Plenary meeting: Priorities for the Evolution of Medical Device Regulatory Approval Systems
ESC Cardiovascular Round Table (CRT) 2024
Brussels, Belgium
17 April 2024

Regulatory Approaches to Facilitate Device Innovation

Andrew Farb, MD
Chief Medical Officer, Office of Cardiovascular Devices
Co-Leader FDA's Early Feasibility Studies Program
US Food and Drug Administration
andrew.farb@fda.hhs.gov

Investigational Device Exemptions (IDE)

FDA 101

- IDE approval by FDA allows use of a *significant risk investigational* device in humans in the US
  - IDE and IRB approval required ***before*** initiating enrollment
- Clinical data collected under IDE can support a marketing application [PMA, De-novo, or 510(k)]
- IDE submissions have a 30-calendar day review period
- No submission or review fees

Innovative Medical Device Evaluation in the US

The Past

- Migration of initial clinical testing of novel devices overseas
- Time lag in the access to beneficial medical devices for US patients
- Delay in physician experience with new products

US was the 42nd nation to approve a transcatheter aortic valve replacement device

Many clinical trial ecosystem factors contributed to these trends including FDA's requirements for non-clinical testing prior to initiating clinical studies of new devices.

The US EFS Program 10-Year Anniversary

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

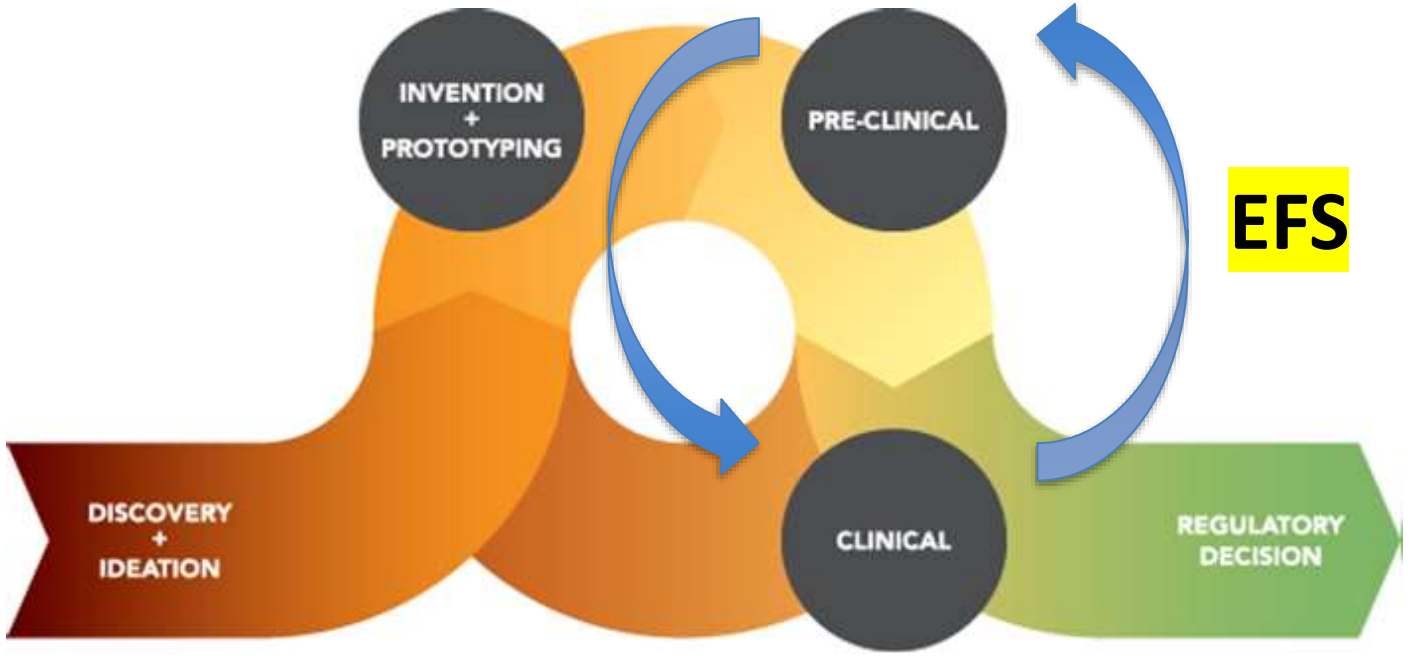
Document issued on: October 1, 2013

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

- Increase early US **patient access** to potentially beneficial medical devices
- Expand US site participation in the early clinical evaluation of innovative medical devices
- Enhance collaboration among device developers, industry, regulators, and investigators



Keys to EFS IDE Approval

Apply benefit/risk thinking throughout regulatory decision-making

- Disease condition (e.g., life-limiting, life-threatening)
- Availability and risks associated with currently available therapies
- Patient tolerance for risk & perspective on benefits

EFS needed when additional nonclinical testing not informative or not available to advance device development

Keys to EFS IDE Approval

- Just-in-time non-clinical testing: Right tests at the right time to support proof-of-principle and basic safety
  - May be acceptable to defer some nonclinical testing until the device design has been finalized for use in a pivotal study
  - Comprehensive testing early in device development may add cost without return
- Just-in-case risk mitigation strategies to enhance study subject protection

The US EFS Value Proposition
For Devices Ultimately Intended for the US

- Travel & language factors
- Data quality & monitoring considerations
- Patient characteristics relevant to the US population
- MDR challenges

