Facilitating Patient Access to Medical Devices:
The Expanded Access, Early Feasibility Study and Breakthrough Devices Programs

FDA Small Business
Regulatory Education for Industry (REdI)
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Maureen L. Dreher, PhD
Policy and Operations Team
Division of Clinical Science and Quality
Office of Clinical Evidence and Analysis
Center for Devices and Radiological Health
U.S. Food and Drug Administration

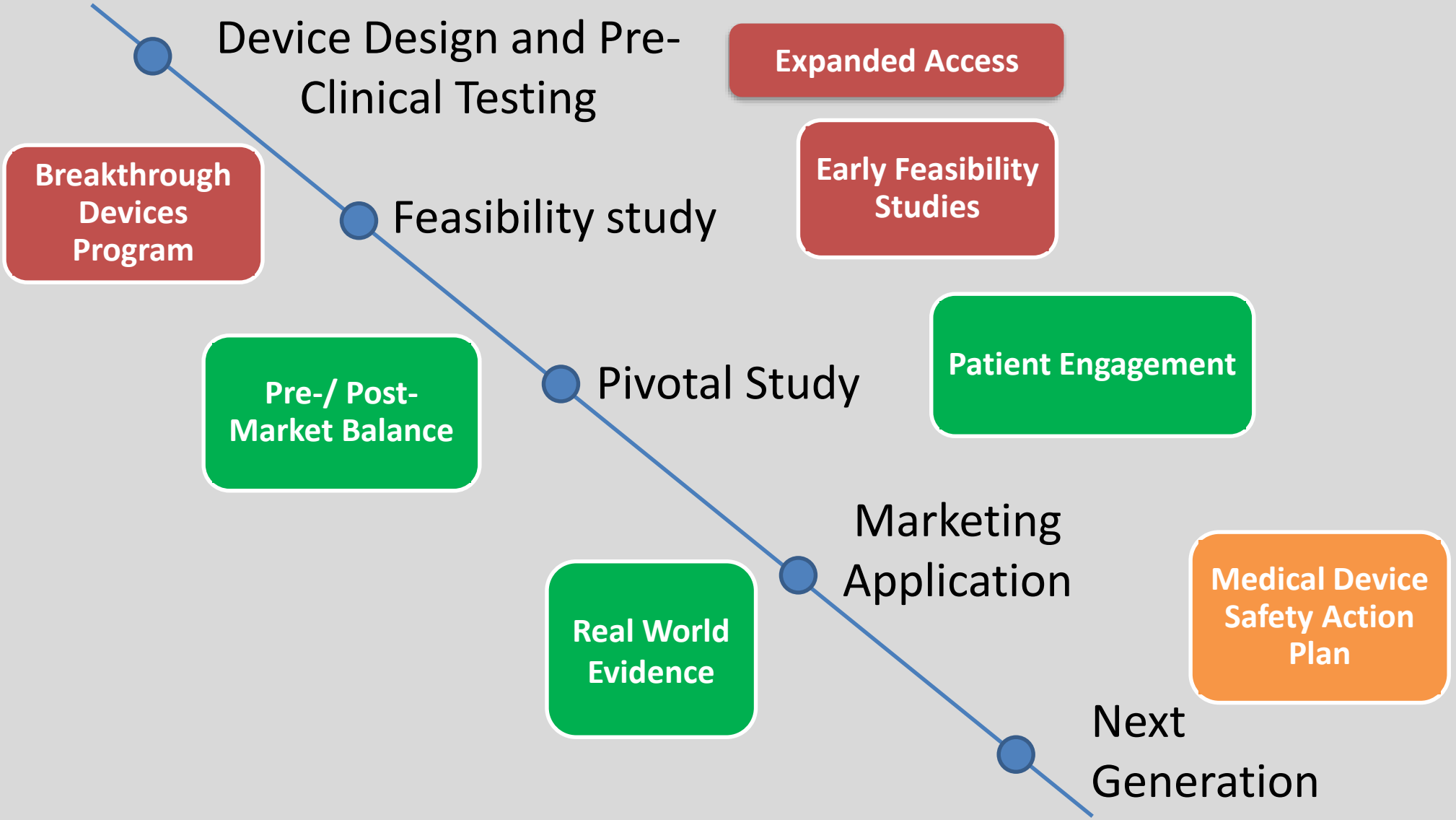
CDRH Vision: Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance, first in the world

Learning Objectives

Understand purpose, key policies and operating principles for:

1. Expanded Access
2. Early Feasibility Study Program
3. Breakthrough Devices Program

Development Milestones and FDA Programs



Expanded Access

Expanded Access

Pathway for patients with serious disease or condition to gain access to an investigational medical device outside of a clinical study

Emergency Use

Compassionate Use

Treatment Use

Expanded Access Criteria – Emergency Use

- **Life-threatening or serious disease or condition**
- **No generally acceptable alternative therapy or diagnosis**
- No time to obtain FDA prior approval:
  - through existing mechanisms
  - due to immediate need to use device

Expanded Access Criteria – Compassionate Use

- Life-threatening or serious disease or condition
- No comparable or satisfactory alternative therapy or diagnosis

Expanded Access Criteria – Treatment Use

- **Life-threatening or serious disease or condition**
- **No comparable or satisfactory alternative therapy or diagnosis**
- Device is under investigation:
  - in an approved IDE for same use, or
  - all clinical trials have been completed
- Sponsor is pursuing marketing approval/clearance with due diligence

Expanded Access – Submission Mechanisms

- **Emergency Use**
  - Doesn't require FDA approval prior to use
  - Treating physician notifies FDA within 5 days of emergency use
- **Compassionate Use**
  - Requires FDA approval prior to use
  - If IDE exists for device, submit a "Compassionate Use Supplement request" to FDA
  - If no IDE, submit request to CDRH Document Control Center
- **Treatment Use**
  - Submit to CDRH Document Control Center:
    - identify request as "Treatment IDE application"
    - identify existing approved IDE for device

