



Post-Approval Studies Update

Ophthalmic Devices Panel

June 10, 2008

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Outline

- Recent Changes

- Post-Approval Studies (PAS) Program
- Postmarket Surveillance (PS) Program

- Ophthalmic Devices PAS/PS Update

Mandated Postmarket Studies

- Post-Approval Studies (PAS)
- Postmarket Surveillance (PS)

PAS Legal Authority

- **Title 21 Section 814.82**
- (a) 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.

PS Legal Authority

- **Title 21 Section 822**

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

(a) Failure of the device would be reasonably likely to have serious adverse health consequences

(b) The device is intended to be implanted in the human body for more than 1 year.

(c) The device is intended to be used to support or sustain life and to be used outside of user facility

2007 FDAAA –

device that is expected to have a significant use in pediatric populations

Major Goals of PAS Program Transformation

- Enhance scientific rigor of PAS
- Establish and maintain accountability for the PAS commitments
- Build PAS information management system
- Build bridges between the postmarket knowledge and premarket device evaluation
- Increase the transparency with the public

Areas of PAS Program Transformation

- Oversight
- Tracking
- Review
- Guidance
- Web Posting
- Postmarket Advisory Panel Updates
- Building Public Health Partnerships

PAS Oversight

January 1, 2005 Initial Transfer

April 2, 2007 Full Transfer

ODE/OIVD



OSB

PAS Tracking System

- Developed & instituted automated tracking system for post-approval study commitments

Premarket Review Process

- Epidemiologist on each PMA team
 - Lead the design of PAS study
 - Work interactively with sponsors
 - Present at Panel meetings
- PAS Protocol/outline finalized at the time of PMA approval
- Agreed upon study timelines

Postmarket Review Process

- Epidemiology lead on all PAS Reports and all PAS Supplements involving changes to PAS protocol
- Postmarket Review Team
 - Epidemiology lead
 - Feedback to premarket

Post-Approval Studies Guidance Document

- Guidance for Industry and FDA Staff:
Procedures for Handling Post-Approval
Studies Imposed by PMA Order
(December 21, 2006, revised August 1,
2007)

<http://www.fda.gov/cdrh/osb/guidance/1561.html>

Reporting Status Definitions

- Report On- time : FDA has received the scheduled Interim or Final Post-Approval Study Status Report by the due date.
- Report Overdue : FDA has not received the Interim or Final Post-Approval Study Status Report by the due date.
- Report Overdue/Received: FDA has received the Interim or Final Post-Approval Study Status Report, although past the due date.
- Final Post-Approval Study Report Submitted : The study has been concluded or terminated, and the Final Post-Approval Study Report has been submitted.

Study Status Definitions

- Protocol Pending: FDA has not approved the study protocol and it has been less than 6 months since the approval of the PMA.
- Protocol Overdue: FDA has not approved the study protocol and it has been 6 months or more since the approval of the PMA
- Study Pending : The protocol has been approved but the study has not begun (i.e., no subjects have been enrolled), and the projected date for completing patient accrual has not passed.
- Study On-time : The study is proceeding according to, or is ahead of, the agreed upon schedule .
- Study Overdue: The study has not been initiated by the projected date for completion of patient enrollment or the study is behind the agreed upon schedule.
- Study Terminated : FDA granted an early termination of the study because the study is either no longer feasible or would no longer provide useful information.
- Study Completed: FDA has reviewed the Final Post-Approval Study Report and determined that the study fulfills the commitment.

PAS Web Page

- Went live on April 6, 2007
- Reporting Schedule Status
- PAS Study Progress
- Post – 2005 Studies

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm



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. <http://www.fda.gov/cdrh/osb/guidance/1561.html>.
- 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.

[A](#) [B](#) [C](#) [D](#) [E](#) [M](#) [O](#) [P](#) [S](#) [T](#) [U](#) [V](#) [W](#) [Z](#)

66 records

[Show All Studies](#)

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Application Number	Applicant Name	Device Name	Medical Specialty	Date PMA Approved	Post-Approval Study Commitment	Study Name	Protocol Approved	Study Population	Study Status
P040038	ABBOTT VASCULAR DEVICES	XACT CAROTID STENT SYSTEM	Cardiovascular	09/06/2005	1. YOU HAVE AGREED TO CONDUCT THE FOLLOWING STUDIES AND TO REPORT ON THESE STUDIES EVERY <input type="checkbox"/>	PROTECT Study	02/05/2007	Transitional Adolescent B: 18-21 yrs, Adult: >21	Study time
						EXACT Study	10/12/2005	Transitional Adolescent B: 18-21 yrs, Adult: >21	Study time
H040006	ABIOMED, INC.	ABIOCOR	Cardiovascular	09/05/2006		Abicor Artificial Heart	09/05/2006	Transitional Adolescent B:	Study time