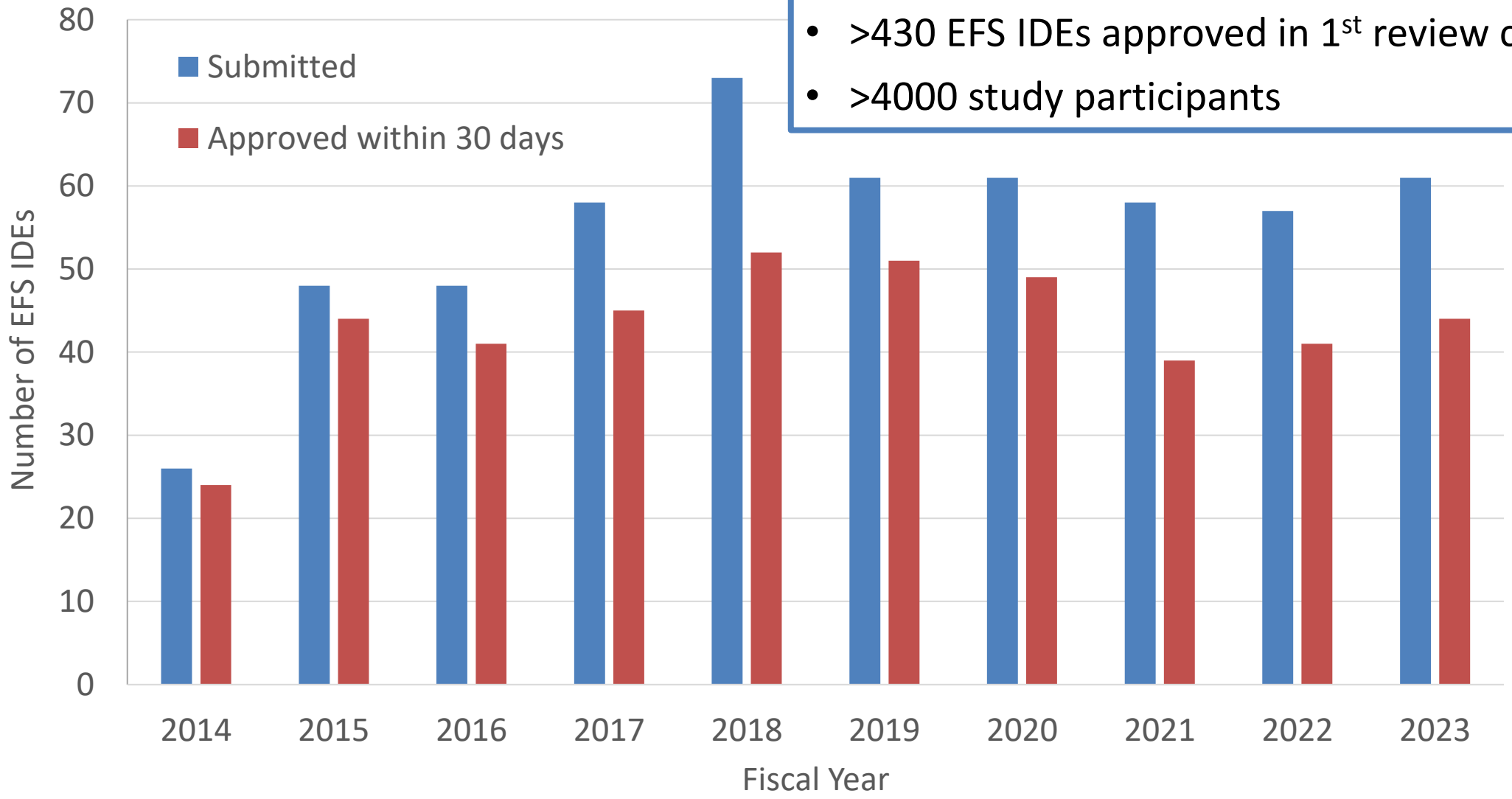
Starting earlier in the US

- Early FDA familiarity with the technology
- Consensus on non-clinical test plan
- US IRB approval & site initiation with accelerated operator learning curves

US EFS and non-US studies can be done in parallel

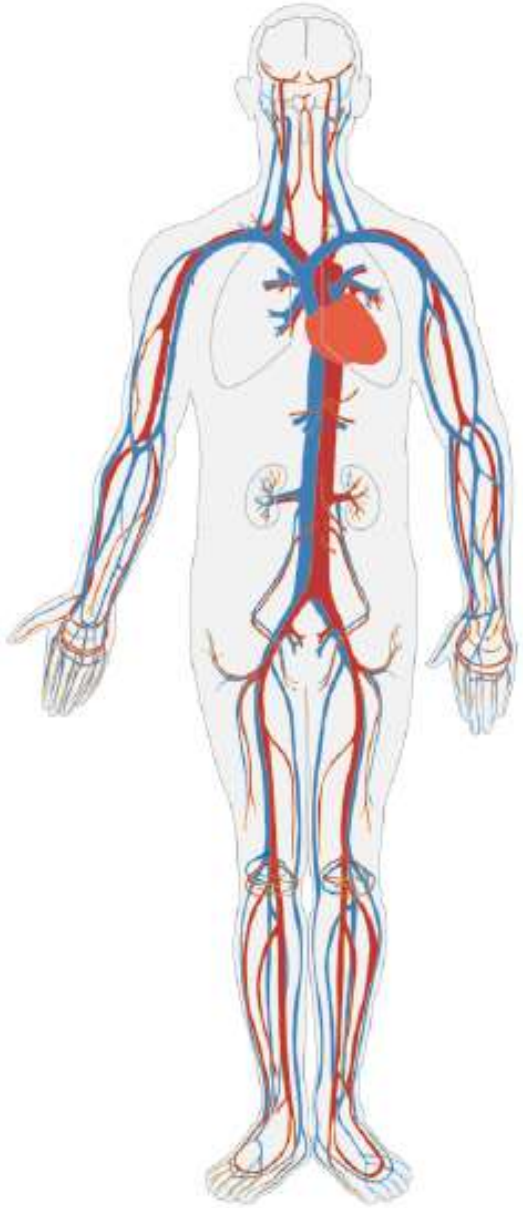
EFS Program Snapshot

- Approx. 60 EFS approved/year since FY17
- >430 EFS IDEs approved in 1st review cycle
- >4000 study participants