Enabling Patient Access

2014-2015 Strategic Priority – *Strengthen the Clinical Trial Enterprise*

- Early Feasibility Study Program

Strike the Right Pre/Post-Market Balance

Provide Excellent Customer Service

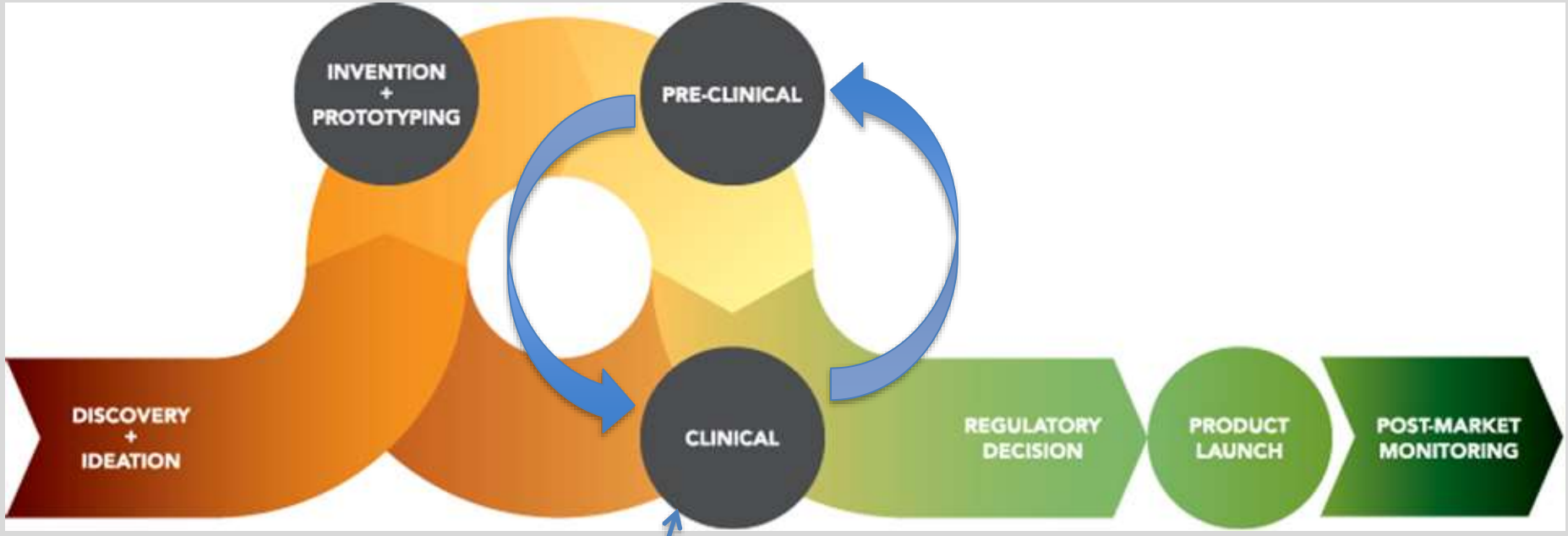
Early Feasibility Study Program

Motivation for Early Feasibility Study Program

- Initial clinical testing of novel devices moved to non-US sites
  - Concern that device innovation may follow and improve outside United States more quickly
- Devices developed for non-US markets
- Growing concern regarding time lag in availability of beneficial medical devices for US patients

Many device clinical trial ecosystem factors contributed to these trends including data requirements for initiating clinical studies in the US

Device Development to Clinical Studies



Feasibility

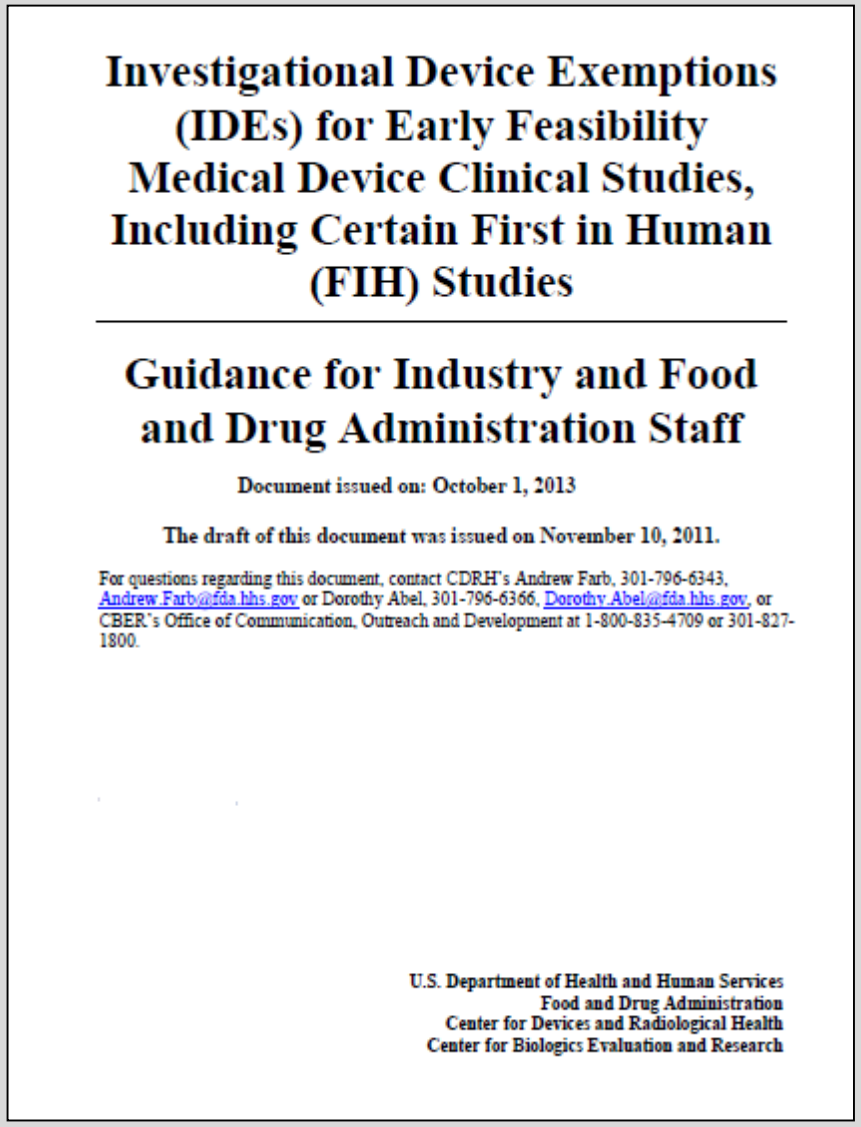
Pivotal

(much more known about device, procedure, indication)

FIH

EFS

Early Feasibility Study Program



Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies

Guidance for Industry and Food and Drug Administration Staff

Document issued on: October 1, 2013

The draft of this document was issued on November 10, 2011.

