Meeting of the Orthopaedic and Rehabilitation Devices Advisory Panel
June 27-28, 2012

Metal-on-Metal Hip Systems

Center for Devices and Radiological Health
U.S. Food and Drug Administration

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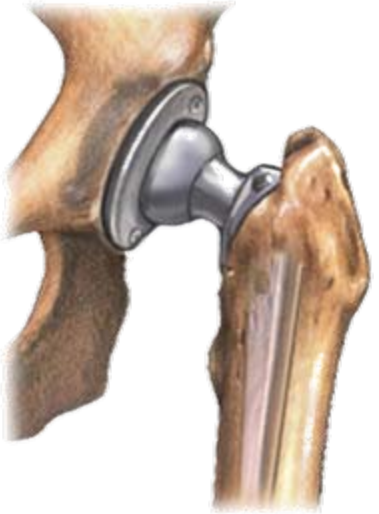
Overview of Hip Arthroplasty

- Hip arthroplasty relieves pain and restores joint function
- Hip arthroplasty has been available in the United States (US) for over 50 years
- Approximately 400,000 hip arthroplasty procedures performed in the US annually

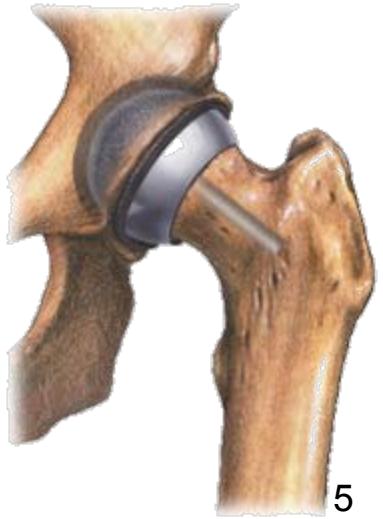
Total Hip Replacement (THR) Surgery

- Diseased femoral head replaced with a femoral head and stem
- Acetabular socket replaced with a metal cup with a polyethylene, metal or ceramic liner
- Different bearing combinations
  - Metal on Polyethylene (MoP)
  - Ceramic on Polyethylene (CoP)
  - Metal on Metal (MoM)
  - Ceramic on Metal (CoM)
  - Ceramic on Ceramic (CoC)



Resurfacing Hip Replacement Surgery

- Replaces only the upper surface of the femoral head
- Preserves more of the native femoral bone
- Requires stronger bone stock, generally younger patients
- Metal on Metal articulating components



General Hip Replacement Risks

- The following short and long term complications are associated with any hip replacement surgery.
  - Infection
  - Venous thrombosis
  - Intra-operative nerve injury
  - Vascular injury/bleeding
  - Post-operative leg length inequality
  - Dislocation of the head from the socket
  - Post-operative nerve palsy
  - Implant wear
  - Prosthesis loosening
  - Implant breakage/fracture
  - Heterotopic ossification
  - Femoral neck fracture (resurfacing hip systems)

MoM THR Systems: Indications for Use

- Skeletally mature patients with the following conditions:
  - Non-inflammatory degenerative joint disease (NIDJD) such as osteoarthritis, avascular necrosis, post-traumatic arthritis, ankylosis, protrusio acetabuli, and painful hip dysplasia
  - Inflammatory degenerative joint disease such as rheumatoid arthritis
  - Correction of functional deformity, and
  - Revision procedures where other treatments or devices have failed

MoM THR Systems: Contraindications

- Bone or musculature compromised by disease, prior infection, or prior implantation that cannot provide adequate support or fixation for the prosthesis
- Any active or suspected infection in or about the hip or distant foci
- Skeletal immaturity
- Metal sensitivity
- Patients who are pregnant or who may become pregnant, and
- Patients with known moderate to severe renal insufficiency

MoM THR Systems: FDA Regulation

- Class III preamendment devices
- Call for Premarket Approval (PMA) Applications has not been proposed
- Regulated as Class III 510(k) devices
- Initial MoM THR design from each manufacturer supported with clinical data
- Modifications to existing systems supported by preclinical testing with clinical data required for significant changes

MoM THR Systems Marketed in the U.S.

- As of May 30, 2012, FDA has cleared 188 510(k) submissions from 21 manufacturers for MoM THR systems
  - Many of these are for additional components or modifications to previously cleared systems
  - Manufacturers have been purchased by other manufacturers or no longer market MoM hip systems

Manufacturers of MoM THR Systems Marketed in the U.S.

