Expedited Access Premarket Approval ("PMA") Program

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Artwork from, Reflections Art in Health
a user-led charity that promotes positive
mental health through the creative arts.

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Agenda

- PMA Refresher
- New April 23, 2014 Expedited Access PMA
- Breakthrough Therapy

FDA Premarket Approval Process

Approval based on FDA determination PMA application contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use.

- PMA approval is a private license granting the applicant (owner) permission to market the device
- Regulations provide FDA 180 review days
- FDA may request an advisory committee to review PMA at a public meeting and make a recommendation
- FDA inspections
  - Bioresearch Monitoring (BIMO)
  - PreMarket approval

http://www.fda.gov/OHRMS/DOCKETS/98fr/06d-0228-gdl0001.pdf

FDA Premarket Approval Process

Class III device

- Supports or sustains human life <or>
- Is of substantial importance in preventing impairment of human health <or>
- Presents a potential unreasonable risk of illness or injury
- General and special controls are insufficient to assure Safety and Effectiveness

PMA application:

- Required under Section 515 of the US Federal Food, Drug, and Cosmetic Act
- Most stringent type of FDA device marketing application

PMA Data Requirements

- Cover Letter
- Table of Contents
- PMA Summary (becomes public information along with labeling)
  - Indications for Use
  - Device Description
  - Alternative Practices and Procedures
  - Marketing History
  - Summary of Non-Clinical and Clinical Studies
  - Conclusions drawn from studies
- Complete Device Description:
  - Including pictures, functional components
  - Properties of device relevant to diagnosis, treatment, prevention, cure, or mitigation of disease or condition
  - Principles of Operation

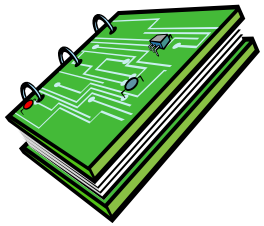
PMA Data Requirements

- Methods, facilities, and controls for manufacturing, processing, packaging, storage, installation.*
- Reference to performance standards or voluntary standards
- Technical Information
  - Non-Clinical Laboratory Studies: Microbiology, toxicity, immunology, biocompatibility, stress, wear, shelf-life, other laboratory or animal tests. Non-clinical studies for safety evaluation must comply to GLPs (21 CFR Part 58)
  - Clinical Investigations: Study protocols, S&E data, adverse reactions and complications, device failures and replacements, patient information, patient complications, tabulation of data from all individual subjects, results of statistical analysis, any other clinical investigational data. Identification of any IDE investigations.

Data Requirements

- Bibliography of published reports
- Copies of all proposed labeling
- Environmental assessment in accordance with 21 CFR 25 (may not be needed if device is of same type and use as previously approved)
- Financial certification or disclosure statements

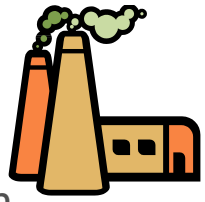
Manufacturing Documents



- Overview of the Quality System
- Quality System Procedures, 820.20 (e)
- Copy of QS procedures (Audit SOP, Management Review SOP, Outline of the structure of QS documentation.
- Quality Manual