For questions regarding this document, contact CDRH's Andrew Farb, 301-796-6343, Andrew.Farb@fda.hhs.gov or Dorothy Abel, 301-796-6366, Dorothy.Abel@fda.hhs.gov, or CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

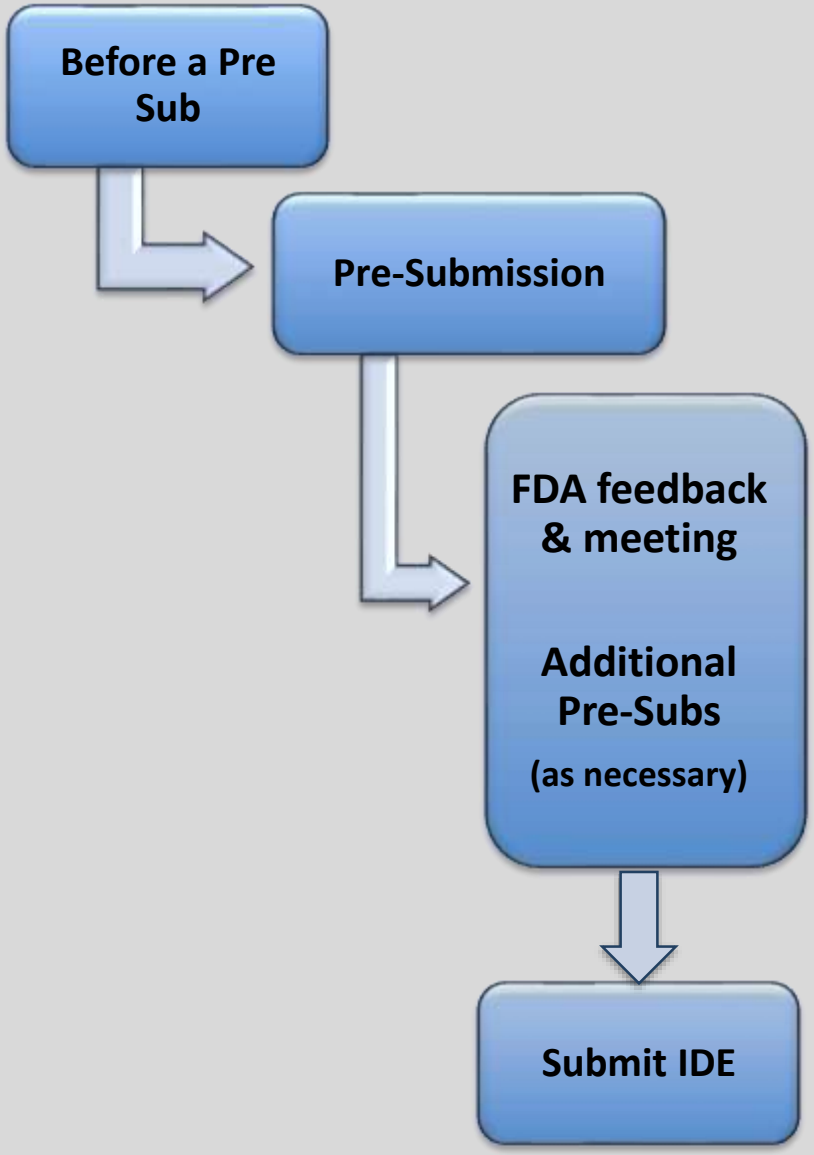
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

- **Voluntary, informal** program for devices:
  - in **early stage** of development
  - to be evaluated in **small human clinical study**
  - **in the US**
- Flexible approaches to address risk while protecting human subjects
- Tools to communicate device evaluation strategy
- Significant training effort and identification of representatives from each premarket review area

What is an EFS IDE?

- EFS are completed under Investigational Device Exemptions (IDEs)
- EFS IDE - A standard IDE application except…
  - May be a greater level of uncertainty about how device will perform
    - Device is generally early in development or
    - Device has a new intended use
  - Small number of subjects in clinical investigation (fewer than 15)
    - Initial indication of safety and/or effectiveness
    - Proof of concept

Recommended EFS Process



Contact EFS Representatives

- Prepare for working with FDA review team

Submit Initial Pre-Submission

- Educate FDA review team on device and clinical context
- Reach agreement on information needed in the Report of Prior Investigations to support study initiation (risk analysis, non-clinical testing, clinical mitigations)

Submit additional Pre-Submissions

- Obtain feedback on test protocols, clinical study plan, informed consent

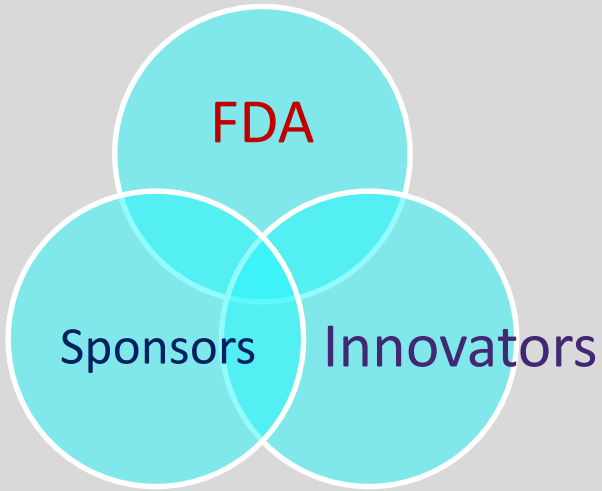
Submit IDE

- Interact with FDA review team to address any concerns

Key Policies for EFS Program

- **“Right Testing at the Right Time”**
  - Comprehensive testing during early phases of device development may add cost without significant return
  - However, informative nonclinical testing should be completed
- **Possible to leverage data from earlier versions of device**
- **Unknowns and risk can be addressed by:**
  - Using clinical mitigations to provide patients with extra protection
  - More frequent/detailed reporting
- **Provides tools for communicating available data to FDA**
  - Device evaluation strategy based approach

EFS Program Benefits



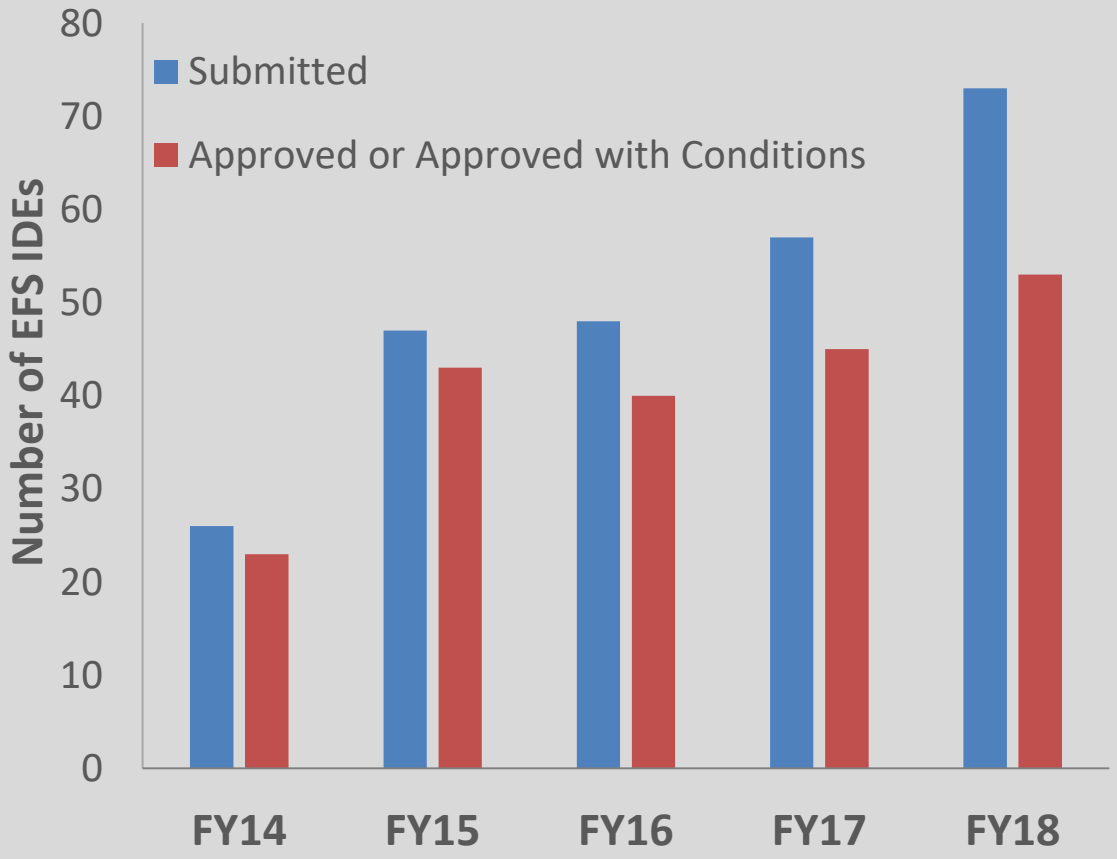
- Familiarity with technology and regulatory considerations
- Results in high quality clinical data