1. Biomet, Inc.
2. DePuy Orthopaedics, Inc.
3. Encore Medical, L.P.
4. Wright Medical Technology, Inc.
5. Zimmer, Inc.

MoM THR Systems: Characteristics

- Acetabular Shell
  - Monoblock
  - Modular with metal liner
  - Modular with metal insert in polyethylene liner (poly sandwich)
  - Articulating component
    - Material: Cobalt-chromium-molybdenum (CoCrMo) alloy
      - ASTM F1537 – Wrought
      - ASTM F75 – Cast
      - High carbon content (0.15 – 0.35 mass percent chemical composition)
    - Inner Diameter ranges from 28-60mm

MoM THR Systems: Characteristics

- Acetabular Shell
  - Shell material
    - Titanium alloy (ASTM F136) or
    - CoCrMo alloy (ASTM F1537 or ASTM F75)
  - Outer Diameter ranges from 44-80mm
  - Methods of Fixation
    - Cemented
    - Porous or non-porous metallic coatings
    - Calcium phosphate coatings

MoM THR Systems: Characteristics

- Femoral Head
  - Cobalt-chromium-molybdenum (CoCrMo) alloy
    - ASTM F1537 – Wrought
    - ASTM F75 – Cast
    - High carbon content
      (0.15 – 0.35 mass percent chemical composition)
  - Diameters range from 28-60mm
  - Range of neck offsets
  - Larger heads may have taper sleeve adapter

MoM THR Systems: Characteristics

- Femoral Stem
  - CoCrMo alloy (ASTM F1537 or ASTM F75)
  - Titanium alloy (ASTM F136)
  - Methods of Fixation
    - Cemented
    - Porous or non-porous metallic coatings
    - Calcium phosphate coatings
- Diametrical Clearances range from 50–250 µm

MoM Hip Resurfacing Systems: Indications for Use

- Intended for reduction or relief of pain and/or improved hip function in skeletally mature patients having the following conditions:
  - Non-inflammatory degenerative arthritis such as osteoarthritis, traumatic arthritis, avascular necrosis, or dysplasia/developmental dislocation of the hip (DDH); or
  - Inflammatory arthritis such as rheumatoid arthritis.
- Resurfacing systems are intended for patients who, due to their relatively younger age or increased activity level, may not be suitable for traditional total hip arthroplasty due to an increased possibility of requiring ipsilateral hip joint revision.

MoM Hip Resurfacing Systems: Contraindications

- Infection
- Skeletal immaturity
- Inadequate bone stock
- Severe osteopenia
- Osteonecrosis or avascular necrosis (AVN) with >50% involvement of the femoral head (regardless of FICAT Grade)
- Cysts of the femoral head (>1cm)
- Vascular insufficiency, muscular atrophy, or neuromuscular disease severe enough to compromise implant stability or postoperative recovery
- Females of child-bearing age
- Moderate to severe renal insufficiency
- Immunosuppressed with diseases such as AIDS or persons receiving high doses of corticosteroids
- Obesity and/or with a BMI>35
- Metal sensitivity (e.g., jewelry)

MoM Hip Resurfacing Systems: FDA Regulation

- Class III devices requiring Premarket Approval (PMA) Applications
- Each manufacturer must demonstrate a reasonable assurance of safety and effectiveness through preclinical and clinical performance data
- Conditions of Approval:
  - Post Approval Studies
    - Long-term outcomes
    - General use of the device
  - Training programs

MoM Resurfacing Systems Marketed in the U.S.

Sponsor	Device	Date of Approval	PMA Number
Smith & Nephew Orthopaedics, Inc.	Birmingham Hip Resurfacing (BHR) System	May 9, 2006	P040033
Corin Medical, Ltd.	Cormet Hip Resurfacing System	July 3, 2007	P050016
Wright Medical Technology, Inc.	CONSERVE Plus Total Resurfacing Hip System	Nov. 3, 2009	P030042

MoM Resurfacing Systems: Characteristics

- Acetabular shell
  - Cast CoCrMo (ASTM F75)
  - 44–66mm outer diameter, 36-58mm inner diameter
  - Metallic coating, with some also having a calcium phosphate coating

- Resurfacing femoral head
  - Cast CoCrMo (ASTM F75)
  - 36–58mm diameter
  - Cemented

