168–177, 1994.

4. Head, W.G., "Wagner Surface Replacement Arthroplasty of the Hip - Analysis of Fourteen Failures in Forty-One Hips," *Journal of Bone and Joint Surgery*, 63-A: 420–427, 1981.

5. Head, W.C., "Total Articular Resurfacing Arthroplasty—Analysis of Component Failure in Sixty-Seven Hips," *Journal of Bone and Joint Surgery*, 66-A: 28–34, 1984.

6. Capello, W.N., G.W. Misamore, and T.M. Trancik, "The Indiana Conservative (Surface Replacement) Hip Arthroplasty," *Journal of Bone and Joint Surgery*, 66-A: 518–528, 1984.

7. Ritter, M.A. and T.J. Gioe, "Conventional Versus Resurfacing Total Hip Arthroplasty: A Long-Term Prospective Study of Concomitant Bilateral Implantation of Prostheses," *Journal of Bone and Joint Surgery*, 68-A: 216–225, 1986.

8. Kim, W.C., T. Grogan, H.C. Amstutz, et al., "Survivorship Comparison of THARIES and Conventional Hip Arthroplasty in Patients Younger Than 40 Years Old," *Clinical Orthopaedics and Related Research*, No. 214: 269–277, 1987.

9. Faris, P.M., M.A. Ritter, R. Bicknell, et al., "Long-Term Follow-Up of the Indiana Conservative Resurfacing Hip Arthroplasty," *Seminars in Arthroplasty*, 1: 12–15, 1990.

10. D.W. Howie, B.L. Cornish, and B. Vernon-Roberts, "Resurfacing Hip Arthroplasty: Classification of Loosening and the Role of Prosthesis Wear Particles," *Clinical Orthopaedics and Related Research*, 255: 144–159, 1990.

11. R. Huiskes, P. Strens, W. Vroemen, et al., "Post-Loosening Mechanical Behavior of Femoral Resurfacing Prostheses," *Clinical Materials*, 6: 37–55, 1990.

12. Wiadrowski, T.P., M. McGee, B.L. Cornish, et al., "Peripheral Wear of Wagner Resurfacing Hip Arthroplasty or Arthroplasty Acetabular Components," *Journal of Arthroplasty*, 6: 103–107, 1991.

13. Kilgus, D.J., F.J. Dorey, G.A.M. Finerman, et al., "Patient Activity, Sports Participation, and Impact Loading on the Durability of Cemented Total Hip Replacements," *Clinical Orthopaedics and Related Research*, 269: 25–31, 1991.

14. Mai, M.T., T.P. Schmalzried, F.J. Dorey, et al., "The Contribution of Frictional Torque to Loosening at the Cement-Bone Interface in Tharies Hip Replacements," *Journal of Bone and Joint Surgery*, 78-A: 505–510, 1996.

15. Campbell, P., J. Mirra, and H.C. Amstutz, "Viability of Femoral Heads Treated With Resurfacing Arthroplasty," *Journal of Arthroplasty*, 15: 120–122, 2000.

16. Watanabe, Y., N. Shiba, S. Matsuo, et al., "Biomechanical Study of the Resurfacing Hip Arthroplasty: Finite Element Analysis of the Femoral Component," *Journal of Arthroplasty*, 15: 505–511, 2000.

17. Amstutz, H.C., B.J. Thomas, R. Jinnah, et al., "Treatment of Primary Osteoarthritis of the Hip," *Journal of Bone and Joint Surgery*, 66-A: 228–241, 1984.

VI. Effective Date

FDA proposes that any final rule that may issue based on this proposal become effective 90 days after its date of publication in the **Federal Register**.

VII. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(8) that this action is of a type that does not individually or cumulatively have a significant effect upon the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 610–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this proposed rule is consistent with the regulatory philosophy and principles identified in the Executive order. In addition, the proposed rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. FDA does not expect to receive any PMAs or notices of completion of

PDPs if this rule becomes final. The device has fallen out of use and is less safe and less effective than other available hip joint prostheses. The agency certifies that the proposed rule will not have a significant impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required. Additionally, this proposed rule will not impose costs of \$100 million or more on the private sector, State, local, and tribal governments in the aggregate. As a result, a summary statement or analysis under section 202(a) of the Unfunded Mandates Reform Act of 1995 is not required.

IX. Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The burden hours required for § 888.3410(c), included in the collection entitled "Pre-market Approval of Medical Devices" (66 FR 42664, August 14, 2001), are reported and approved under OMB control number 0910–0231.

X. Comments

You may submit written or electronic comments regarding this proposal or requests for a change in classification of the device to the Division of Dockets Management (see **ADDRESSES**). Submit a single copy of electronic information or two paper copies of any mailed information, except that individuals may submit one paper copy. Comments or requests are to be identified with the docket number found in brackets in the heading of this document. Received comments or requests may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 888

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 888 be amended as follows:

PART 888—ORTHOPEDIC DEVICES

1. The authority citation for 21 CFR part 888 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Section 888.3410 is revised to read as follows:

§ 888.3410 Hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis.

(a) *Identification.* A hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis is a two-part device intended to be implanted to replace the articulating surfaces of the hip while preserving the femoral head and neck. The device limits translation and rotation in one or more planes via the geometry of its articulating surfaces. It has no linkage across the joint. This generic type of device includes prostheses that consist of a femoral cap component made of a metal alloy, such as cobalt-chromium-molybdenum, or a ceramic material, that is placed over a surgically prepared femoral head, and an acetabular resurfacing polymer component. Both components are

intended for use with bone cement (§ 888.3027).

(b) *Classification.* Class III.

(c) *Date PMA or notice of completion of a PDP is required.* A PMA or a notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [date 90 days after date of publication of the final rule in the **Federal Register**], for any hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis that was in commercial distribution before May 28, 1976, or that has, on or before [date 90 days after date of publication of the final rule in the **Federal Register**], been found to be substantially equivalent to a hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis that was in commercial distribution before May 28, 1976, or that

has, on or before [date 90 days after date of publication of the final rule in the **Federal Register**], been found to be substantially equivalent to a hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis that was in commercial distribution before May 28, 1976. Any other hip joint metal/polymer or ceramic/polymer semiconstrained resurfacing cemented prosthesis must have an approved PMA or a declared completed PDP in effect before being placed in commercial distribution.

Dated: February 13, 2004.

Beverly Chernaik Rothstein,

Acting Deputy Director for Policy and Regulations, Center for Devices and Radiological Health.

[FR Doc. 04-4885 Filed 3-4-04; 8:45 am]

BILLING CODE 4160-01-S