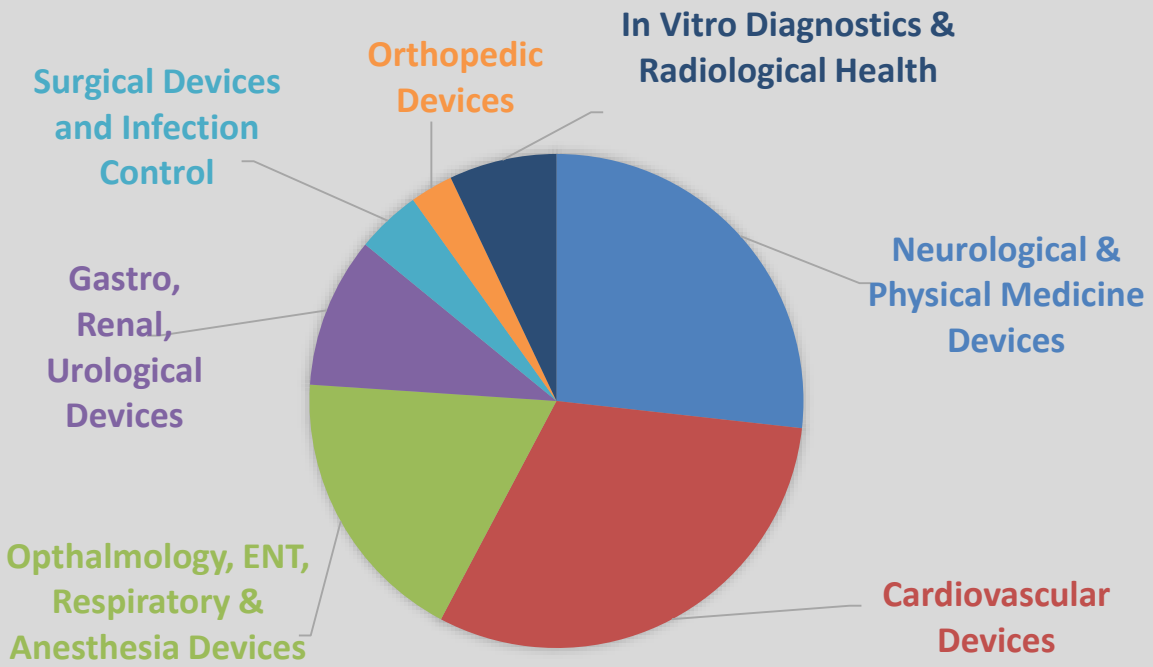
- New opportunity to address unmet needs
- Early experience with innovative technology

- Encourages development of high quality medical products
- Early access to potentially beneficial medical devices

EFS Program at a Glance

Significant FDA interaction from first Pre-Submission to EFS IDE review
Over 200 EFS approved



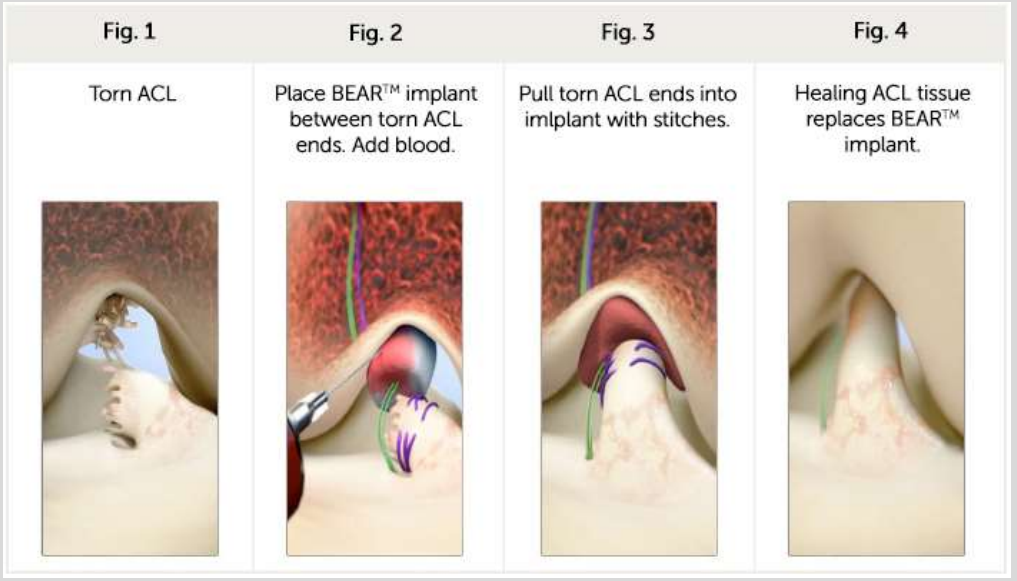


Based on FY18 data

1st EFS Device to Pivotal Trial

Bridge-Enhanced(TM) ACL Repair

- Experimental use of a bridging scaffold to repair the ACL
- Potential benefit: No need to harvest a tendon
- Physician Investigator-led study (Murray et al Orthop J Sports Med, 2016)
- EFS is complete:
  - currently in a pivotal trial



www.childrenshospital.org/centers-and-services/anterior-cruciate-ligament-program/bridge-enhanced-acl-repair-trial