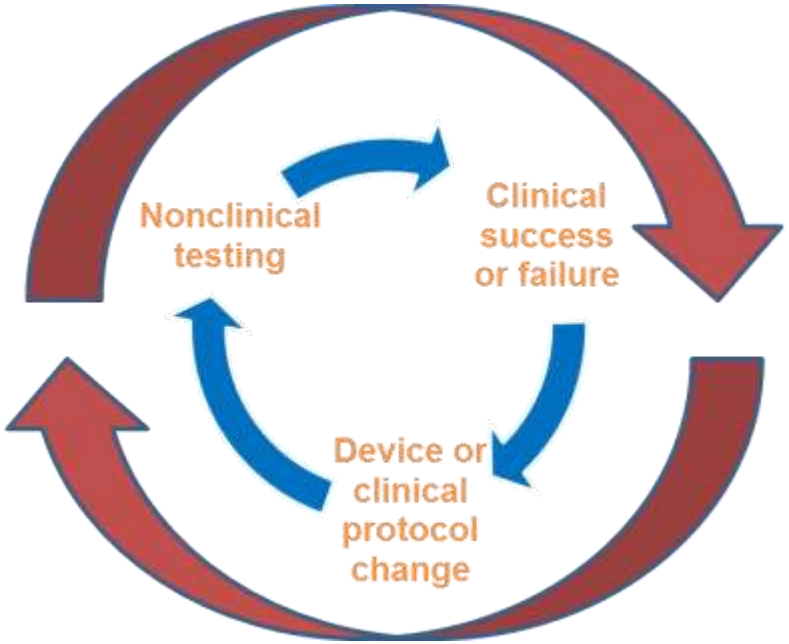
Cutting Edge CV Device & Clinical Condition EFS

- Carotid baroreflex
- Cardiac valves
- Acute heart failure
- LAA Closure
- CAD
- Hemodialysis access



- Aortic endografts
- Vena caval valves
- MCS devices
- VT ablation
- PAD
- Venous insufficiency

Next Steps in the US EFS Journey



Learn-as-you-go: Continue EFS with a modified device or procedure

Continue EFS with expanded enrollment

- Add new sites and investigators
- Gain further clinical experience
- Refine safety and effectiveness event rate estimates for pivotal trial planning

Transition to a pivotal trial to support product approval

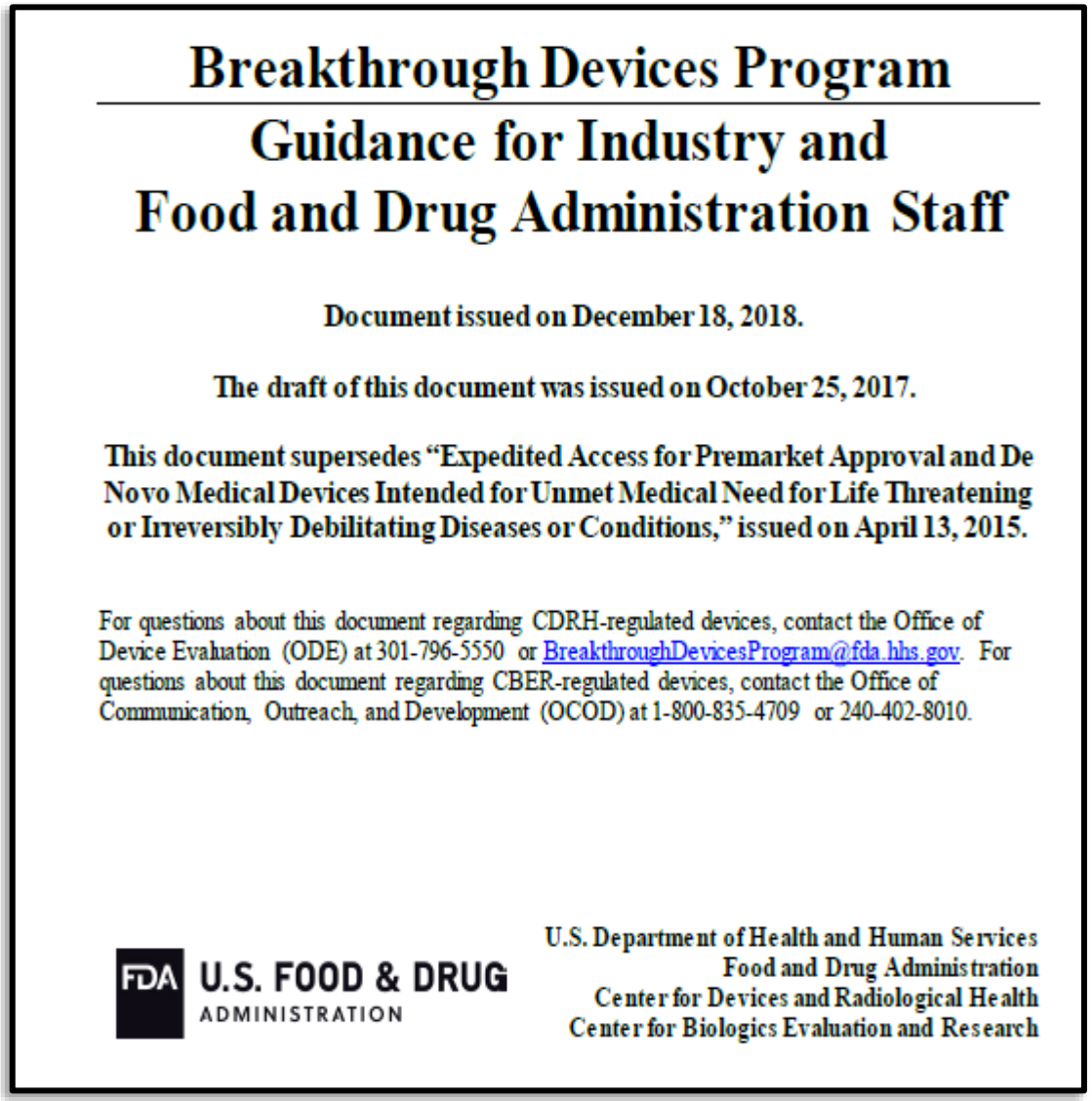
Finalized:

