Regulation of UHMWPE Biomaterials in Total Joint Arthroplasty

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Outline

- Regulatory background
- The 510(k) Flowchart
- Simple regulatory examples
- Taking crosslinked UHMWPE through the chart
- Taking Vit. E UHMWPE through the chart
Device Regulation History

- With the amendment of The Food, Drug and Cosmetic Act of 1976 FDA began to regulate medical devices.

- All devices on the market prior to May 28, 1976 were sorted into a device regulation and assigned a risk class. 

- Any new devices that are not substantially equivalent to pre-amendment are placed into the highest risk class.
Hips were sorted into different regulations depending on:

- **Bearing material**
  - metal on poly, ceramic on poly, metal on metal, ceramic on ceramic, metal on articular cartilage, ceramic on articular cartilage

- **Degree of constraint**
  - semiconstrained, constrained

- **Fixation Method**
  - cemented or uncemented
## Risk Class

<table>
<thead>
<tr>
<th>Class</th>
<th>Risk</th>
<th>Device Example</th>
<th>Regulatory Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Low</td>
<td>Scalpel</td>
<td>Registration with FDA (GMP)</td>
</tr>
<tr>
<td>II</td>
<td>Moderate</td>
<td>Metal on poly hip</td>
<td>510(k) (substantial equivalence)</td>
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<tr>
<td>III</td>
<td>High</td>
<td>Ceramic on ceramic hip</td>
<td>Premarket Approval (PMA) or de Novo</td>
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</table>
### 510(k) vs. PMA

<table>
<thead>
<tr>
<th></th>
<th>Submission Cost</th>
<th>Review Time</th>
<th>Clinical data</th>
<th>GMP</th>
<th>Labeling</th>
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<tbody>
<tr>
<td>510(k)</td>
<td>$4,348</td>
<td>90/360 days</td>
<td>10%</td>
<td>On file</td>
<td>Draft</td>
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<tr>
<td>PMA</td>
<td>$236,298</td>
<td>180/360 days</td>
<td>100%</td>
<td>Reviewed</td>
<td>Final</td>
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PMAs must stand on their own, while 510(k)s may borrow from other 510(k) devices.
The 510(k) Flowchart (abbreviated)

- New indications for Use?
  - Yes: Alter therapeutic effect?
    - Yes: New intended use
      - Yes: PMA required
      - No: New types of S&E questions?
        - Yes: Substantially equivalent
        - No: Scientific methods exist?
          - Yes: Performance data demonstrate equivalence?
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Simple Screw Example

- Device modification: Addition of screw lengths and diameters to screw system
  - New screws have larger diameter
  - New screws have equivalent thread lengths
- Predicate device: Cleared screw System
- Indications: Same as predicate
Simple Screw Example

New indications for Use? yes

Alter therapeutic effect? no

New intended use yes

PMA required

Same technological characteristics? yes

Can characteristics affect safety and efficacy (S&E)? no

Substantially equivalent yes

Scientific methods exist? yes

New types of S&E questions?

Can characteristics affect safety and efficacy (S&E)? yes

Performance data demonstrate equivalence? no

Adequate descriptive characteristics? no

Need more data

Performance data demonstrate equivalence? yes

Adequate descriptive characteristics? no

New indications for Use? no
Simple Total Hip Example

- Device modification: Addition of larger femoral heads and acetabular liners to hip system
  - Same articulating material
  - Same offsets
- Predicate device: Cleared hip System
- Indications: Same as predicate
Simple Hip Example

New indications for Use? yes

New intended use yes

PMA required yes

New types of S&E questions? yes

Substantially equivalent yes

Scientific methods exist? yes

Need more data no

Adequate descriptive characteristics? yes

Same technological characteristics? no

Can characteristics affect safety and efficacy (S&E)? yes

Performance data demonstrate equivalence? yes

Alter therapeutic effect? no

Performance data demonstrate equivalence? no
Ceramic on Metal Hip Example

- Device modification: Change of the femoral head from metal to ceramic
  - Different articulating material
  - Geometry is changed
- Predicate device: Cleared MoM hip System
- Indications: Same as predicate
Ceramic on Metal Example