1st EFS Device to Market

Angel® Catheter

- Retrievable, Inferior Vena Cava (IVC) filter, coupled with a triple lumen, central venous access catheter
- Benefits: Pulmonary embolism protection. Ability to remove filter.
- Small company
- EFS and pivotal studies complete. 510(k) cleared (K160747)

www.bio2medical.com/angel-catheter/

Morales JP & Farb A, JVIR 2017

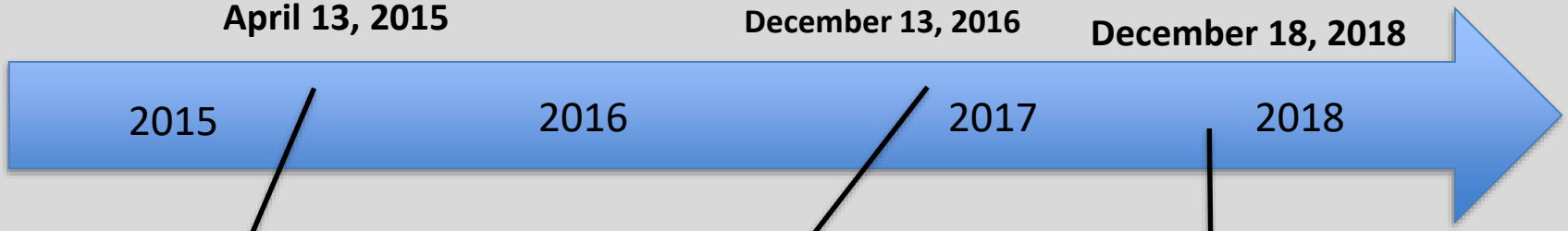
Breakthrough Devices Program

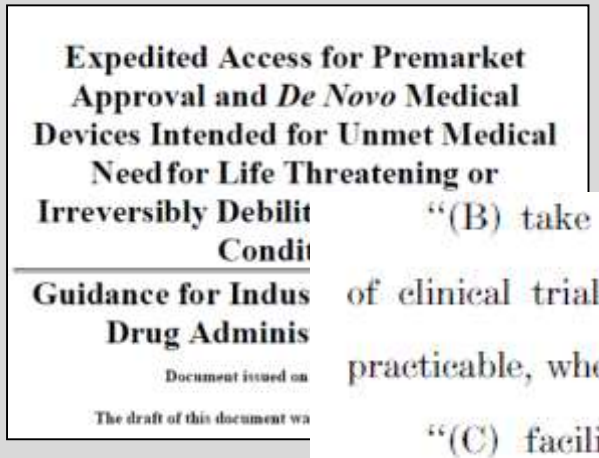
Breakthrough Devices Program

FDA's EAP Final Guidance April 13, 2015

21st Century Cures Act December 13, 2016

Breakthrough Devices Program Guidance December 18, 2018




Expedited Access for Premarket Approval and *De Novo* Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilit Condit

Guidance for Indus Drug Adminis

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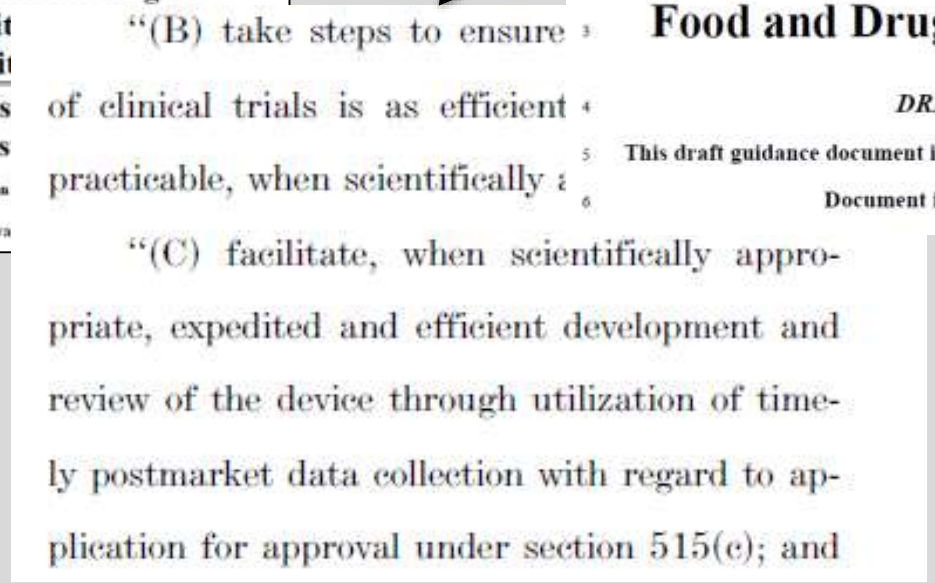
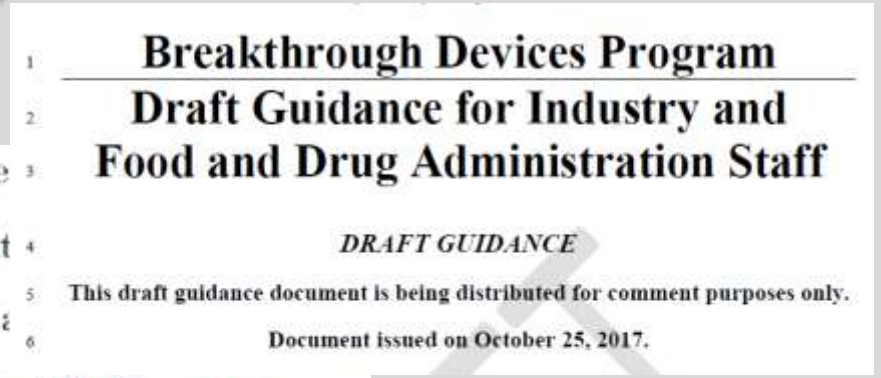

"(B) take steps to ensure

of clinical trials is as efficient

practicable, when scientifically a

"(C) facilitate, when scientifically appropriate, expedited and efficient development and review of the device through utilization of timely postmarket data collection with regard to application for approval under section 515(e); and


Breakthrough Devices Program

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on October 25, 2017.

Breakthrough Devices Program: Purpose

- Help patients have more timely access to devices
- Expedite device development and review for certain medical devices
- Work with sponsors to define roadmap to FDA marketing authorization
  - Breakdown perceived barriers
  - Collaboration and interaction in a positive feedback loop

Program Definition

- Voluntary program
- Devices and device-led combination products
  - Provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions
- Enable more timely access
- Expedite breakthrough device development, assessment, and review
- Preserve statutory standards for PMA, 510(k), and De Novo

Breakthrough: Eligibility and Criterion 1

Eligibility:

- Devices subject to PMA, De Novo and 510(k) that:

Criterion 1

- "provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions; and

Section 515B(b) FD&C Act

Breakthrough: Criterion 2

Meet One of the Following:

2A: that represent breakthrough technologies; or

2B: for which no approved or cleared alternatives exist; or

2C: that offer significant advantages over existing approved or cleared alternatives, including the potential, compared to existing approved alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients' ability to manage their own care (such as through self-directed personal assistance), or establish long-term clinical efficiencies; or

2D: the availability of which is in the best interest of patients."