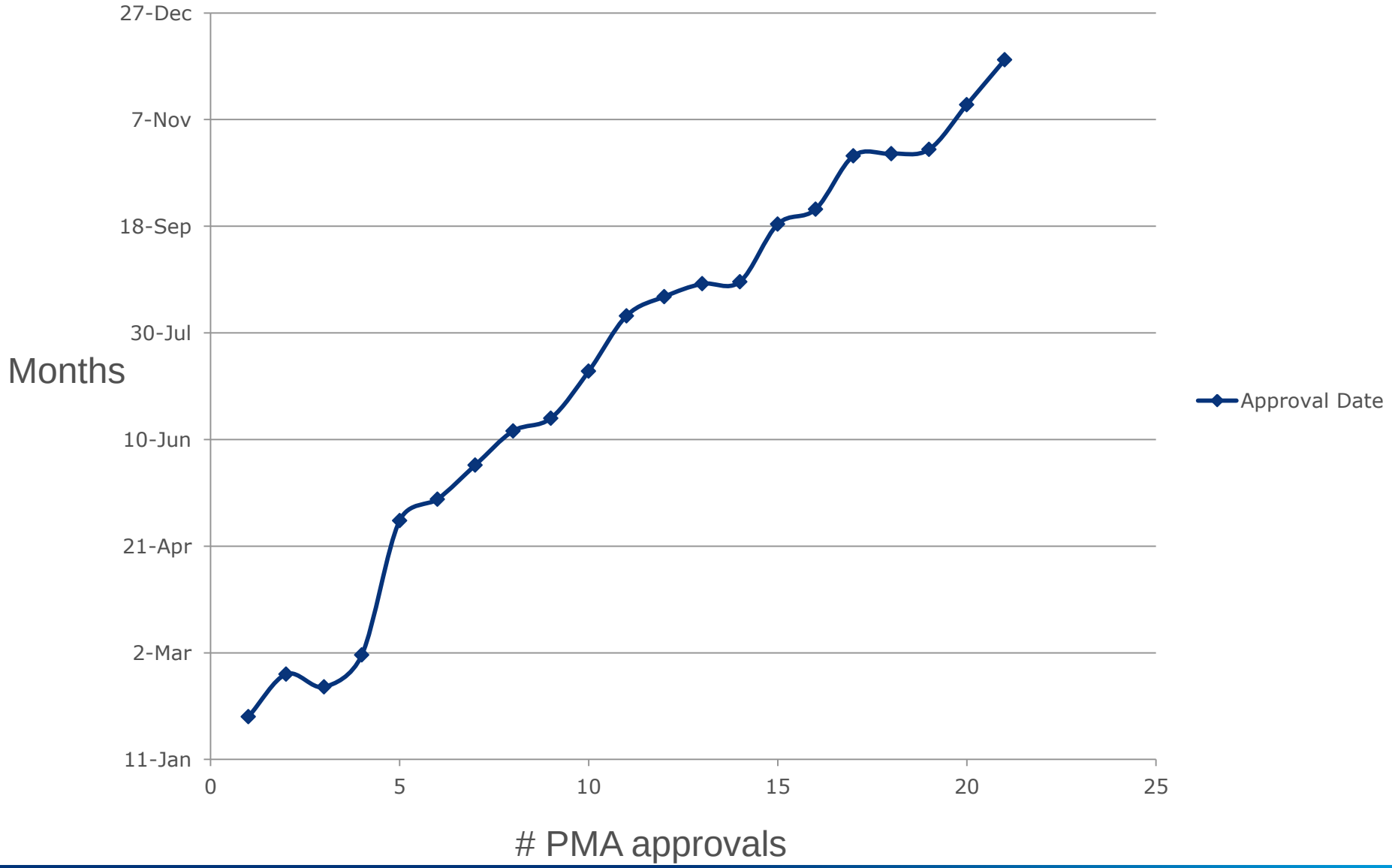
Including: Title and scope of application, TOC, Outline of the structure of the QM, Quality Policy and Objectives, Organizational structure and responsibilities or authority, References to basic QS SOPs, etc.