Postmarket Advisory Panel Updates

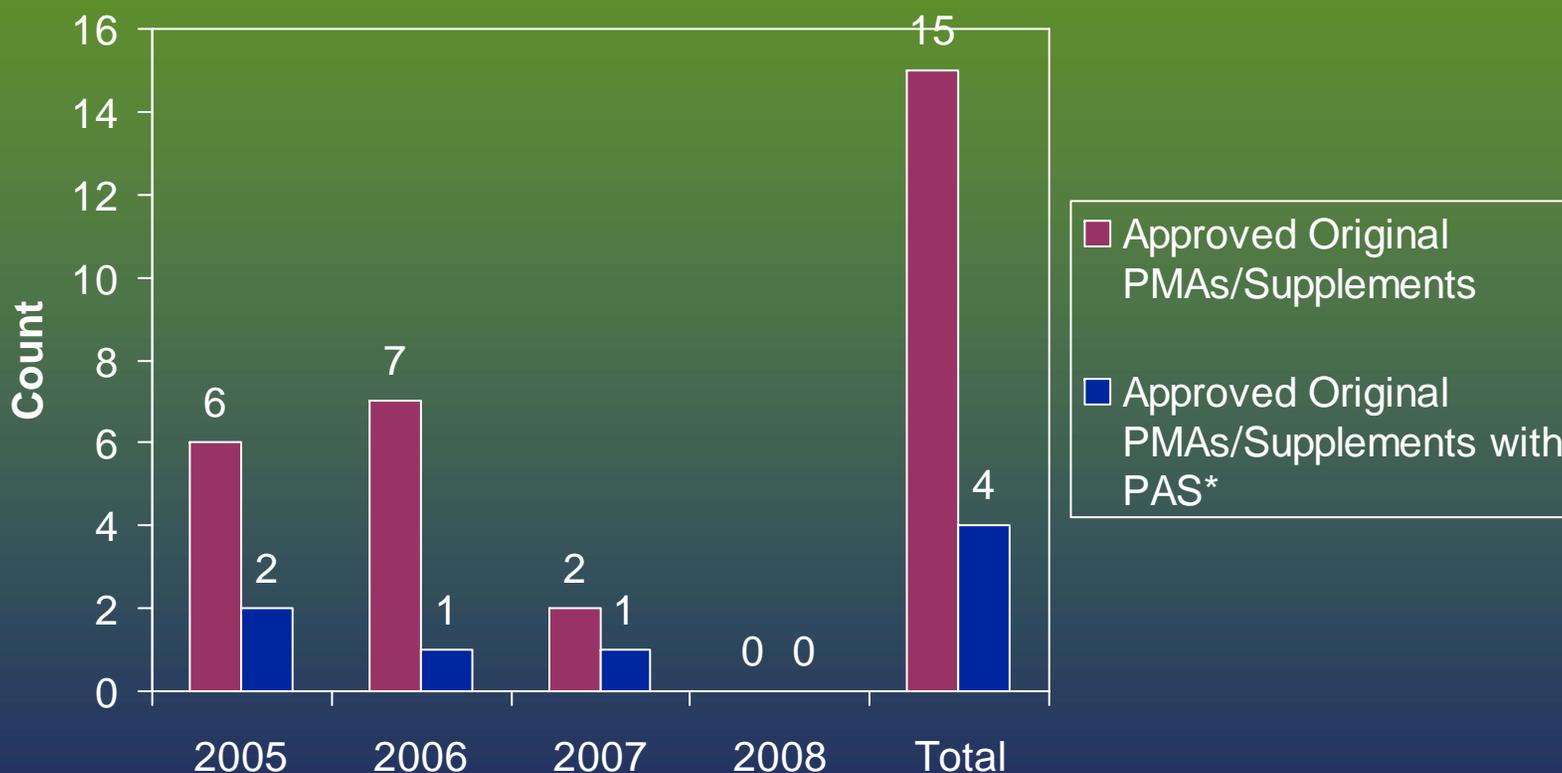
- General PAS Updates
 - First presented November 24, 2007
 - At every Panel meeting
- Specific PAS Updates
 - January 26, 2007
 - December 14, 2007



