Opportunities To Increase Regulatory Predictability

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Overview

- Expedited Access Pathway
- Clinical Trials Program
- Direct DeNovo

Expedited Access Pathway (EAP)

- A voluntary program for certain medical devices that demonstrate the potential to address unmet medical needs for life threatening or irreversibly debilitating diseases or conditions

- Only for devices that are subject to premarket approval applications (PMA) or are eligible for *de novo* requests

Two New Guidance Documents

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

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

  clarifies FDA's current policy on balancing premarket and postmarket data collection during FDA review of premarket approval applications (PMAs).

EAP

- Maintain the statutory standard of reasonable assurance of safety and effectiveness
- Innovation Pathway
- Role of Postmarket Data
  - Least burdensome
  - Benefit-risk

Criteria

- The device is intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition.
- The device meets at least one of the criteria for addressing an unmet need.
- The sponsor submits an acceptable draft Data Development Plan.

Unmet Need

- Must meet at least 1 of the following criteria:
  - No approved alternative treatment or means of diagnosis exists.
  - The device represents a breakthrough technology that provides a clinically meaningful advantage over existing legally marketed technology.
  - The device offers significant, clinically meaningful advantages over existing legally marketed alternatives.
  - The availability of the device is in the best interest of patients (e.g., addresses an unmet medical need).

Draft Data Development Plan

- Explanation and justification for proposed pre- and postmarket data collection
- Data collection plan
- Timeline

Features of EAP

- Interactive review
- Senior management involvement
- Case manager
- Priority review
- Expectation for applicants to be timely in interactions

Benefit-Risk Considerations

- Postmarket data collection
- Uncertainty
- Ways to reduce probable risk of harm

Clinical Evidence

- Intermediate and surrogate endpoints
- Two-phase studies
- In Vitro Diagnostics
- Sources of clinical evidence

Conditions of Approval (for PMAs)

- Post-Approval Studies (PAS)
- Reporting Requirements for PAS
- Labeling
- Use of Registries

Postmarket Actions

- Submission of a PMA supplement*
- Safety Communications
- Panel Meeting*
- Administrative and Enforcement Actions

* PMA only

Clinical Trials Program

Strengthening the Clinical Trial Enterprise

- Goal: Improve the efficiency, consistency, and predictability of the IDE process to reduce the time and number of cycles needed to reach appropriate IDE full approval for medical devices, in general, and for devices of public health importance, in particular.
- Goal: Increase the number of early feasibility/first-in-human IDE studies submitted to FDA and conducted in the U.S.

The IDE Challenge

- The IDE review process is an important part to protecting subjects in investigational device studies
- We also recognize, the sooner an IDE is approved, the sooner a potentially important technology can be available to US patients
- The IDE process has at times led to avoidable bottlenecks in the process
- We can and should look for ways to improve the process of FDA's decision making for IDEs

