

Panel Questions for the August 8th Panel

Reclassification Petition for Metal/Metal Semi-Constrained Hip Joint Prostheses

Overall Risks and Controls

1. Risks to Health have been identified by the petitioner and the July 1987 Orthopedic and Rehabilitation Panel. The petition lists the following risks for metal/metal semi-constrained hips:

- loosening,
- migration,
- revision,
- dislocation,
- failure,
- fracture,
- wear,
- osteolysis,
- sensitivity,
- infection,
- pain,
- nerve impingement/damage,
- vascular disorders,
- pulmonary embolism, and
- gastrointestinal/genitourinary complication

These risks are based on literature articles for first and second generation hips and unpublished clinical studies of second generation hips. Are these all of the risks associated with these types of devices? If not, then what are other risks, and what are the controls to minimize those risks?

Long Term Risks

2. The petition lists migration, loosening and wear among others as possible risks associated with metal/metal hips. These risks are most often seen in long term clinical data as shown by the petitioner in literature articles. The original petition has literature articles on first and second generation hip designs and two year data on two contemporary second generation devices. The special controls listed in the petition that specifically try to minimize these long term risks are laboratory testing (i.e., kinematics testing, push-out testing, cyclic wear testing, and hip simulator tests); materials; and design parameters. Do these controls accurately predict all the possible long term risks for the second generation devices? If not, what controls are appropriate to minimize these risks?

Wear

3. Runaway wear is a potential risk for metal/metal hips. The generation of wear particles can be a major cause of hip failure at greater than or equal to two years after implantation. The wear proposal in the petition does not allow for a positive control to determine whether the results obtained in the wear tests are predictive of "good" hip designs. Hip simulator testing is proposed in the petition to minimize the risk of wear. The wear proposal in the petition compares an investigational device to a legally marketed contemporary second generation hip design using ASTM 1714-96 *Standard Guide for Gravimetric Wear Assessment of Prosthetic Hip-Designs in Simulator Devices*. The wear proposal also only requires the testing of hips that have certain design parameters that are descriptive of second generation devices. Does the wear proposal act as an adequate control for long term wear data for second generation hip designs, taking into account the lack of a positive control (i.e., a first generation device that proved not to be clinically successful? If not, what other controls can be implemented to minimize the long term wear risks? In addition, how does the wear proposal differentiate from a "bad" hip design and a "good" hip design?

Loosening

4. Early literature articles provided in the petition stated that many of the hips were revised were due to loosening. In the unpublished clinical studies, radiolucencies were seen in a high percentage of patients at 24 months both in the femur and acetabulae. Radiolucencies have been considered predictors of implant loosening. The controls proposed by the sponsor to minimize the risk of loosening includes sterility, good manufacturing practices, labeling controls, warning and precaution statements. Are these sufficient controls to minimize the risk of loosening? Are there other controls to minimize this risk?

Low Follow-up

5.* In the petition, there are four unpublished clinical studies out to two years. For Study A, the follow-up rates are 36.7% and 46.0% for Metal/Metal and Metal/Poly groups, respectively. For study B, the follow-up rate is 42.5% for the Metal/Metal group. For Study C, the follow-up rates are 47.2% and 56.1% for the Metal/Metal and Metal/Poly groups, respectively. This clinical data is to support the second generation hip designs and show their safety and effectiveness over the first two years. Given the low follow up rates, can these unpublished clinical data be used to address the risks associated with second generation metal/metal constrained hips?

* Amendment 3 was sent to the FDA on July 10, 2001 and has not yet been reviewed by the FDA. The amendment contains new follow-up tables for Study A, Study B, and Study C. This question might be updated at the time of the panel meeting.