- Device
- Procedure
- Target patient population

❑ Adequate info for a pivotal study with statistically validated endpoints

❑ Nonclincal testing gaps filled

CDRH Breakthrough Devices Program



Breakthrough Devices Program

Guidance for Industry and Food and Drug Administration Staff

Document issued on December 18, 2018.

The draft of this document was issued on October 25, 2017.

This document supersedes "Expedited Access for Premarket Approval and De Novo Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions," issued on April 13, 2015.

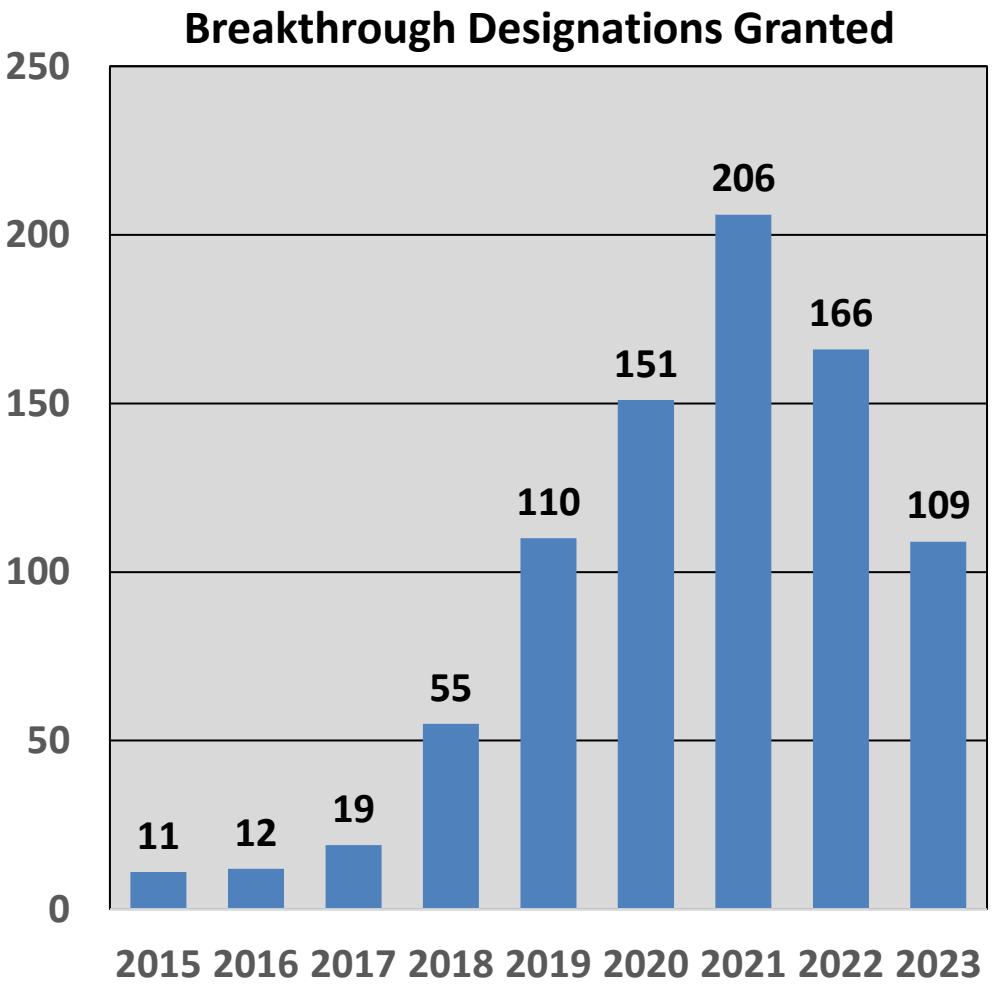
For questions about this document regarding CDRH-regulated devices, contact the Office of Device Evaluation (ODE) at 301-796-5550 or BreakthroughDevicesProgram@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