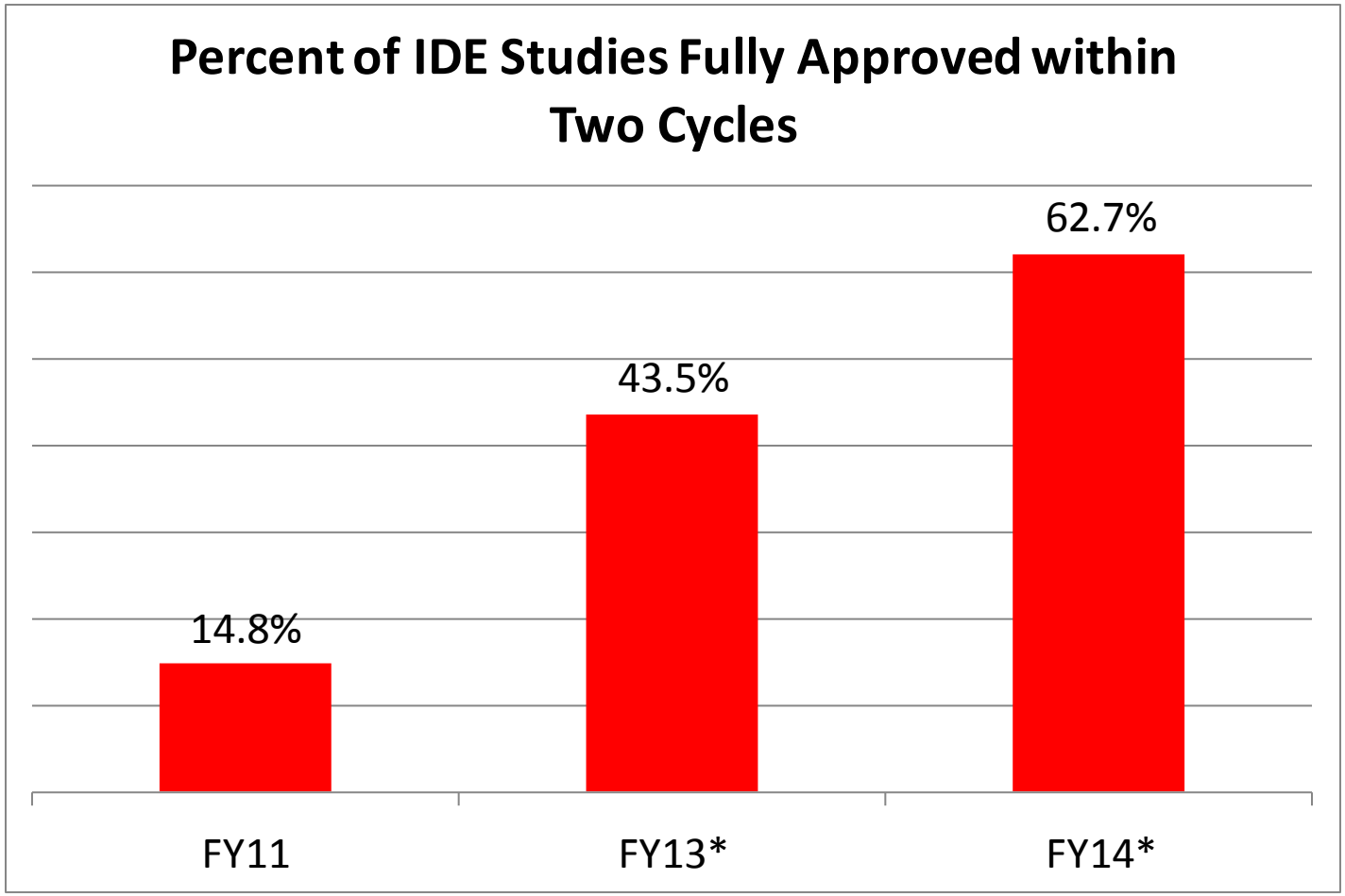
What is CDRH doing?

- Established Clinical Trials Program and Clinical Trials Director (CTD)
- Established SOP for CTD involvement and review of certain IDE decisions. Focus on:
  - Ensuring CDRH is “in the right place”
  - Ensuring flexibility is applied where appropriate
  - Increased communication with sponsors
- Established Early Feasibility Study (EFS) coordinators within Clinical Trials Program