Intended Benefits of MoM Hip Systems

- Relieve pain and improve function
- Larger diameter heads closely mimic natural anatomy
- Intended to improve stability and reduce incidence of dislocation
- Resurfacing systems provide for greater preservation of femoral bone stock

Issues Associated with MoM Hip Systems

- Wear of articulating components may lead to the production and accumulation of metal ions and debris
- Cup malpositioning may increase wear rates
- Reaction to particulate is patient specific
  - No reaction
  - Mild hypersensitivity
  - Severe inflammatory response
- Increases in potential safety issues, include:
  - Local complications, such as pseudotumors and aseptic lymphocytic vasculitis-associated lesions (ALVAL)
  - Commonly referred to as adverse local tissue reaction (ALTR) or adverse reaction to metal debris (ARMD)
  - Early device failure and need for revision surgery
  - Systemic complications from metal ion exposure

Regulatory Actions – Australian Therapeutic Goods Administration (TGA)

- Review of data from Australian National Joint Replacement Registry (NJRR) showed higher revision rates for the DePuy ASR hip implants.
- Withdrawal of DePuy ASR hip implants from Australian market (Dec 2009)

Regulatory Actions – U.K. Medicines and Healthcare products Regulatory Agency

- April 2010 MHRA Alert
  - Local and soft tissue reactions and revision surgery
  - Recommendations regarding metal ion testing and cross-sectional imaging
- May & Sept 2010 MHRA Alerts – Patients implanted with DePuy ASR hip implants
- February 2012 MHRA Alert
  - Revised recommendations regarding metal ion testing and cross-sectional imaging
  - Specific recommendations for patients with large diameter total hip systems (≥ 36mm), standard THR systems, resurfacing systems and the ASR

MHRA

Regulatory Actions – Health Canada

Health Canada Issued Public Communication on Metal-on-Metal Hip Implants

May 9, 2012

Subject: Important Safety Information regarding Metal-on-Metal Hip Implants

Dear patients,

Health Canada has issued a Health Care Professional letter to Canadian orthopaedic surgeons informing them about potential health risks and recommending patient management strategies following metal-on-metal (MoM) hip implant surgery

Health Canada Santé Canada

Regulatory Actions - FDA

- April 2009 – 515(i) Call for Safety and Effectiveness Information
  - FDA called for safety and effectiveness information on all Class III preamendment devices for which the classification process has not been finalized
  - Applies to MoM THR systems
  - Five orthopedic manufacturers submitted information recommending downclassification of MoM THR systems
  - Proposed rule under review, **NOT** the subject of this panel meeting

Regulatory Actions - FDA

- Two MoM THR device recalls in US
  - Zimmer Durom Total Hip System (July 2008)
    - Inadequate instructions for use
    - Device currently available to surgeons who complete surgeon training program
  - DePuy ASR Total Hip System (August 2010)
    - Higher than expected revision rates
    - THR system no longer marketed in the US
    - Resurfacing system never marketed in US

Regulatory Actions - FDA

- Sept 2010 – FDA met with professional societies
- Feb 2011 – FDA posted public health communication on its website
- May 2011 – FDA issued 522 postmarket surveillance orders for MoM THR Systems

Goals for this Advisory Panel Meeting

- Review currently available data regarding MoM hip systems
- Open and transparent dialogue of issues
- Characterize any potential and real safety risks
- Generate scientifically based recommendations for the clinical and patient communities on how to best communicate and mitigate risks
- NOTE: This panel meeting is **NOT** intended to address specific regulatory issues regarding MoM systems including prior market entry data, regulatory decisions or classification.

Advisory Panel Meeting Overview

- Transparent dialogue between:
  - Advisory Panel Members
  - FDA
  - International Regulatory Bodies
  - Professional Societies
  - Industry
  - Scientific Experts
  - Academia
  - Consumer Groups
  - Public

Advisory Panel Meeting Overview

- Scientific Sessions:
  - MoM Device Mechanics and Failure Modes
  - Soft Tissue Imaging of the Hip
  - Metal Ion Testing Methodology
  - Outcomes: Local and Systemic Complications
- International Consortium of Orthopaedic Registries (ICOR) Revision Outcomes
- Literature Review

Advisory Panel Meeting Goals

- Recommendations for patient follow-up (symptomatic and asymptomatic)
  - Total hip replacement systems
  - Resurfacing hip systems
- Discussion of patient risk factors to take into account when considering MoM Hip Systems as an option
- Recommendations for modifications to current product labeling