Building Public Health Partnerships

- First FDA/FDLI PAS Conference, May 10-11, 2007
- Continued dialogue with stakeholders
- Two conferences 2008/2009

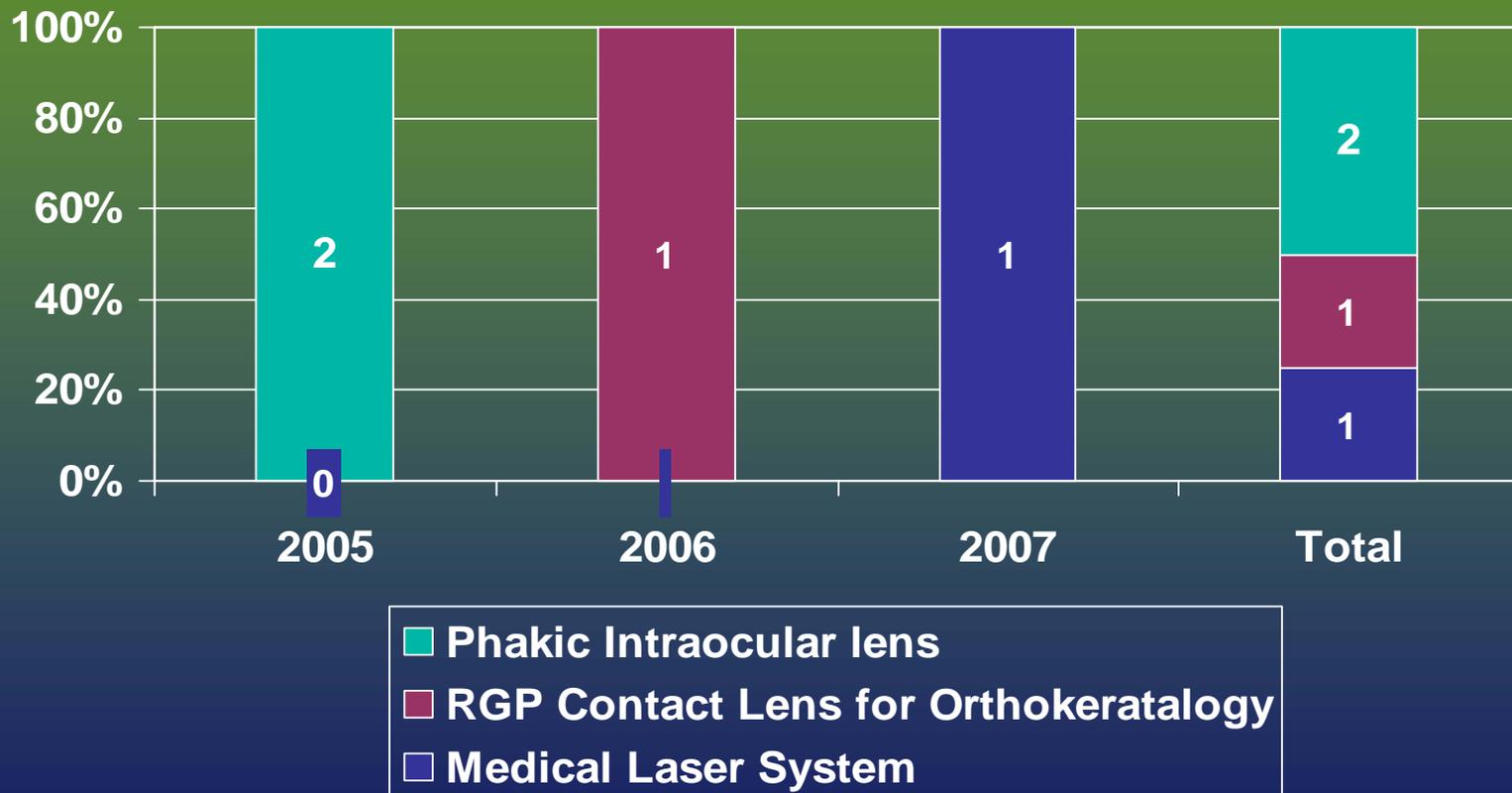
Ophthalmic Original PMAs and Supplements Approved CY2005 - 2008