U.S. FOOD & DRUG ADMINISTRATION

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

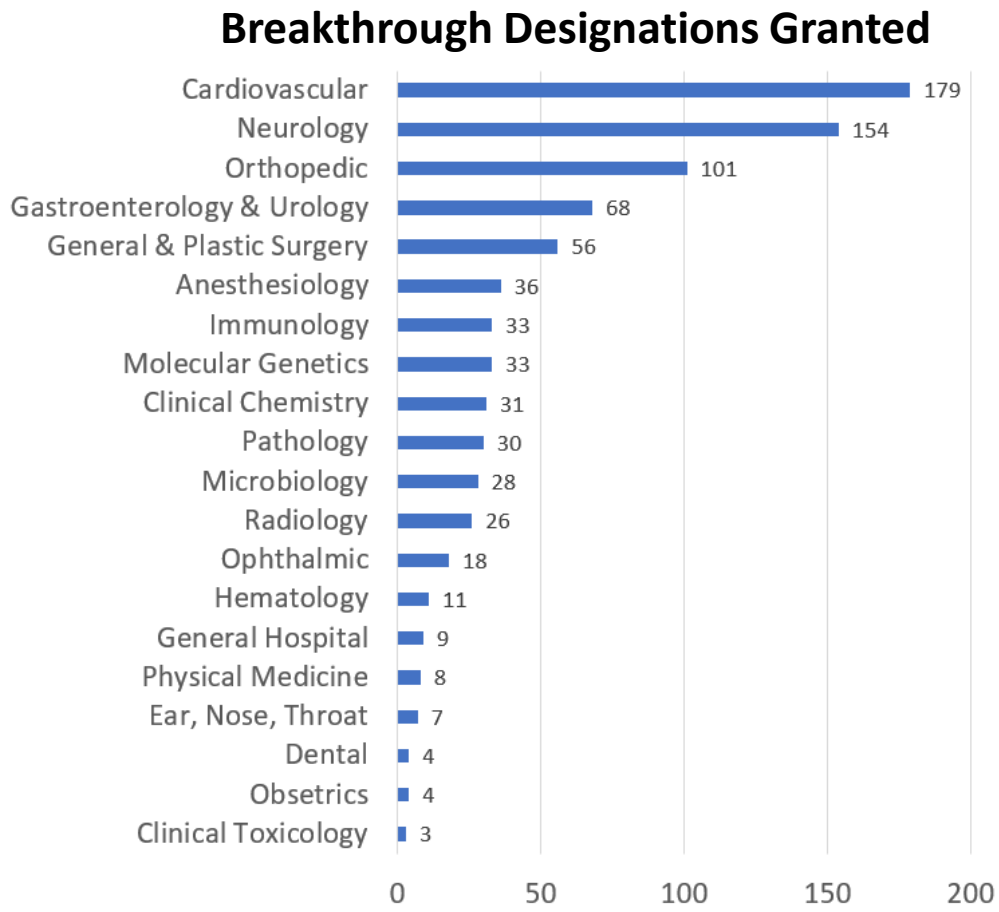
- Established by 21st Century Cures Act; superseded Expedited Access Pathway
- Accelerated pathway for devices that could provide more effective treatments for or diagnose life-threatening or irreversibly debilitating diseases or conditions, particularly those that address unmet needs
- Highly interactive
  - Sprint discussions to facilitate agreement between FDA and sponsors on product development topics
  - Regular status update meetings

CDRH Breakthrough Devices Program



839
Designated Devices

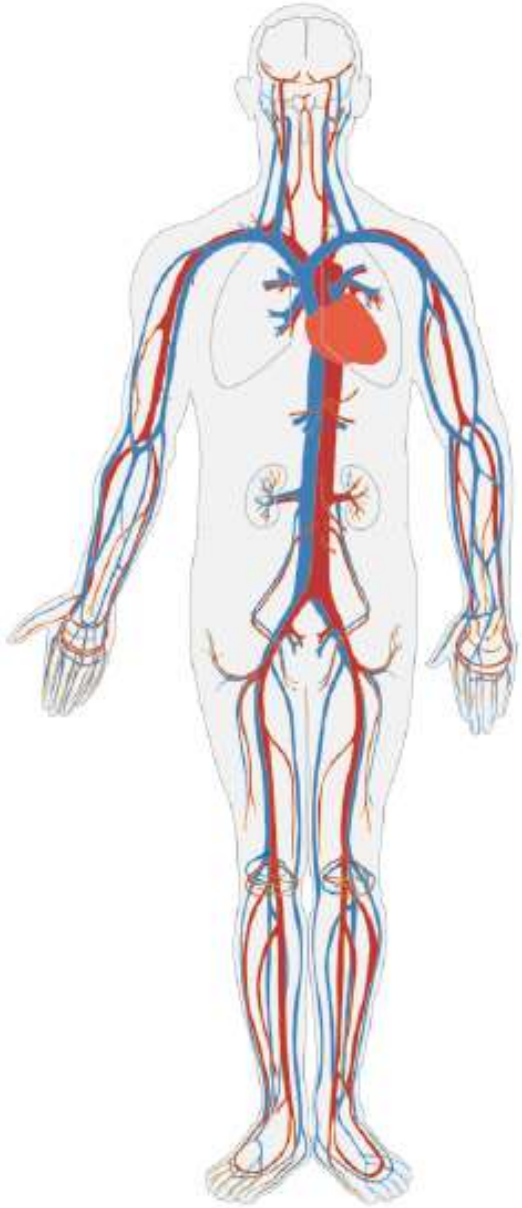
79
Marketing Authorizations
24 PMAs
28 510(k)s
27 De Novos