Manufacturing Documents

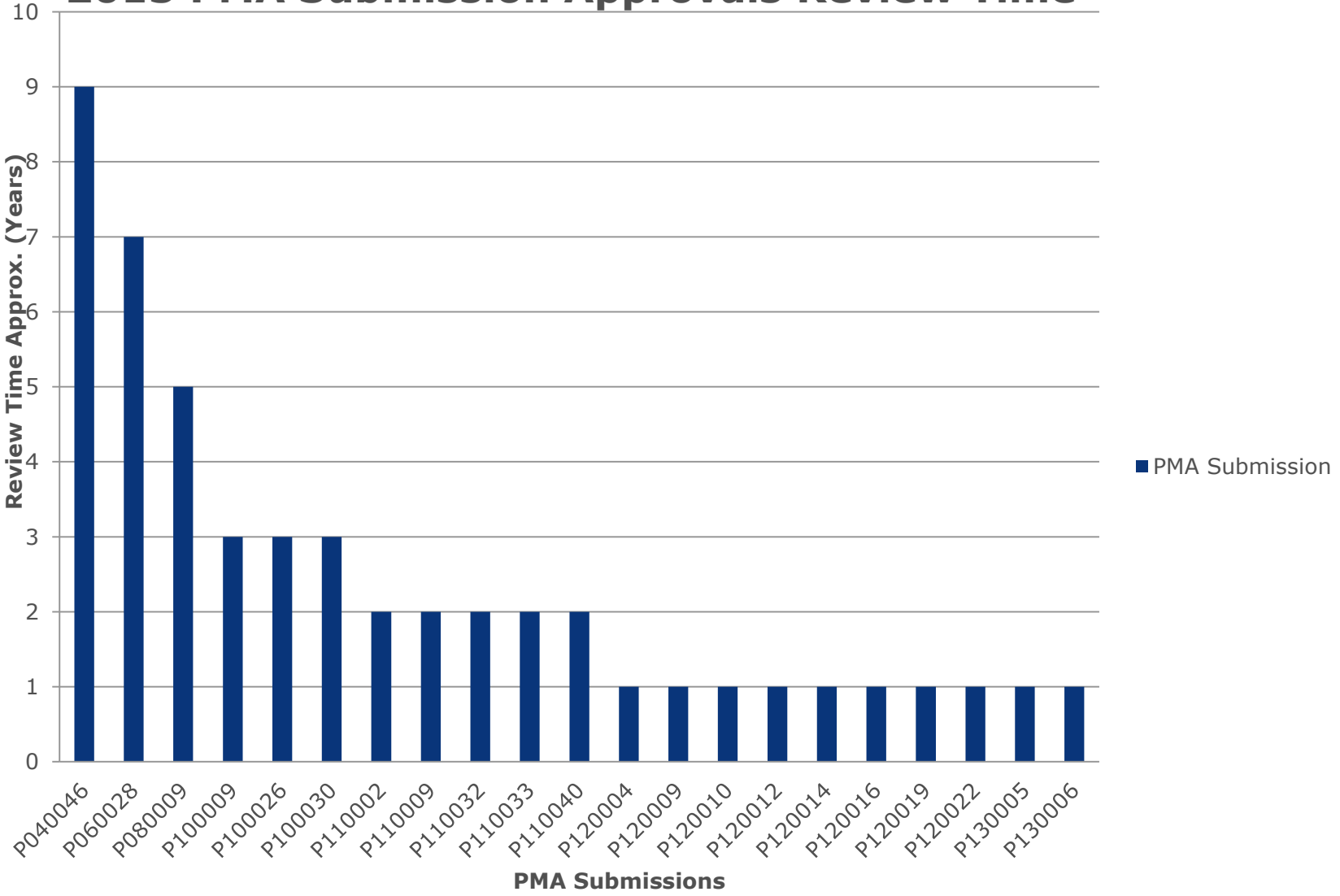


- Overview of the Manufacturing facilities with a Production Flow Diagram showing important aspects of the process
- Purchasing Controls -Copy of the Procedure
- Production and Process Controls -Copy of the Procedure
- Inspection, Measuring, and Test Equipment -Copy of the Procedure
- Final Acceptance Activities -Copy of the Procedure
- Nonconforming Product and CAPA -Copy of the Procedures
- Complaint Files -Copy of the Procedure
- Process Validation - Copy of the Process Validation plans and reports
- Receiving Acceptance Activities -Copy of the Procedure

2013 Original PMA Approvals



2013 PMA Submission Approvals Review Time



Expedited Access PMA

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM393978.pdf

Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Document issued on: April 23, 2014

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document concerning devices regulated by CDRH, contact the Office of the Center Director at 301-796-5900. For questions about this document concerning devices regulated by CBER, contact the Office of Communication, Outreach and Development (OCOD) by calling 1-800-835-4709 or 301-827-1800.

U.S. Department of Health and Human Services
Food and Drug Administration

Center for Devices and Radiological Health

Center for Biologics Evaluation and Research

Executive Summary - “EAP” program

New, voluntary program designed to expedite patient access to certain medical devices intended for unmet medical needs and are subject to premarket approval (PMA) applications.

- FDA believes the program "will help patients have more timely access to these medical devices by expediting their development, assessment and review, while preserving the statutory standard of reasonable assurance of safety and effectiveness for premarket approval."

- "Getting the right balance between premarket and postmarket data collection-specifically, where appropriate, a greater reliance on postmarket collection-can reduce the extent of premarket data submission and directly impact when patients will have access to high-quality, safe and effective medical devices.“

- “Not a new pathway to market," "collaborative approach to facilitate product development" using existing regulatory authority granted to it by Congress

Request Designation and Eligible for the EAP Program (1)

- Sponsors first needs to request a designation from FDA that their device is an "EAP Device," known as "EAP Designation."

Eligibility:

- "Life threatening" is defined as a high likelihood of death unless the disease course is interrupted.

- "Irreversibly debilitating" means a morbidity that has substantial impact on day-to-day functioning.

FDA notes that short-lived and self-limiting morbidities will usually not be sufficient.

Eligible for the EAP Program (2)

EAP Sponsor demonstrates the device meets one of four criteria:

(1) the device represents a breakthrough technology that provides a clinically meaningful advantage over existing technology;

(2) no approved alternative treatment or means of diagnosis exists;

(3) the device offers significant, clinically meaningful advantages over existing approved alternatives; or

(4) the availability of the device is in the best interest of patients (e.g., addresses an unmet medical need). Note: IVDs are eligible for EAP and may find justification through this fourth criteria.