New indications for Use? yes no

Same technological characteristics? no yes

Adequate descriptive characteristics? no yes

Need more data

Alter therapeutic effect? no yes

Can characteristics affect safety and efficacy (S&E)? no yes

Performance data demonstrate equivalence? no yes

Substantially equivalent? no yes

Scientific methods exist? no yes

New intended use yes no

PMA required yes no

New types of S&E questions? no yes
**XLPE Example**

- **Device modification:** 100 kGy irradiation followed by melt (150 °C)
  - Same head/liner dimensions
  - Same liner/cup locking mechanism

- **Predicate device:** Conventional hip system (25 – 40 kGy gamma sterilization and package in inert environment)

- **Indications:** Same as predicate
## XLPE Material Testing

<table>
<thead>
<tr>
<th>Safety and Efficacy Question</th>
<th>Tensile properties</th>
<th>Oxidation resistance</th>
<th>Fatigue resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific Method</td>
<td>Tensile testing, small punch testing</td>
<td>Accelerated aging, OI, free radical content</td>
<td>Fatigue crack propagation testing, Izod impact test</td>
</tr>
</tbody>
</table>

See ASTM F2565
### XLPE Material Testing

<table>
<thead>
<tr>
<th>Safety and Efficacy Question</th>
<th>Radiation modification of material</th>
<th>Crystallinity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific Method</td>
<td>Swell ratio, TVI</td>
<td>Thermal properties</td>
</tr>
</tbody>
</table>

See ASTM F2565
<table>
<thead>
<tr>
<th>Safety and Efficacy Question</th>
<th>Wear rate</th>
<th>Liner/Cup interlocking</th>
<th>Rim fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific Method</td>
<td>Hip simulator testing</td>
<td>Push out, lever out, torque out testing</td>
<td>Rim fatigue testing</td>
</tr>
</tbody>
</table>
New indications for Use?

Alter therapeutic effect?

New intended use

PMA required

Same technological characteristics?

Can characteristics affect safety and efficacy (S&E)?

New types of S&E questions?

Substantially equivalent

Scientific methods exist?

Adequate descriptive characteristics?

Performance data demonstrate equivalence?

Need more data
Vit. E XLPE Example

- Device modification: 0.1 wt% Vit. E before molding, 100 kGy irradiation followed by anneal (120 °C), EtO sterilized
  - Same head/liner dimensions
  - Same liner/cup locking mechanism
- Predicate device: XLPE hip system (100 kGy, remelted, EtO sterilization)
- Indications: Same as predicate
# Vit. E XLPE Material Testing

<table>
<thead>
<tr>
<th>Safety and Efficacy Question</th>
<th>Tensile properties</th>
<th>Oxidation resistance</th>
<th>Fatigue resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific Method</td>
<td>Tensile testing, small punch testing</td>
<td>Accelerated aging after loading and after extraction, OI, free radical content</td>
<td>Fatigue crack propagation testing, Izod impact test</td>
</tr>
<tr>
<td>Safety and Efficacy Question</td>
<td>Modification of material</td>
<td>Biocompatibility</td>
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<td></td>
</tr>
<tr>
<td>Scientific Method</td>
<td>Swell ratio, TVI, VEI, consolidation verification, thermal properties</td>
<td>Exhaustive extract analysis (GCMS, LCMS), toxicological risk assessment, cytotoxicity, sensitization, irritation, acute toxicity, chronic toxicity, genotoxicity, implantation, and carcinogenicity</td>
<td></td>
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<tr>
<td>Safety and Efficacy Question</td>
<td>Wear rate</td>
<td>Liner/Cup interlocking</td>
<td>Rim fracture</td>
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<tr>
<td>Scientific Method</td>
<td>Hip simulator testing (normal &amp; abrasive), wear particle analysis</td>
<td>Push out, lever out, torque out testing</td>
<td>Rim fatigue testing</td>
</tr>
</tbody>
</table>
Vit. E XLPE Example

New indications for Use? yes

no

Same technological characteristics? yes

no

Can characteristics affect safety and efficacy (S&E)? yes

no

Substantially equivalent

yes

no

Performance data demonstrate equivalence?

yes

no

Adequate descriptive characteristics?

yes

no

Need more data

Scientific methods exist?

yes

no

New types of S&E questions?

PMA required
Summary

- All medical devices were originally sorted into three classes according to risk
- New moderate risk devices are those that can rely on the proven clinical history of substantially equivalent moderate risk devices
- Devices are deemed high risk when they are not substantially equivalent to marketed devices with clinical history
- Devices that employ technological characteristics that raise new types of safety and effectiveness questions cannot rely on another device’s clinical history
Questions?