Section 515B(b) FD&C Act

Program Principles

- Interactive and timely communication: begins at designation request and carries onto subsequent submissions
  - Review team support
  - Senior management involvement
  - Engaging external experts during review

- Prioritized review of subsequent submissions
  - Examples: Q-Submissions, Investigational Device Exemptions (IDE), marketing submission

Section 515B(e), FD&C Act

Program Principles

- Opportunities for the following as scientifically appropriate:
  - Premarket and postmarket balance of data collection
  - Application of flexible and efficient clinical study design
  - Expedited manufacturing and quality systems compliance review for breakthrough devices subject to PMA

Program Overview

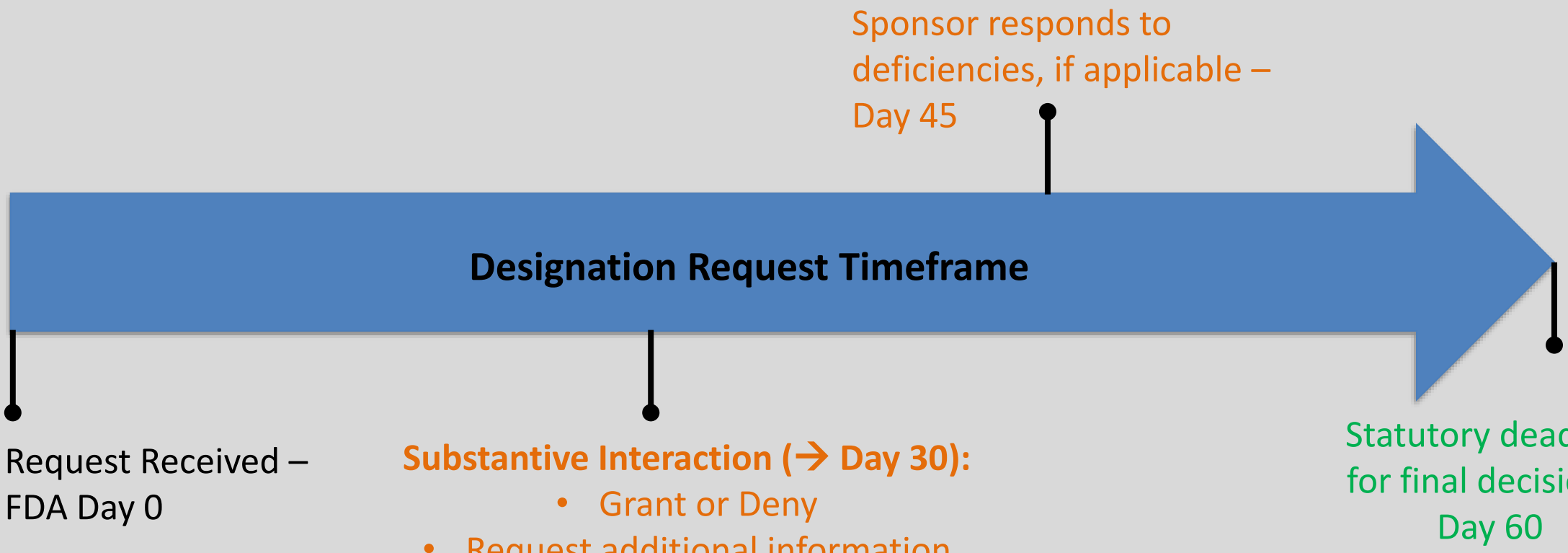
- For granted breakthrough devices,
  - Designation tracks with device for subsequent submissions
  - Prioritized review and other benefits
- If denied, traditional pathways still available for obtaining FDA feedback (for example, Pre-Submissions) and marketing submission

Considerations for Designation Request Review

- ***"Designation Request for Breakthrough Device"*** Q-Sub
  - Distinct submission that focuses solely on designation request
  - Don't include additional requests for feedback

- **Focused on:**
  - Device description
  - Proposed indication for use and clinical context
  - Justification for how device meets statutory criteria

Breakthrough Device Designation: Request Process



Banyan Brain Trauma Indicator

De Novo classification granted February 14, 2018

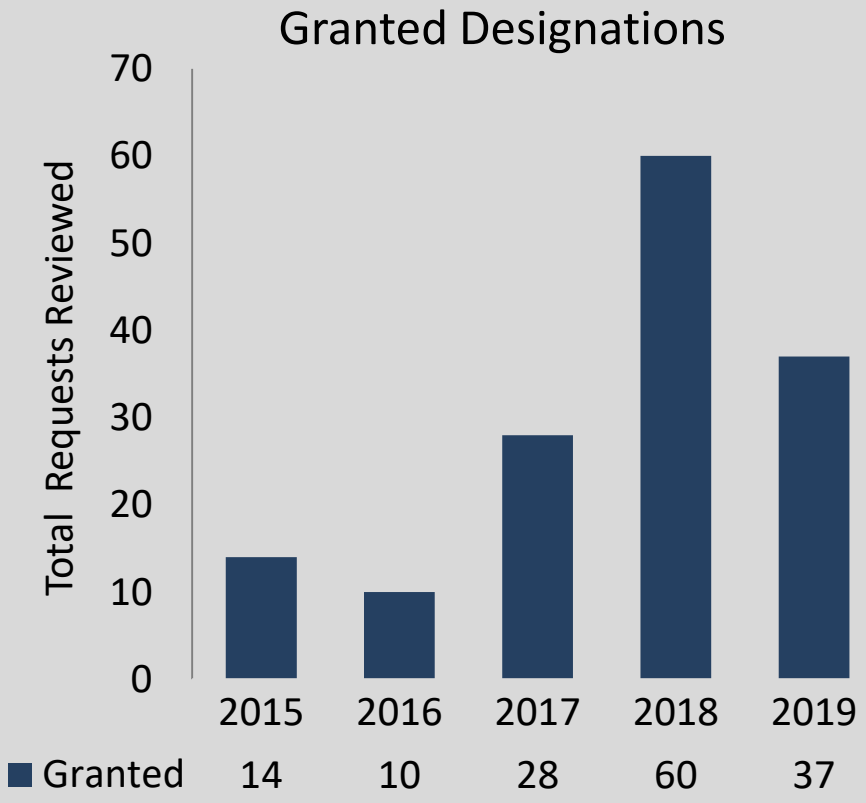
The Banyan BTI is an in vitro diagnostic chemiluminescent enzyme-linked immunosorbent assay (ELISA). The assay provides a semi-quantitative measurement of the concentrations of ubiquitin C-terminal hydrolase-L1 (UCH-L1) and glial fibrillary acidic protein (GFAP) in human serum, and is used with the Synergy 2 Multi-mode Reader.