These criteria are based on priority review criteria in Section 515(d)(5) of the Federal Food, Drug, and Cosmetic Act

Data Development Plan

- The program will involve sponsors and FDA working closely together, both to communicate and resolve issues as they arise and in the development of a "data development plan specific to the device" that will outline the clinical data that the sponsor intends to use in support of the device's approval and when that data will be collected (premarket or postmarket).

- Data development plan is a key aspect of the EAP; the plan will "help assure predictable, efficient, transparent and timely device assessment and review." Crucial to the plan is determining which data can be collected *after* the device is granted approval.

10 Factor Device Evaluation of Probable Benefit-Risk:

1. Premarket (clinical or non-clinical) data demonstrate probability of serious harm is low.
2. Postmarket patient device exposure is small prior to required postmarket data submission.
3. Device is non-implantable.
4. Sponsor has a proven track record of a robust quality system.
5. Data Safety Monitoring Board will be used in the postmarket study.
6. User training to help mitigate the probable device risks, described in the proposed labeling.
7. Sponsor provides patient labeling.
8. Valid scientific evidence demonstrates intended patient population is willing to tolerate probable harm and a level of uncertainty about probable benefits.
9. High likelihood that postmarket surveillance can quickly identify instances of serious patient harm.
10. Timely completion of required postmarket data. Proposed postmarket data study is well-designed and feasible (including likelihood of patient participation once device approved.)

How can the PMA review be accelerated?

- EAP Device SE. FDA intends to accept surrogate endpoints, intermediate endpoints, smaller clinical trials, quicker clinical trials, and companion diagnostics to help bring devices to market more quickly.

- EAP designation affords companies an interactive review
  - "Least burdensome" approach to development
  - Priority review status
  - Potential involvement of senior FDA management officials and a cross-disciplinary case manager.

- FDA may:
  - Permit device manufacturers to "provide less manufacturing information in their PMA application,"
  - If Sponsor has history of GMP compliance, no premarket inspections of manufacturing sites.

Breakthrough Therapies

EAP PMA Program Modeled on Drug Breakthrough Therapies and Accelerated Programs

- EAP Program utilizes certain features from CDRH's 2011 Innovation Pathway, program designed to help expedite the development and review of breakthrough medical devices.
- Breakthrough Therapies: Drug breakthrough therapies program was created by the Food and Drug Administration Safety and Innovation Act ("FDASIA") and signed into law July 9, 2012.
- Accelerated Approval: Accelerated approval provides for drug approval based on an effect on a surrogate or intermediate clinical endpoint that is reasonably likely to predict a drug's clinical benefit.
- Fast-Track: The fast-track program includes frequent interactions with the FDA drug review team, priority review, and rolling review.

Guidance for Industry

Expedited Programs for Serious Conditions – Drugs and Biologics

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2014
Procedural

OMB Control No. 0910-0765
Expiration Date: 03/31/2017
See additional PRA statement in section X of this guidance.

IV. OVERVIEW OF EXPEDITED PROGRAMS

The table provides an overview of the four expedited programs. Additional details on the specific programs are found in the sections that follow. Note that a drug development program may qualify for more than one expedited program.

Comparison of FDA's Expedited Programs for Serious Conditions

	Fast Track	Breakthrough Therapy	Accelerated Approval	Priority Review
Nature of program	Designation	Designation	Approval Pathway	Designation
Reference	• Section 506(b) of the FD&C Act, as added by section 112 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) and amended by section 901 of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA)	• Section 506(a) of the FD&C Act, as added by section 902 of FDASIA	• 21 CFR part 314, subpart H • 21 CFR part 601, subpart E • Section 506(c) of the FD&C Act, as amended by section 901 of FDASIA	• Prescription Drug User Fee Act of 1992
Qualifying criteria	• A drug that is intended to treat a serious condition **AND** nonclinical or clinical data demonstrate the potential to address unmet medical need **OR** • A drug that has been designated as a qualified infectious disease product[a]	• A drug that is intended to treat a serious condition **AND** preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies	• A drug that treats a serious condition **AND** generally provides a meaningful advantage over available therapies **AND** demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM) that is reasonably likely to predict an effect on IMM or other clinical benefit (i.e., an intermediate clinical endpoint)	• An application (original or efficacy supplement) for a drug that treats a serious condition **AND**, if approved, would provide a significant improvement in safety or effectiveness **OR** • Any supplement that proposes a labeling change pursuant to a report on a pediatric study under 505A[b] **OR** • An application for a drug that has been designated as a qualified infectious disease product[c] **OR**

Thank You

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