As of 6/30/2023

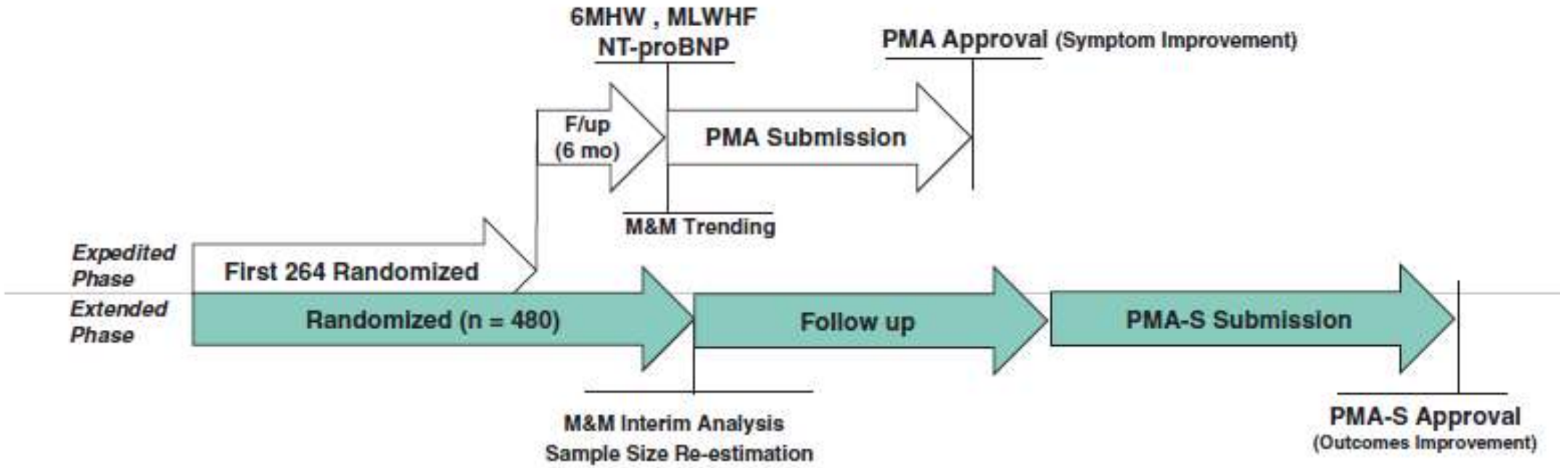
Breakthrough CV Device Approval Examples

- Coronary drug-coated balloons
- TV replacement & repair
- Renal denervation for HTN
- Pulse field ablation
- Aortic endographs
- PAD revascularization devices
- AV fistula support devices



Breakthrough CV Device 2-Phased Pivotal Trial

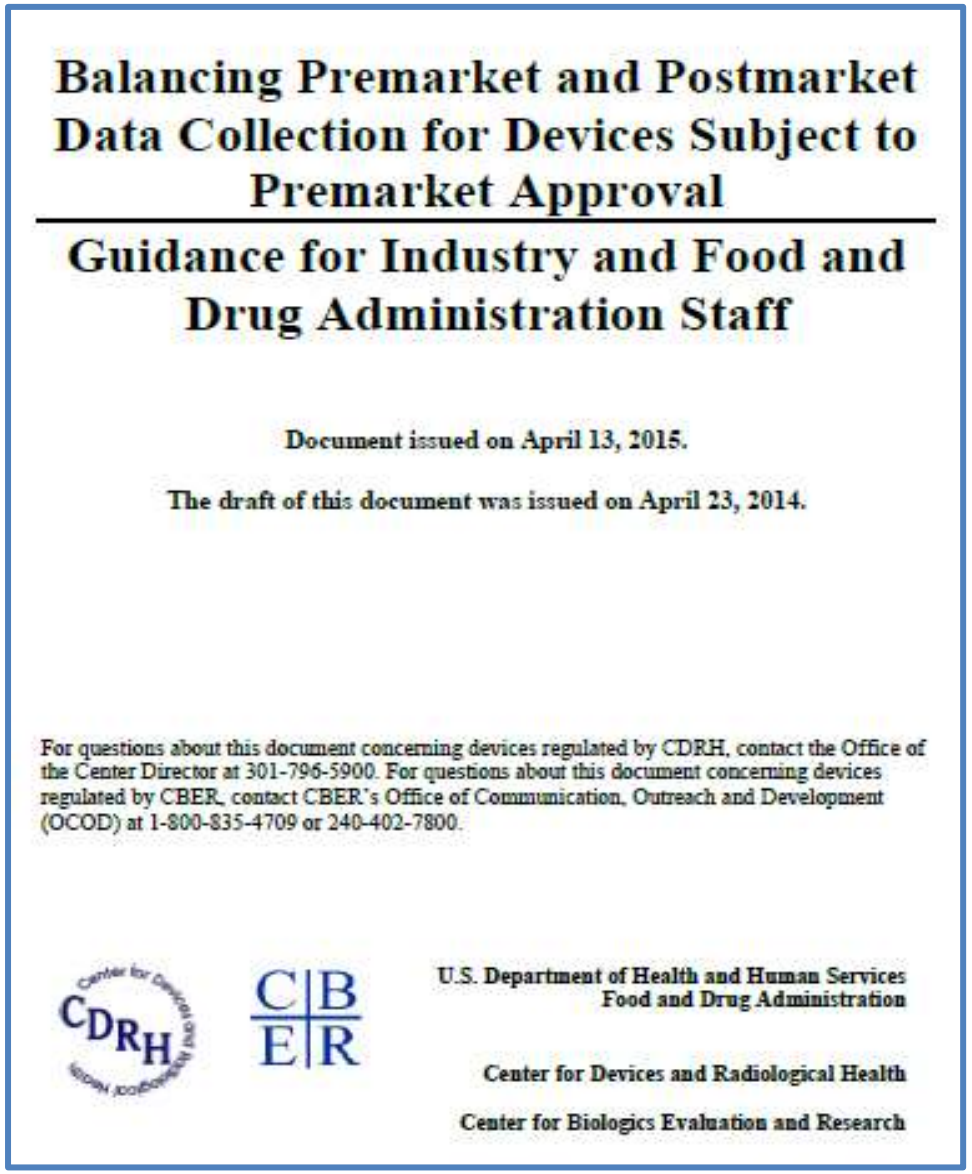
BEAT-HF Breakthrough Device Trial Design



Heart failure morbidity & cardiovascular mortality

Zile M, et al. Am Heart J 2018;204:139-50

Appropriate Pre/Post-Market Balance



Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval

Guidance for Industry and Food and Drug Administration Staff

Document issued on April 13, 2015.