*There are 15 PMAs/Panel Track Supplements and 4 post-approval studies

As of June 6, 2008

Ophthalmic Devices with Post-Approval Studies



As of June 6, 2008

Visian ICL for Myopia Follow-Up Post-Approval Study

Objective	<ul style="list-style-type: none">■ Provide data on long-term safety of Visian ICL, especially corneal endothelial cell loss, out to 5 years post-operation
Study Design	<ul style="list-style-type: none">■ Prospective, multi-center, one-arm cohort study■ Each subject's pre-operative status serves as control for post-surgical outcomes
Population	<ul style="list-style-type: none">■ 294 subjects from IDE cohort (526 eyes total)■ 14 US investigational sites
Endpoints	Corneal Endothelial Cell loss at 5 years
Follow-up Duration and Visits	<ul style="list-style-type: none">■ Duration: 5 years■ 36, 48, 60 months post-operation

Visian ICL for Myopia Adverse Event Post-Approval Study

Objective	Estimate the incidence of major adverse events in the postmarket environment under conditions of general use
Study Design	<ul style="list-style-type: none">■ Prospective, multi-center study■ Each subject's pre-operative status serves as control for post-surgical outcomes
Population	5,000 US patients implanted with Visian ICLs, with goal of obtaining complete five-year data for 2,000 patients

Visian ICL for Myopia Adverse Event Post-Approval Study

Primary Endpoints	Cataract, retinal detachment, corneal decompensation, chronic uveitis, persistent elevated IOP, secondary surgical intervention
Follow-up Duration and Visits	<ul style="list-style-type: none">■ Duration: 5 years■ 6, 12, 18, 24, 36, 48, 60 months post-operation

Paragon Z RGP Lens for Orthokeratology Post-Approval Study

Objective	Compare incidence of microbial keratitis (MK) in pediatric patients (age < 18 yrs) and adult patients wearing corneal reshaping lenses and fitted in 2004 and 2005
Study Design	Controlled, multicenter, retrospective, cohort study
Selection of Practitioners	■ Randomly selected stratified (by practice volume: <25 vs. ≥25 lens orders) sample of 200 practitioners in Paragon database of accounts
Selection of Subjects	■ If practice volume <25, enroll all patients ■ If practice volume: ≥ 25, randomly select up to 50 patients from of practice lens orders

Paragon Z RGP Lens for Orthokeratology

Post-Approval Study

Population	<ul style="list-style-type: none">■ 1,000 pediatric patients and 1,000 Adult patients with sufficient follow-up to provide 1,000 patient years of exposure in each group■ Randomly selected from lens orders of selected practitioners
Primary Study Endpoints	<ul style="list-style-type: none">■ Incidence of MK■ Relative Risk of MK in juveniles compared to adults
Data collection	<ul style="list-style-type: none">■ Practitioner survey to determine if patient still wearing lenses, patient's last visit, absence or presence of MK■ If patient had MK+: complete Event form

CustomVue™ Monovision LASIK Post-Approval Study

Objective	Estimate proportion of CustomVue Monovision LASIK patients w/ visual disturbances, diplopia
Study Design	<ul style="list-style-type: none">■ Multi-center, single-arm prospective study■ Each subject's pre-operative status serves as control for post-surgical outcomes■ consecutive subject enrollment
Population	<ul style="list-style-type: none">■ 525 subjects■ ~15 US clinical sites 2 academic, 6 corporate, 7 private practice
Primary Study Endpoints	<ul style="list-style-type: none">■ Vision-related Quality of Life: % of subjects with poor post operative quality of life outcomes, driving difficulties, and diplopia

CustomVue™ Monovision LASIK Post-Approval Study

Primary Study Endpoints	<ul style="list-style-type: none">■ Vision-related Quality of Life: % of subjects with poor post operative quality of life outcomes, driving difficulties, and diplopia
Secondary Study Endpoints	<ul style="list-style-type: none">■ Uncorrected and best corrected vision (monocular and binocular) at distance and near, manifest refraction
Follow-up Duration and Visits	<ul style="list-style-type: none">■ Duration: 6 months■ Pre-operative visit, 6 months post-operation
Quality of Life Questionnaire	<ul style="list-style-type: none">■ NEI Refractive Quality of Life (RQL)■ NEI- Visual Function Quality of Life (VFQ)■ Unvalidated diplopia questionnaire

