FDA Panel Questions

1. The applicant planned to conduct a prospective, non-randomized, concurrently controlled clinical study to evaluate the Cormet 2000 Hip Resurfacing System. The control subjects were to receive a cleared metal-on-metal or metal-on-polyethylene total hip replacement; however, no subjects were ever actually enrolled in the control arm of the study. In the original PMA submission, the applicant proposed and used metal-on-metal hip data as a historical control. In Amendments 8 and 13 of the PMA, the sponsor reanalyzed their clinical data using another device, Osteonics ABC Ceramic-on-Ceramic System (Alumina Bearing Couple, approved in PMA P000013 on February 3, 2003), as the historical control.

   Please discuss the appropriateness of changing the controls during the study progression as well as after the original data analyses were performed and how this impacts the ability to interpret the data. Please also comment on the relevance of using the Osteonics ABC System as an appropriate control for a clinical study using the Cormet 2000 Hip Resurfacing System as the investigational arm.

2. Various radiographic measurement techniques and criteria have been used to evaluate the success/failure of resurfacing hip devices. The original IDE approved protocol included the following radiographic success criteria:

   a. Acetabular component
      - Migration <5mm vertical or horizontal
      - Migration <5°in varus/valgus
      - No new or progressive radiolucencies >1mm in **any** zones

   b. Femoral component
      - Subsidence <5mm
      - Tilting <1° in varus/valgus
      - No new or progressive radiolucencies >2mm in **any** zones

   In Amendments 8 and 13 of the PMA submission, the sponsor provided a new radiographic technique and then analyzed the radiographs according to the following revised endpoints:

   a. Acetabular component
      - Migration <5mm vertical or horizontal
      - Migration <5^{o} in varus/valgus
      - No new complete radiolucencies >1mm in **all three** zones

   b. Femoral component
      - Subsidence < 5mm **and** tilting < 1° in varus/valgus
      - No new complete radiolucencies >2mm in **all three** zones

   Based on this information:

   a. Please discuss the appropriateness of changing the study radiographic measurement techniques and success/failure criteria after the study completion.

   b. Please comment on whether the final proposed endpoints are accurate to predict the success/failure of this resurfacing hip system.

3. The applicant provided additional analyses of the learning curve and explored risk factors that may help investigate the revision rates observed for the Cormet 2000 Hip Resurfacing System. For subjects in the Pivotal Unilateral Cohort with 24+ month follow-up data, there was a 7.9% (24/302) revision rate.

    a. Please discuss the significance of these revision rates and any safety concerns they raise. As part of this discussion, please also consider the observation that femoral neck fractures were present in 2.3% of the Cormet 2000 Hip Resurfacing System.

    b. The applicant's analysis of patient selection criteria demonstrates the device revision rate is higher than average for females, patients requiring use of smaller device components, patients with diagnoses other than osteoarthritis, patients with low function HHS scores and patients with leg length discrepancies $\geq$ 1 cm. Please comment on the significance of these risk factors, given the applicant's proposed indications for use:

        "The Cormet 2000 Hip Resurfacing System is intended for use in resurfacing hip arthroplasty for reduction or relief of pain and/or improved hip function in skeletally mature patients having the following conditions:

        1. Non-inflammatory degenerative arthritis such as osteoarthritis, and avascular necrosis (AVN);
        2. Inflammatory arthritis such as rheumatoid arthritis.

        Hip resurfacing arthroplasty is intended as a primary joint replacement for patients who are at risk of requiring more than one hip joint replacement over their lifetime. While it is not possible to predict if a patient will require a future hip joint revision, several factors such as gender, age, weight, and activity level may increase the risk of the need for revision."

4. Under CFR 860.7(e)(1) effectiveness is defined as reasonable assurance that, in a significant portion of the population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results. Considering the study design and endpoints discussed today, please discuss whether the clinical data in the PMA provide reasonable assurance that the device is effective.

5. Under CFR 860.7(d)(1) , safety is defined as reasonable assurance, based on valid scientific evidence, that the probable benefits to health under conditions of the intended use, when accompanied by adequate directions for use and warnings against unsafe use, outweigh any probable risks. Considering the revision rates and femoral neck fractures for the subject device, please discuss whether the clinical data in the PMA provide reasonable assurance that the device is safe.