SECTION IV

REGULATORY HISTORY OF DEVICES

The use of metal/metal hip joint replacement devices predates the Medical Device Amendments of 1976. Prior to the enactment of these regulations, the FDA chartered the Orthopaedic Device Classification Panel to study orthopedic devices and to make recommendations on their classification.

Although the Orthopedic Device Classification Panel was terminated by the FDA in 1978 in favor of reestablishment as the Orthopedic Device Section of the Surgical and Rehabilitation Devices Panel (The Panel), review of device classification continued. On July 2, 1982, after reviewing the recommendations of the Panel, the FDA issued a Proposed Rule (47 FR 29052) classifying 77 orthopedic devices. Metal/metal hip joint replacement prostheses with cemented acetabular components (CFR 888.3320) and metal/metal hip joint replacement prostheses with uncemented acetabular components (CFR 888.3330) were proposed for class III.

The Final Rule classifying orthopedic devices was published September 4, 1987 (52 FR 33686). Although this formally established metal/metal hip joint replacement prostheses as preamendment class III devices, no date was established for a call for PMAs for these devices. Since that time manufacturers were allowed to market metal/metal semi-constrained total hip joint replacement prostheses via the premarket notification, i.e., the 510 (k) provision of the Act, provided the FDA determined them to be substantially equivalent to preamendment predicate devices. FDA disclosed to applicants filing premarket notifications that data from a clinical trial of the device, or from a similar device, would be required in support of substantial equivalence to a preamendment device.

On April 19, 1994, a memorandum from the Acting Director of the Office of Device Evaluation was released outlining the strategy for implementation of the provision of the Safe Medical Devices Act of 1990 that mandated further activity on these class III devices. This strategy was also published May 6, 1994 (59 FR 23731). Three groups were created regarding these devices:

Group 1	Devices that have fallen into disuse and are unlikely to result in viable PMAs or reclassification petitions;
Group 2	Devices that FDA believed to have a high potential for reclassification; and
Group 3	Devices not at the time considered for reclassification and for which PMAs would be called.

The memorandum also set forth dates on which the FDA would take various actions on these groups of devices. Metal/metal semi-constrained total hip prostheses (21 CFR 888.3320 and 888.3330) were placed in Group 3 with a call for PMAs or completed PDPs scheduled for 1994.

On September 7, 1995 FDA published a Proposed Rule (60 FR 46717) that outlined the date on which PMAs or PDPs for 43 class III devices would be required. The period for written comments closed on January 5, 1995. On September 27, 1996, the Final Rule was published (61 FR 50704) for 41 of the 43 class III devices requiring PMAs or completed PDPs by December 26, 1996.

The Orthopedic Surgical Manufacturers Association (OSMA) formed seven committees to work on several reclassification petitions for orthopedic devices that were subject to calls for PMAs or completed PDPs. In January 2000, one of those committees was assigned the responsibility of submitting a reclassification petition for metal/metal semi-constrained total hip joint prostheses.

The petition for downclassification was submitted on September 25 and filed by the agency on December 1, 2000. On December 26, 2000, the agency, in a letter to Mr. Tom Craig, then the president of OSMA, concluded that the petition lacked information needed to determine whether all of the risks associated with the device had been identified and how these risks may be controlled for the purpose of reclassification. Additional amendments were submitted on November 28, 2000, May 23, 2001 and July 10, 2001, and the submission was accepted. Then pursuant to the statute, the petition was reviewed at an Orthopedic and Rehabilitation Devices Panel meeting on August 8, 2001. The panel recommended five to two that the hip joint metal/metal semiconstrained prostheses not be reclassified from class III to class II. On September 6, 2002 the FDA published their denial of the Request for Change in Classification in the Federal Register (Vol 67, No. 173). In that notice the Deputy Director announced that the petition was denied because OSMA failed to provide reasonable assurance of the safety and effectiveness of the devices. There were a number of recommendations. The panel determined that there were insufficient clinical and preclinical testing information to establish special controls. In addition, the panel concluded that the length and rate of long term patient follow-up data were inadequate. In terms of preclinical testing, the panel also concluded that validation of wear simulation, non-ideal preclinical wear testing (off angle), and biological evaluation of metallic wear debris generated by the device were not established.

Since then, OSMA task force members have been in contact with the agency to discuss a second petition. Letters have been sent to Mr. Phil Phillips, Office of Regulatory Affairs, updating him as to OSMA's intent. The latest was sent in December 2003. A testing protocol was submitted to the agency in April 2003, and a number of suggestions were made. There were proposals for certain test methods and a request for longer term clinical data. Additional comments were received by OSMA from the agency in September 2003. In November 2003, OSMA and FDA representatives conducted a telephone conference to review all comments regarding proposed testing. This second

petition is the result of these meetings and is designed to address the concerns of the panel and the Food and Drug Administration. Dr. Harry McKellop, Vice President for Research, Los Angeles Orthopaedic Hospital, UCLA is assisting OSMA as a paid consultant in compiling preclinical testing information to justify certain special controls and Dr. Pat Campbell, also a paid consultant, from that same institution has prepared a report on the short and long-term effects of metal-on-metal total hip replacement from human retrieval and in-vitro studies. OSMA now is in the possession of longer term clinical data to meet the requirements of the panel and this information is included. The format for the presentation of clinical data was discussed with the agency at a meeting with FDA officials on January 23, 2002 and subsequent teleconferences held on April 25 and September 4, 2002. OSMA was advised to present a device survivorship analysis of the metal-on-metal hip devices from the clinical studies described in the original submission. We have added two studies of considerably longer duration sponsored by Zimmer (formerly Centerpulse).