Post-Approval Studies (PAS) Program Update

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Circulatory Devices Advisory Panel
January 25, 2011
Post-Approval Studies: Legal Authority

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: Legal Authority

21 C.F.R. § 814.82

FDA may impose post-approval requirements at the time of approval of the PMA or by regulation subsequent to approval and may include:

- (2) Continuing evaluation and reporting on the safety, effectiveness, and reliability of the device for its intended use. FDA will state the reason and the number of patients to be evaluated.

- (9) Other requirements as FDA determines necessary to provide (continued) reasonable assurance of the safety and effectiveness of the device.
PAS - Established Need

- Gather essential postmarket information
  - Longer-term performance including effects of re-treatments & product changes
  - Real-world device performance (patients and clinicians)
- Effectiveness of training programs
- Sub-group performance
- Outcomes of concern (safety and effectiveness)
PAS Public Health Value

- Evaluate medical devices as they enter a “real-world” utilization
- Contribute to better design of premarket studies
- Can provide infrastructure for nesting premarket clinical trials
- Can detect real-time signals (actionable)
- Help identify over-arching regulatory science needs
- Help prioritize CDRH epidemiologic research resources
Recent PAS Developments

- 2005 Oversight transferred to postmarket
- 2005 Began raising scientific rigor of PAS
- 2006 Developed and instituted tracking system
- 2006 Issued PAS Guidance document
- 2007 Created public website
- 2007 Instituted Advisory Panel updates
- 2008 Initiated BIMO inspections of PAS
- 2008 Increased focus on infrastructure building
- 2009 Increased focus on methods development
- 2010 PAS transparency initiative
- 2010 MDEpiNet initiative
Post Approval Studies

- The new Center for Devices and Radiological Health (CDRH) Post-Approval Studies Program encompasses design, tracking, oversight, and review responsibilities for studies mandated as a condition of approval of a premarket approval (PMA) application. The program helps ensure that well-designed post-approval studies (PAS) are conducted effectively and efficiently and in the least burdensome manner.
- On January 1, 2005, the oversight responsibility was transferred to CDRH’s Office of Surveillance and Biometrics (OSB) and the PAS review functions were integrated into the medical device epidemiology program. Guidance on report format and content was developed to ensure optimal PAS reporting and review.
- CDRH has established a new automated tracking system that efficiently identifies the reporting status of active PAS studies ordered since January 1, 2005. This system represents CDRH’s effort to ensure that all PAS commitments are fulfilled in a timely manner. The effective tracking system is based on study timelines incorporated in study protocols and agreed upon by the CDRH and manufacturer.
- In addition to this internal tracking system, CDRH launched this publicly available webpage to keep all stakeholders informed of their progress. It displays not only the report status, but also study status (based on protocol-driven timelines) of each PAS.

<table>
<thead>
<tr>
<th>Application Number</th>
<th>Applicant Name</th>
<th>Device Name</th>
<th>Medical Specialty</th>
<th>Date PMA Approved</th>
<th>Post-Approval Study Commitment</th>
<th>Study Name</th>
<th>Protocol Approved</th>
<th>Study Population</th>
<th>Study Status</th>
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</thead>
<tbody>
<tr>
<td>P040038</td>
<td>ABBOTT VASCULAR DEVICES</td>
<td>XACT CAROTID STENT SYSTEM</td>
<td>Cardiovascular</td>
<td>09/06/2005</td>
<td>1. YOU HAVE AGREED TO CONDUCT THE FOLLOWING STUDIES AND TO REPORT ON THESE STUDIES EVERY</td>
<td>PROTECT Study</td>
<td>02/05/2007</td>
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<td>Stud time</td>
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<td>H040006</td>
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<td>Stud time</td>
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</table>
# PAS Transparency Initiative