Distribution of PAS Study Designs

N= 4 Studies



As of June 6, 2008

Reporting Status of PAS

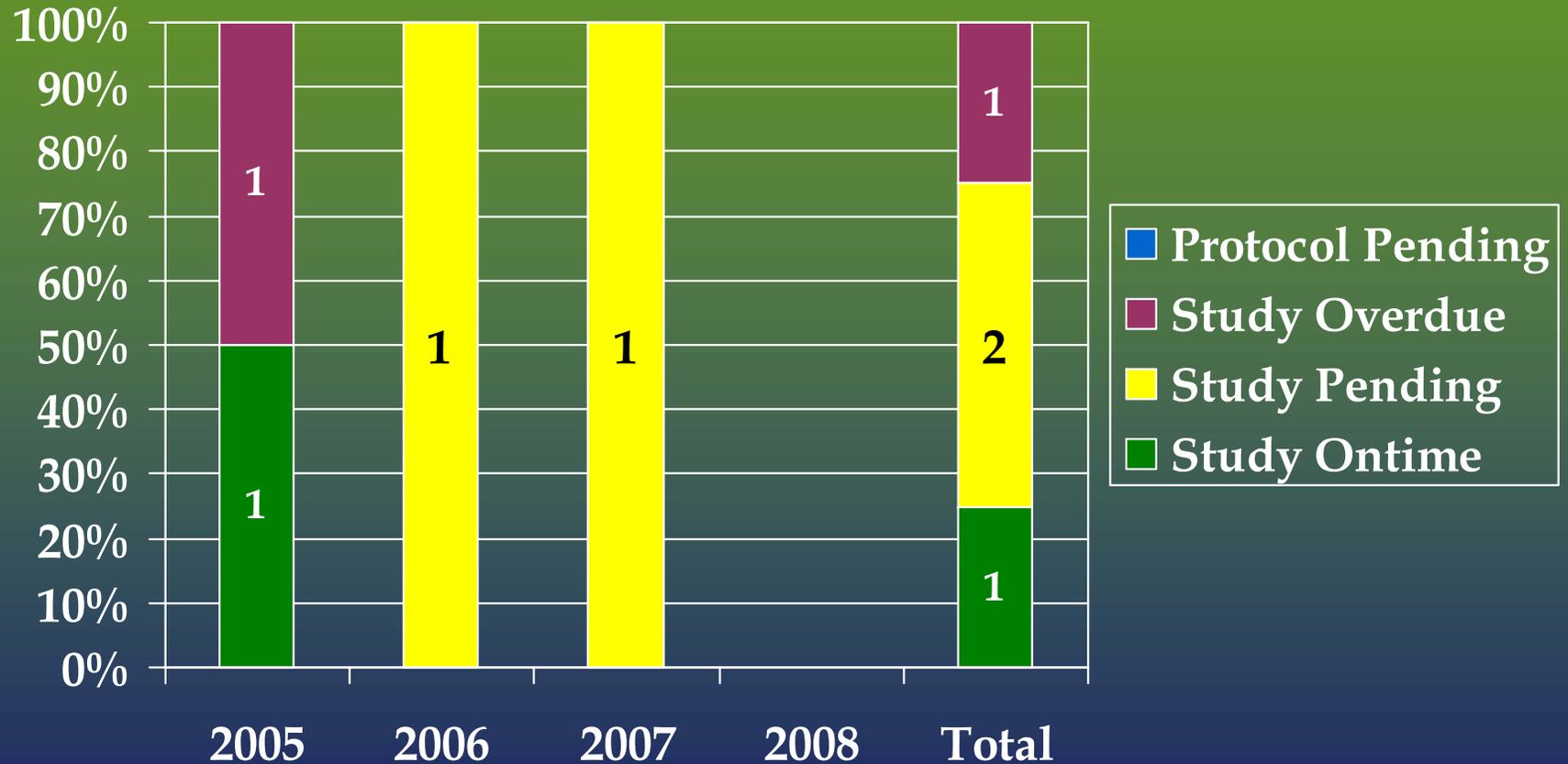
N= 4 Studies



As of June 6, 2008

Progress Status of PAS

N=4



As of June 6, 2008

Post- Approval Studies Vision

- Important postmarket questions are addressed
- Studies are realistic & founded on good science
- Studies are timely, accurate, & provide useful results
- Reports are clearly identified & effectively tracked
- Stakeholders are kept apprised
- Collaboration is stressed throughout
- Enforcement options are rarely used

Questions, Suggestions, Ideas?



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