The draft of this document was issued on April 23, 2014.

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 CBER's Office of Communication, Outreach and Development (OCOD) at 1-800-835-4709 or 240-402-7800.

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

Center for Devices and Radiological Health

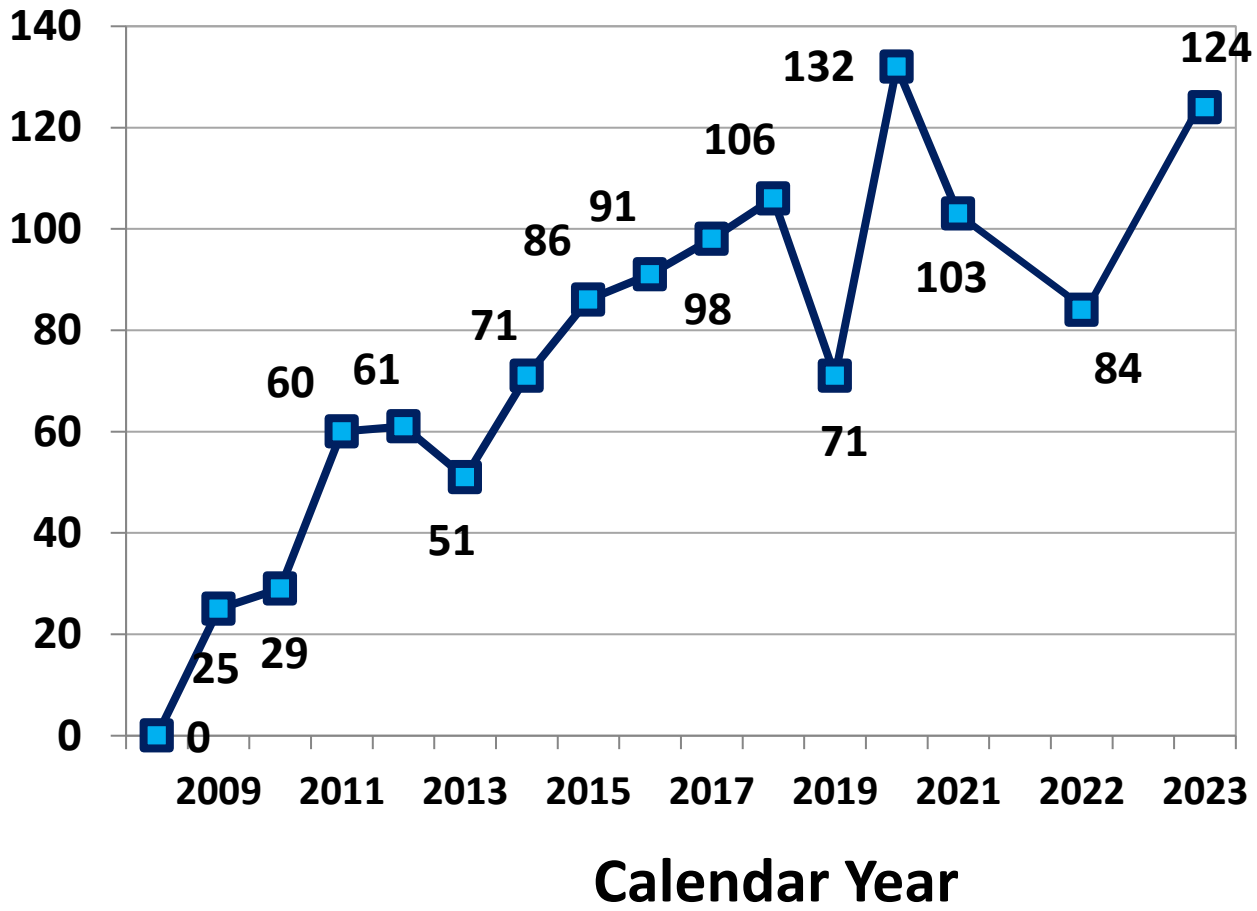
Center for Biologics Evaluation and Research

"FDA may consider it acceptable to collect certain data in the postmarket setting, rather than premarket under certain circumstances when FDA has uncertainty regarding certain benefits or risks of the device, but the degree of uncertainty is acceptable in the context of the overall benefit-risk profile of the device at the time of premarket approval."

Increased Novel Device Authorizations

Novel devices include original PMAs, panel track supplement PMAs, De Novos, HDEs, breakthrough 510(k)s, and specific EUAs

US the 1st nation to approve TAVR in low-risk patients



Digital Health Technology

https://www.fda.gov/medical-devices/digital-health-center-excellence

FDA authorized AI/ML-enabled Medical Devices

- ECG and EGM analysis
- Echo acquisition guidance
- Heart sounds/phonocardiography analysis
- LAAO placement guidance
- Critical care indexes
- Interventional calculations (e.g., imaging-based FFR)

OPPORTUNITIES

- Significant positive impact on health care
  - Earlier disease detection
  - More accurate diagnosis
  - Personalized diagnostics and therapeutics
- Applications across all medical fields
- Ability to learn, adapt, and improve performance

CHALLENGES

- Fit-for-purpose data sets for development and testing, including diversity
- Identification and minimization of bias
- Providing oversight for an adaptive system
- Opacity of some algorithms and ensuring transparency
- Patient data protection