Clinical Trials Program Outcomes

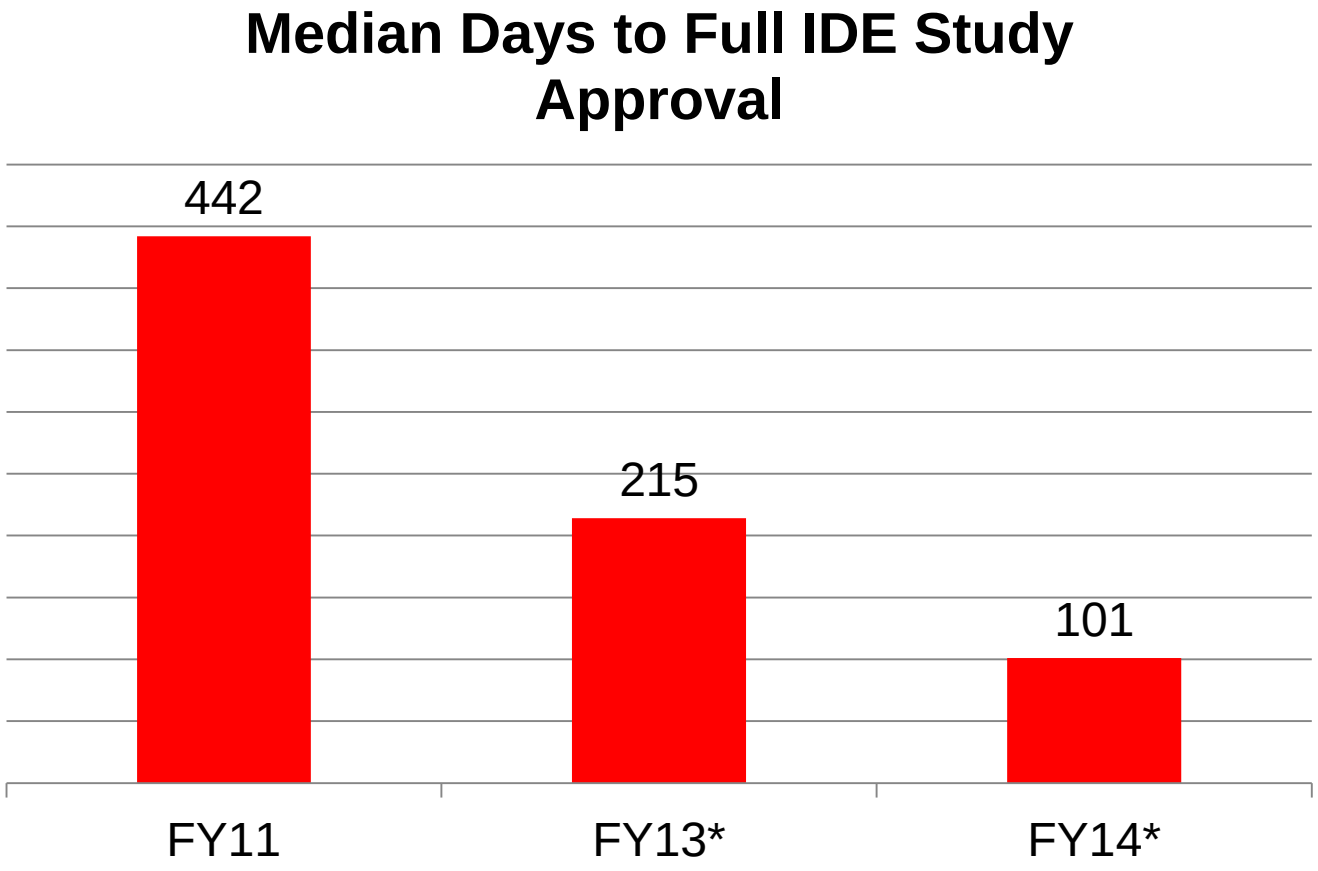
- Helps ensure consistency in decision-making
- Facilitates sharing of best practices across divisions
- Encourages higher levels of interaction
- Helps prepare sponsor to respond