## Expanded PAS Webpage- December 20, 2010

<table>
<thead>
<tr>
<th>Ongoing Studies</th>
<th>Completed Studies</th>
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</thead>
<tbody>
<tr>
<td><strong>Detailed Study Protocol Descriptions:</strong></td>
<td><strong>Detailed Study Protocol Descriptions:</strong></td>
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<tr>
<td>Study Population</td>
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<tr>
<td>Sample Size (sites and patients)</td>
<td>Sample Size (sites and patients)</td>
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<tr>
<td>Study Endpoints</td>
<td>Study Endpoints</td>
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<tr>
<td>Data Collection and Follow-up Visits</td>
<td>Data Collection and Follow-up Visits</td>
</tr>
</tbody>
</table>

**Final Data Summary:**
- Number of Sites and Enrolled Patients
- Study Final Results
- Study Strengths and Limitations
- Recommended Labeling Changes

http://www.fda.gov/devicepostapprovalstudies
Number of Approved Original PMAs and Panel-Track Supplements (2005-present)

<table>
<thead>
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<th>Calendar Year</th>
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<th>Number Approved with PAS</th>
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<td>14</td>
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<td>2010</td>
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</tbody>
</table>
Number of Original PMAs and Panel-Track Supplements Approved with PAS Order

- 2005: 14 Approved w PAS, 20 Individual PAS Requirements
- 2006: 14 Approved w PAS, 36 Individual PAS Requirements
- 2007: 12 Approved w PAS, 19 Individual PAS Requirements
- 2008: 15 Approved w PAS, 21 Individual PAS Requirements
- 2009: 14 Approved w PAS, 21 Individual PAS Requirements
- 2010: 8 Approved w PAS, 13 Individual PAS Requirements

Division of Epidemiology
Food and Drug Administration
Study Progress for Ongoing PAS

As of Jan 23, 2011

Number

In Compliance: 106
Out of Compliance: 33
Total: 139

Food and Drug Administration
Division of Epidemiology
PAS for Cardiovascular Devices
Number of Approved Cardiovascular Original PMAs and Panel-Track Supplements

As of Jan 24, 2011

Number of Approved Cardiovascular Original PMAs and Panel-Track Supplements

<table>
<thead>
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<th>Calendar Year</th>
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</table>
Number of Cardiovascular Original PMAs and Panel-Track Supplements Approved with PAS Order

As of Jan 24, 2011

Food and Drug Administration
Division of Epidemiology

Center for Devices and Radiological Health

- App with PAS Order
- # Individual PAS Requirements
PAS Progress: Cardiovascular

As of Jan 24, 2011
PAS Infrastructure Building: Critical Role of Registries in Device Surveillance

- Provides product-specific device identification (to the make/model level)
- Provides clinically-rich information (about patient & procedure)
- Fills critical void in absence of UDI in automated healthcare databases
- Acts as a data “module” in healthcare databases (akin to enrollment files, pharmacy dispensing files, lab files)
CDRH Ongoing Registry Efforts

- Use existing registries for PAS studies and surveillance
  - INTERMACS (NIH, CMS, FDA)
- Facilitate new registry development
  - Atrial Fibrillation Registry (ACC, HRS, STS)
  - American Joint Replacement Registry (AAOS)
  - Diagnostic and Therapeutic Bronchoscopy Registry (ACCP)
  - Uro-Gynecological Mesh Registry (U Mass; AUS)
  - IMPACT Registry (ACC)
CDRH Ongoing Registry Efforts (cont)

- Use existing registries for discretionary studies
  - ICD Registry (ACC-NCDR)
  - Adult Cardio-Thoracic Database (STS)
  - Total Joint Replacement Registry (Kaiser)
  - Hospital for Special Surgeries Registry (Cornell)
  - OUS Orthopedic Registries (Australia, Denmark)

- Explore registry capabilities
  - Active surveillance: short-term and longitudinal
  - Linkages studies with Medicare claims data

- Advocate for registries
  - AHRQ guidebook
  - Compendium of pediatric registries
MDEpiNet Initiative

Creation and support of MDEpiNet, FDA/academia epidemiology consortium, to advance innovative methodologies for scientific computing and evidence synthesis based on the best principles of evidence-based medicine, comparative effectiveness research and advances in health informatics.
MDEpiNet Next Steps

- Pilot projects underway
- RFI posted, January 2011
- MDEpiNet – 2nd Annual Conference April 29, 2011
- Establish network by April 15, 2011
Thank you!

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