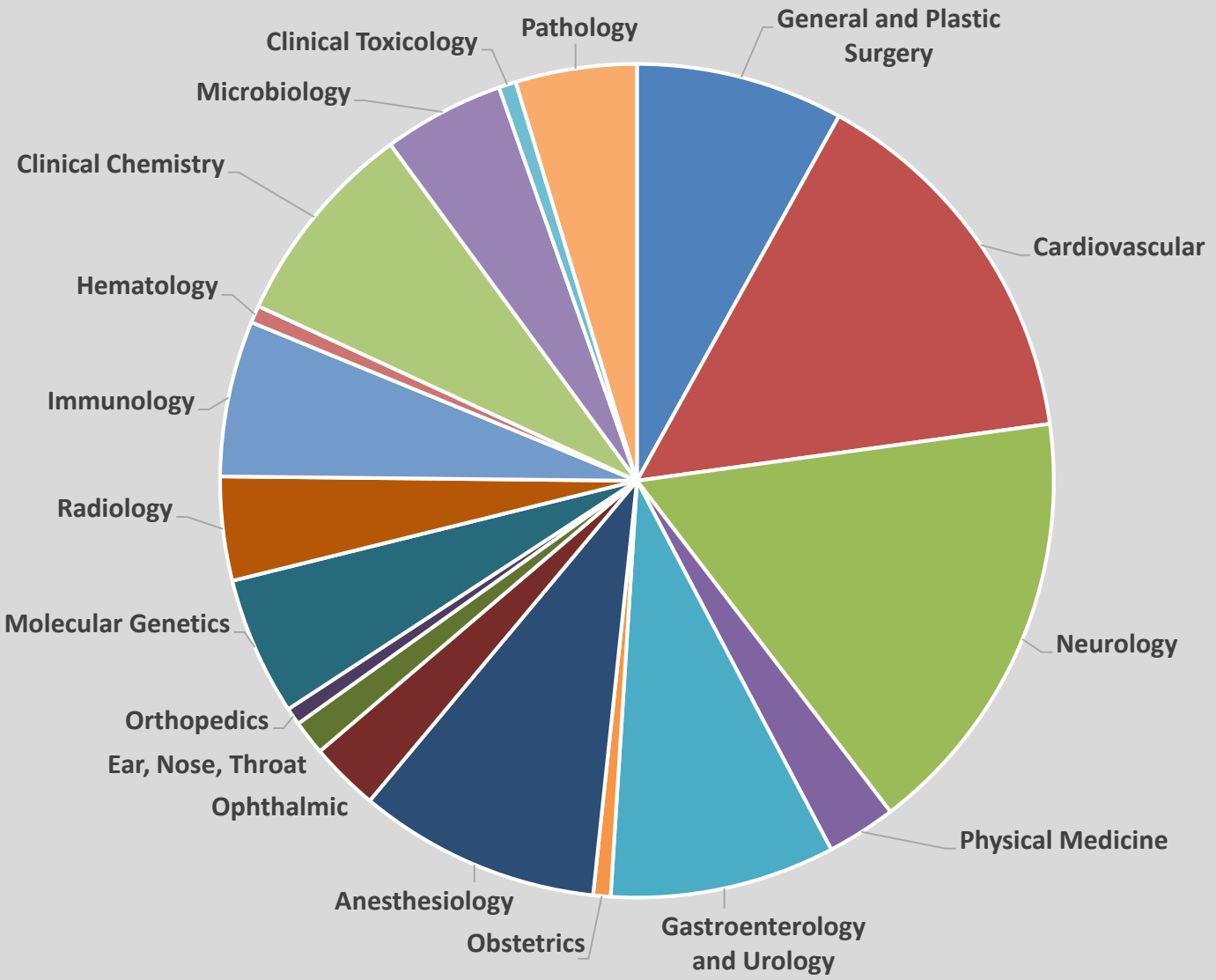
The assay results obtained from serum collected within 12 hours of suspected head injury are used, along with other available clinical information, to aid in the evaluation of patients 18 years of age and older with suspected traumatic brain injury (Glasgow Coma Scale score 13-15). A negative assay result is associated with the absence of acute intracranial lesions visualized on a head CT (computed tomography) scan.

The Banyan BTI is for prescription use only.

Program at a Glance – Granted Designations

as of May 1, 2019





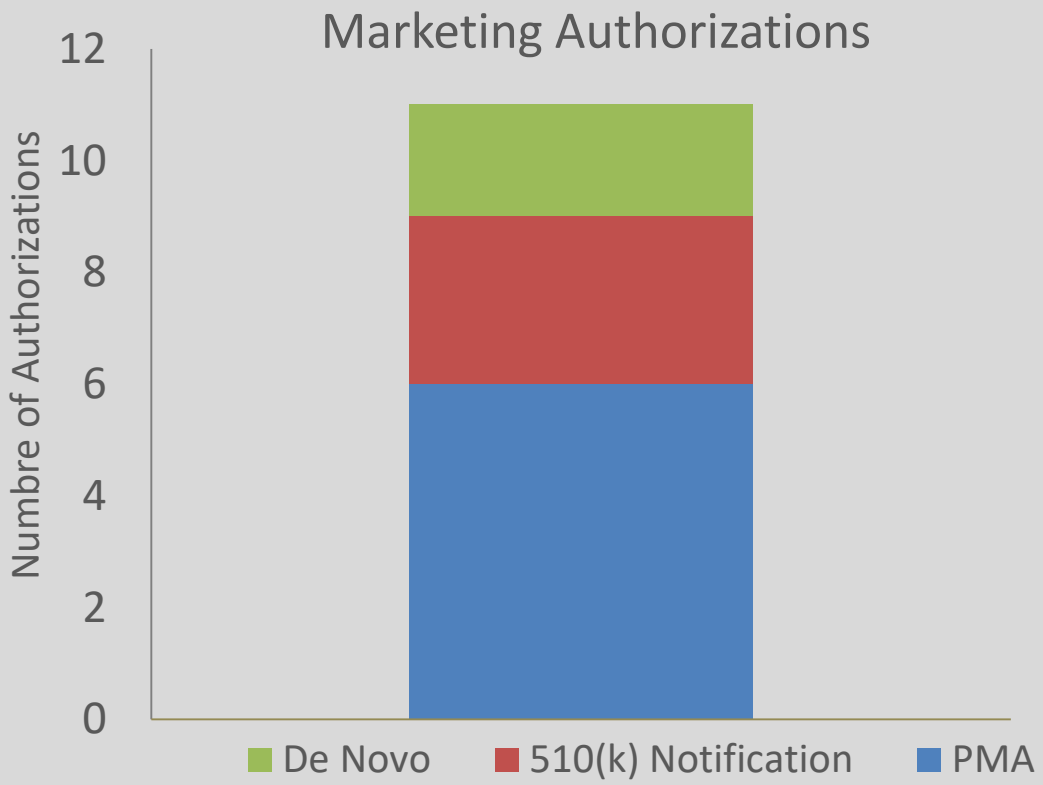
2015 reflects data from publication of final EAP Guidance on 4/13/2015