FY14 Performance



* Values calculated on 10/31/13 and 10/31/14 respectively

FY14 Performance



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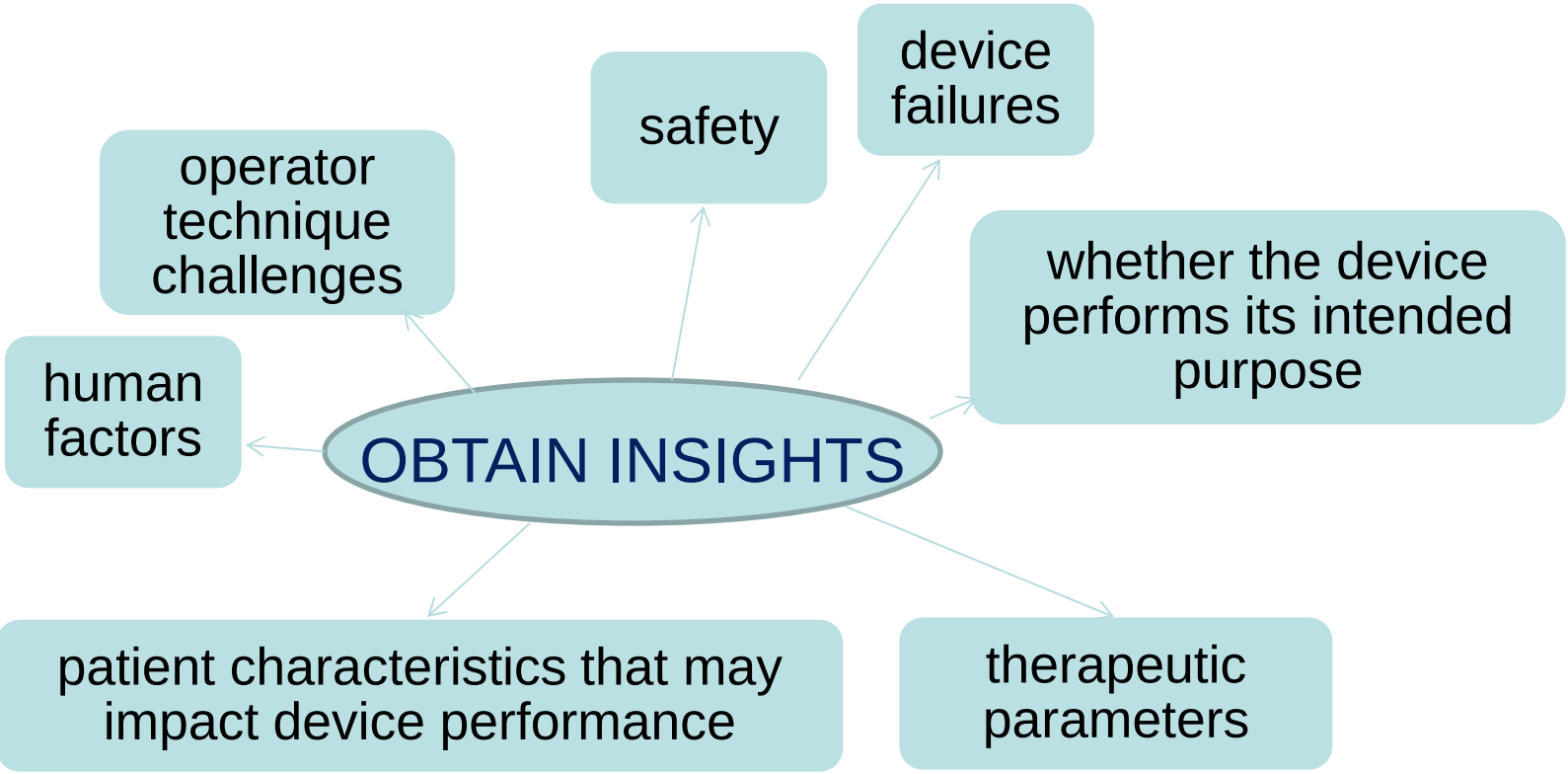
FY2015 Goals

- By June 30, 2015, compared to FY13 performance, CDRH seeks to:
  - Reduce the number of IDEs requiring more than two cycles to an appropriate full approval decision by 50%
  - Reduce the overall median time to full appropriate IDE approval to 30 days.
  - Increase the number of early feasibility/first-in-human IDE studies submitted to each premarket Division

Early Feasibility Study (EFS) Program

- **Intent -** To facilitate US EFS under the IDE regulations
- **Scope -** Elements that define an early feasibility study:
  - Small number of subjects
  - Device that may be early in development, typically before the device design has been finalized
  - Does not necessarily involve the first clinical use of a device

Purpose of Early Feasibility Studies



Why focus on EFS?

- **EFS is often a critical step in device innovation and development**
- When EFS are conducted in the US, important new technologies may become available to US patients sooner.

What is CDRH doing to support EFS in US?

- Issued Guidance to outline FDA's thinking on EFS and how FDA can be more flexible
- Established and trained EFS experts in each ODE review division to assist sponsors and review teams
- Currently developing "CDRH-learn" module focused on EFS

EFS Guidance

- **Key Guidance Principle -** Approval of an early feasibility study IDE may be based on less nonclinical data than would be needed to support the initiation of a larger clinical study of a more final device design
- **Guidance Provisions -** A regulatory toolkit that enables sponsors and regulators to think in new ways about device development
  - Justifying the appropriate evidence needed to move from bench to clinical study
  - Allowing timely device and clinical protocol modifications

The Right Testing at the Right Time

- Comprehensive testing during early phases of device development may add cost without significant return
- It may be acceptable to defer some nonclinical testing until the device design has been finalized
- An early feasibility study incorporates enhanced risk mitigation strategies and patient protection measures as compared to a pivotal study

EFS Process

- Sponsors contact EFS coordinators and interact informally to:
  - Discuss the EFS guidance policies and principles
  - Help with understanding the device evaluation strategy (DES) concept and developing the DES table
  - Prepare for initial interactions with the review team
- Submit the initial Pre-Sub
  - Reach agreement on the information needed in the Report of Prior Investigations to support study initiation
  - Supplement Pre-Sub as needed
- Submit the original IDE and continue interacting with CDRH throughout the conduct of the EFS

