Post-Approval Studies
Program Update

Orthopedic and Rehabilitation Devices Advisory Panel, May 12, 2011

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Director, Division of Epidemiology
Post-Approval Studies

- Clinical study or other investigation required in an approval order to gather specific information to address precise study objectives
- Added by the Food and Drug Administration Modernization Act (FDAMA), and the post-approval requirements regulations at 21 C.F.R. Part 814.82(a)
Post-Approval Studies – Established Need

- Gather essential postmarket information
  - Longer-term performance including effects of retreatments & product changes
  - Real-world device performance (patients and clinicians)
  - Effectiveness of training programs
  - Sub-group performance
  - Outcomes of concern (safety and effectiveness)
### Recent PAS Developments

<table>
<thead>
<tr>
<th>Year</th>
<th>Event Description</th>
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<tbody>
<tr>
<td>2005</td>
<td>Integrated PAS program established</td>
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<td>2005</td>
<td>Began raising scientific rigor of PAS</td>
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<tr>
<td>2006</td>
<td>Developed and instituted PAS tracking</td>
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<td>2006</td>
<td>Issued PAS Guidance document</td>
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<td>2007</td>
<td>Created PAS public website</td>
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<td>2007</td>
<td>Instituted Advisory Panel updates</td>
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<td>2008</td>
<td>Initiated BIMO inspections of PAS</td>
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<td>2008</td>
<td>Increased focus on infrastructure building</td>
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<td>2009</td>
<td>Increased focus on methods development</td>
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<tr>
<td>2010</td>
<td>MDEpiNet Initiative</td>
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<tr>
<td>2011</td>
<td>ICOR Initiative</td>
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Number of Approved Original PMAs and Panel-Track Supplements (PTS), 2005-Present

*As of 5/9/2011
<table>
<thead>
<tr>
<th>Year</th>
<th># Individual PAS Requirements</th>
<th>Approved w PAS</th>
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<tbody>
<tr>
<td>2005</td>
<td>20</td>
<td>14</td>
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<td>2010</td>
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<tr>
<td>2011</td>
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*As of 5/9/2011

Number of Original PMAs and PTS Approved with PAS Order and Number of Individual Requirements, 2005 to Present
Compliance with PAS Requirements Issued 2005 to Present, N=198

- In-Compliance: 168, 85%
- Non-Compliance: 30, 15%

As of 5/9/2011
PAS for Orthopedic Devices
Approved Orthopedic Original PMAs and Panel-Track Supplements

* Through 5/9/11
Orthopedics Original PMAs and Panel-Track Supplements Approved with PAS Requirements

Number

<table>
<thead>
<tr>
<th>Year</th>
<th>Approved</th>
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<td>2011*</td>
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*Through 5/9/11
Compliance with PAS Orthopedic Requirements Issued 2005 to Present N=30

As of 5/9/2011

18, 60%

12, 40%

In-Compliance

Non-Compliance
Number of PAS by Device Area and Study Status

- Orthopedic
- Ophthalmic
- Obstetrics/Gynecology
- Neurology
- Microbiology
- Immunology
- General & Plastic Surgery
- Gastro/Urology
- Ear Nose & Throat
- Clinical Chemistry
- Dental
- Cardiovascular
- Pathology

In Compliance: 82
Out of Compliance:

Legend:
- In Compliance
- Out of Compliance
Recent CDRH Orthopedic Efforts

- Identify and evaluate existing U.S. orthopedic implant registries
- Assess HMO capabilities to study orthopedics
- Explore the utility of OUS orthopedic registries
- Assess orthopedic device identification (registry-specific methods)
- Explore the utility of CMS data and linking
- Quantify prognostic ability of models that integrate all existing data (premarket, PAS, registry, claims, published literature)
- Apply automated surveillance techniques
- International Consortium of Orthopedic Registries (ICOR)
MDEpiNet Initiative – launched 2010

- Medical Device Epidemiology Network
- To bridge evidentiary gaps and develop datasets and innovative methodological approaches for conducting analytic studies to improve FDA understanding of safety and effectiveness of medical devices throughout their life cycle through leverage of expertise from academia and other stakeholders.

- 2nd FDA Public Meeting - held April 25, 2011
- MDEpiNet Public Private Partnership
ICOR Initiative

- Establish International Consortium of Orthopedic Registries (ICOR) to:
  - leverage data from existing registries
  - advance methods to study device performance and patient outcomes
  - help enhance and harmonize the registry data worldwide
  - improve research collaboration

- FDA Public Workshop - held May 9, 2011
  - 35 registries present
  - All major stakeholders
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Section 522 of FFDCA

Authority to order postmarket surveillance of any class II and class III medical device that meets any of the following criteria:

- Failure of the device would be reasonably likely to have a serious adverse health consequence
- Expected to have significant use in pediatric populations
- Intended to be implanted in the body for more than one year
- Intended to be a life-supporting device used outside of a user facility
Moving Forward

- The 522 Order
  - Section 522 of the FD&C Act allows FDA to order manufacturers to conduct postmarket surveillance for devices under certain circumstances

  - CDRH issued 522 orders to all MoM total hip manufacturers on May 6, 2011, asking them to address specific questions relating to:
    - Types and rates of adverse events in patients with MoM total hips
    - Ion levels at baseline and over time of MoM hip patients, including:
      - Patients with revisions compared with those without revision
      - Patients with pain/local ARMD compared with those without
    - Association of demographics/clinical characteristics to metal ion levels
    - Modes and causes of failure