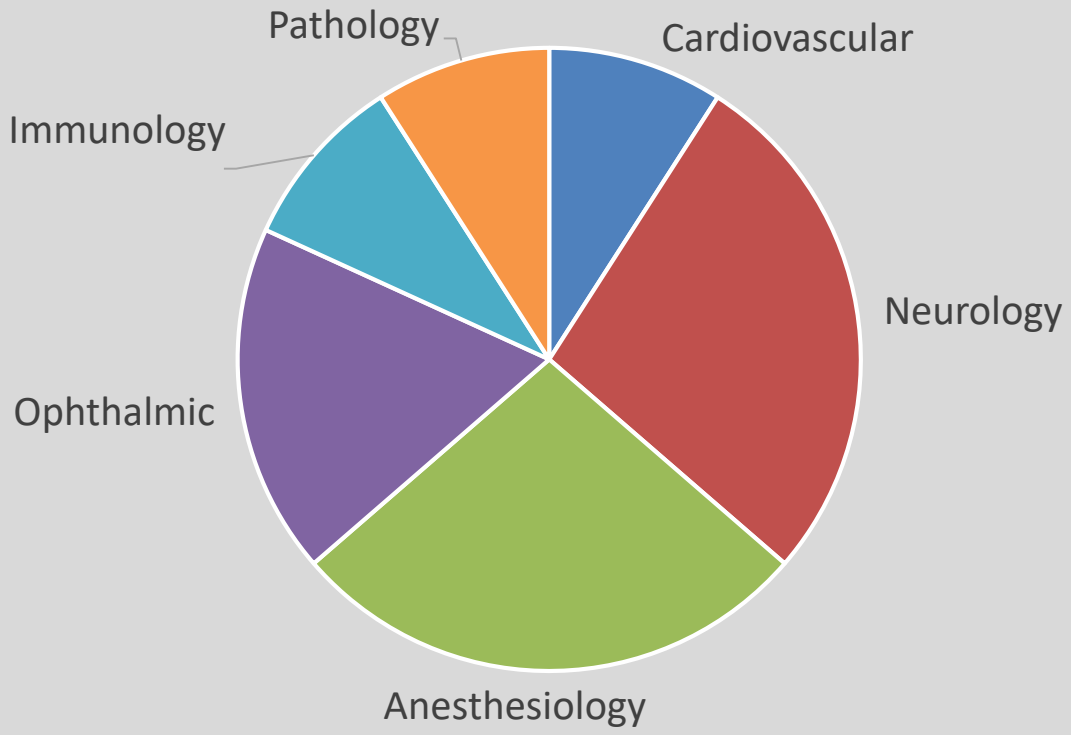
2019 reflects data from first 4 months

Program at a Glance – Marketing Submissions

as of May 1, 2019

11 breakthrough devices have obtained FDA marketing authorization





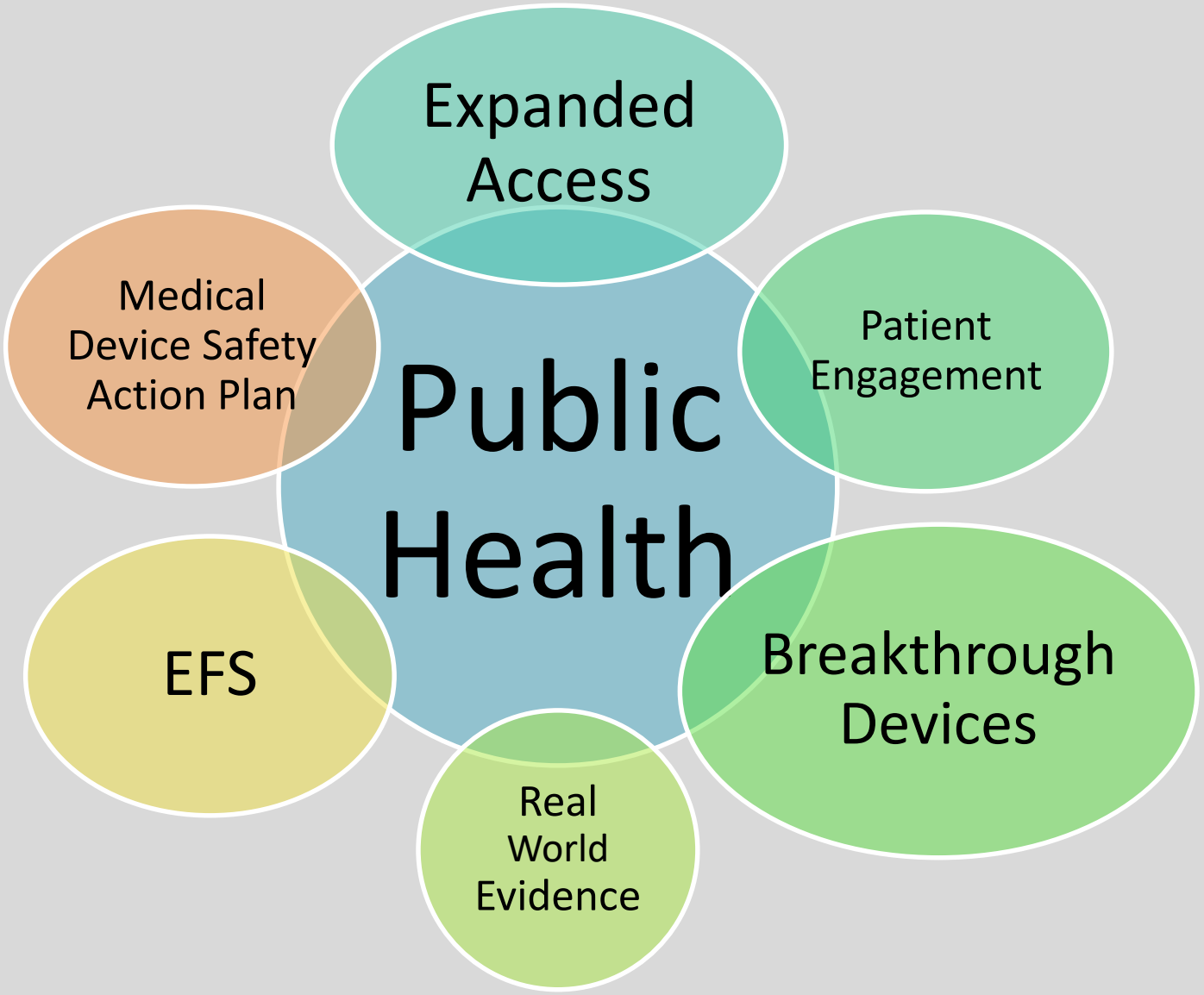
Summary

- FDA has developed three programs designed to increase timeliness of patient access to medical devices:
  1. Expanded Access
  2. Early Feasibility Study Program
  3. Breakthrough Devices Program

- Each program features policies and operational milestones

- Each program has an important role that supports CDRH's vision

How Does it all Fit Together?



Multiple options available
Quality data
Patient access

Questions

Maureen.Dreher@fda.hhs.gov

~~Your~~ Our Call to Action

Innovation

Flexibility

Collaborations


FDA
U.S. FOOD & DRUG
ADMINISTRATION