Guidance, Guidance, Guidance

15 Digital Health Guidance Documents Published Since FY2018

GUIDANCE DOCUMENT

Content of Premarket Submissions for Device Software Functions

DRAFT

GUIDANCE DOCUMENT

Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions

GUIDANCE DOCUMENT

Cybersecurity in Medical Devices: Refuse to Accept Policy for Cyber Devices and Related Systems Under Section 524B of the FD&C Act

GUIDANCE DOCUMENT

Clinical Decision Support Software

GUIDANCE DOCUMENT

Policy for Device Software Functions and Mobile Medical Applications

GUIDANCE DOCUMENT

Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices

DRAFT

GUIDANCE DOCUMENT

Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions

DRAFT

GUIDANCE DOCUMENT

Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Draft Guidance for Industry, Investigators, and Other Stakeholders

GUIDANCE DOCUMENT

Multiple Function Device Products: Policy and Considerations

GUIDANCE DOCUMENT

Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act

GUIDANCE DOCUMENT

General Wellness: Policy for Low Risk Devices

GUIDANCE DOCUMENT

Off-The-Shelf Software Use in Medical Devices

GUIDANCE DOCUMENT

Medical Device Accessories - Describing Accessories and Classification Pathways

GUIDANCE DOCUMENT

Software as a Medical Device (SAMD): Clinical Evaluation

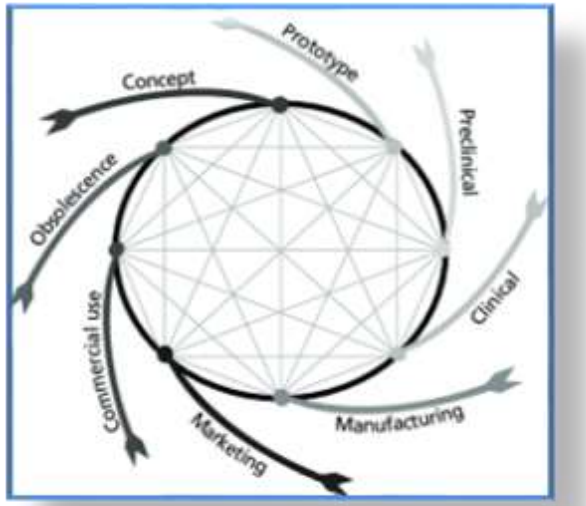
GUIDANCE DOCUMENT

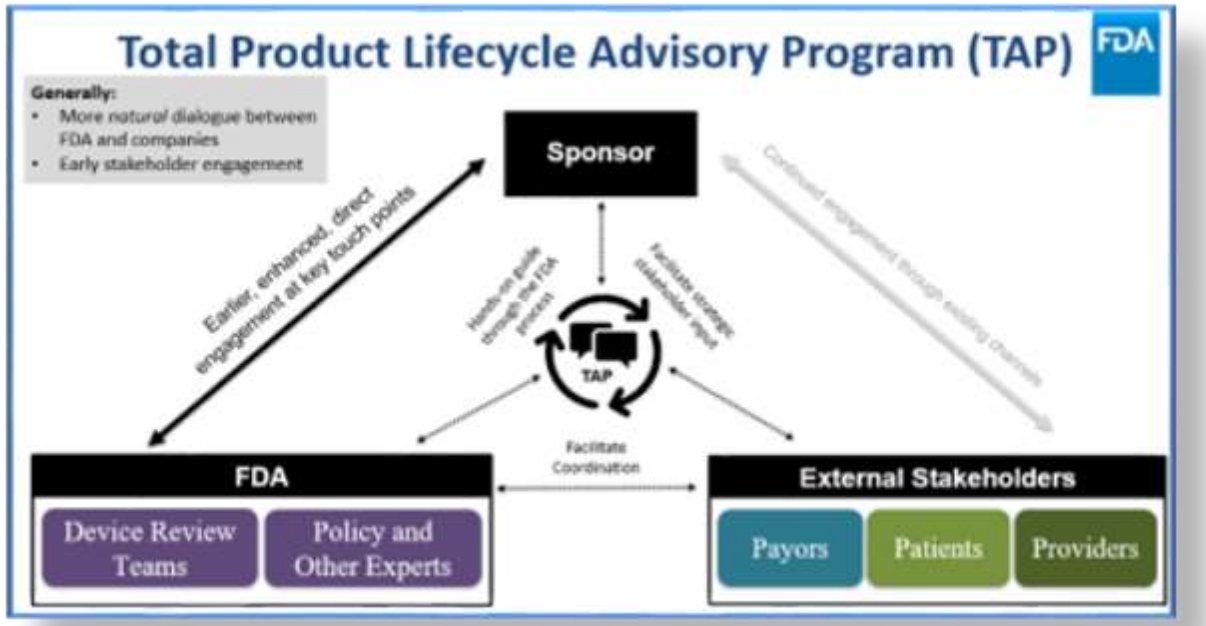
Deciding When to Submit a 510(k) for a Software Change to an Existing Device

Reimagining the Device Innovation Ecosystem

The Total Product Lifecycle Program (TAP) for Breakthrough Devices

- More transparent and predictable data requirements for regulators and payors for innovative products
- Fulfill the promise of total product lifecycle regulatory approaches





https://www.fda.gov/medical-devices/how-study-and-market-your-device/total-product-life-cycle-advisory-program-tap

Reimagining the Device Innovation Ecosystem

Global data streams to support
device innovation and evaluation

FDA U.S. FOOD & DRUG ADMINISTRATION + Devices

andrew.farb@fda.hhs.gov