Clinical Trials Program: Future Plans

- Continued monitoring of performance for IDEs in general and EFS IDEs
- Draft Benefit-Risk Guidance for IDEs
- Development of additional clinical trials training for CDRH review staff and external stakeholders
- Submission quality improvements

De Novo

De Novo Background

FD&C Act – Modified in 1997

Food and Drug Administration Modernization Act (FDAMA)

Section 513(f)(2): established **de novo** classification process

- Also known as "Evaluation of Automatic Class III Designation"
- Provided regulatory authority for FDA to classify devices that were automatically classified into Class III per Section 513(f)(1) (new devices)
- To Class I or II using criteria of Section 513(a)(1)(A-B)

Excludes devices already classified into Class III

(e.g., PMA-approved devices)

De Novo Background

FD&C Act – Further modified in 2012

Food and Drug Administration Safety and Innovation Act (FDASIA)

Section 513(f)(2) – *de novo* provision

What changed

- Removed requirement for sponsor to submit 510(k) prior to submission of de novo request.
- Created two pathways for de novo submissions: post-510(k) NSE and direct de novo.
- Timeframe for review set at 120 days.

Goal: to streamline and increase efficiency in process

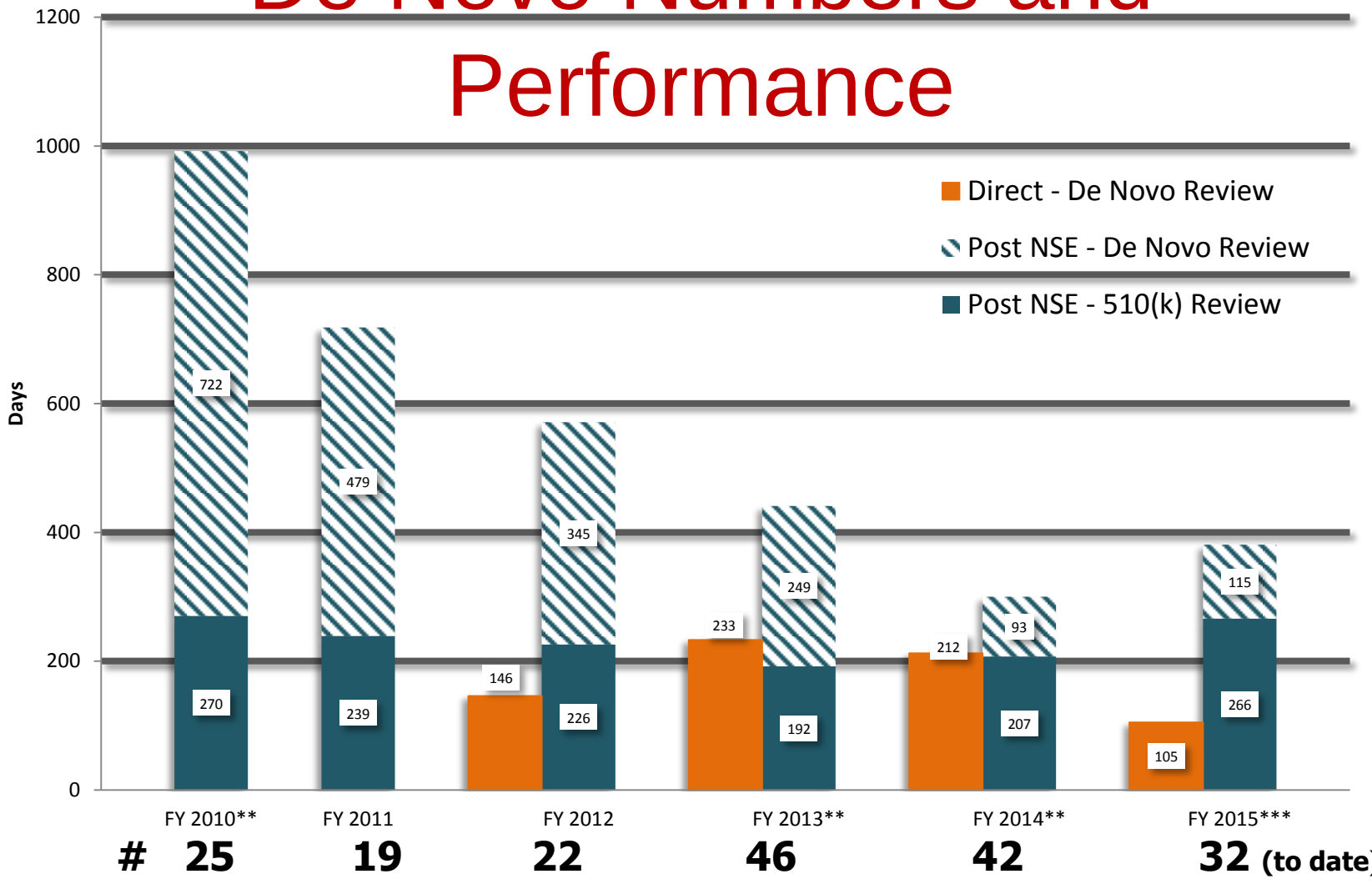
De Novo Draft Guidance

Published 2014

Major Items

- Removes requirement for 510(k) submission prior to de novo
- FDA has 120 days to make classification decision
- Decision Options: **grant** or **decline**
- Pre-Submission meeting process
- New term: "**direct *de novo***" (no 510(k) prior to de novo submission)

De Novo Numbers and Performance



**cohort still open

Strategies for Success

***De Novo* Submission Should Provide:**

- Evidence that establishes reasonable assurance of safety and effectiveness
- Information typically submitted in traditional 510(k) submission including regulatory history, device description, labeling, etc.
- Performance testing (bench, animal, clinical, as appropriate)
- Characterize **risks to health** associated with use of new device
- Characterize how the risks may be **mitigated**
- Provide **rationale** for why device does not fit into existing regulation (either 510(k) or PMA)
- If propose Class II classification, then identify the **special controls** to mitigate the risks to health

Strategies for Success

Remember that, a *de novo*, if granted:

- Establishes a new “device type” along with classification, regulation, and product code
- Device is eligible to serve as a predicate for new medical devices, where appropriate [510(k) process]

After De Novo is Granted

- New device is legally marketed
  - Subject to requirements applicable to that device and class (including general controls, special controls as applicable)
- New device establishes new classification regulation
  - New device is eligible to serve as a predicate for future similar devices
- FDA publishes order announcing new classification, controls
- FDA generates decision summary that is publicly available

Classification Order and Decision Summary

Device Name	DEN#	Classification Order	Decision Summary
Dexcom Share Direct Secondary Displays	DEN140038	Classification Order (http://www.accessdata.fda.gov/cdrh_docs/pdf14/DEN140038.pdf)	Decision Summary (http://www.accessdata.fda.gov/cdrh_docs/reviews/DEN140038.pdf)
HeartFlow FFR_{CT} v.1.4	DEN130045	Classification Order (http://www.accessdata.fda.gov/cdrh_docs/pdf13/DEN130045.pdf)	Decision Summary (http://www.accessdata.fda.gov/cdrh_docs/reviews/DEN130045.pdf)
Eeva® System	DEN120015	Classification Order (http://www.accessdata.fda.gov/cdrh_docs/pdf12/DEN120015.pdf)	Decision Summary (http://www.accessdata.fda.gov/cdrh_docs/reviews/DEN120015.pdf)
Infrascanner Model 1000	DEN100002	Classification Order (http://www.accessdata.fda.gov/cdrh_docs/pdf8/K080377.pdf)	Decision Summary (http://www.accessdata.fda.gov/cdrh_docs/reviews/K080377.pdf)
Zeltiq™ Dermal Cooling Device	DEN090002	Classification Order (http://www.accessdata.fda.gov/cdrh_docs/pdf8/K080521.pdf)	
AirPurge System	DEN080009	Classification Order (http://www.accessdata.fda.gov/cdrh_docs/pdf8/K080644.pdf)	Decision Summary (http://www.accessdata.fda.gov/cdrh_docs/reviews/K080644.pdf)
Bio-Seal Lung Biopsy Tract Plug System	DEN090007	Classification Order (http://www.accessdata.fda.gov/cdrh_docs/pdf8/K082438.pdf)	Decision Summary (http://www.accessdata.fda.gov/cdrh_docs/reviews/K082438.pdf)
Erchonia ML Scanner	DEN090008	Classification Order (http://www.accessdata.fda.gov/cdrh_docs/pdf8/K082609.pdf)	

http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm232269.htm

Conclusion

- Opportunities To Increase Regulatory Predictability
  - Expedited Access Pathway
    - PMA and DeNovo
  - Clinical Trials Program
    - Early Feasibility
    - Reduced time to full study approval
  - Direct DeNovo
    - Increase efficiency of review process