# FDA Submissions and Pre-Submissions: Pathways for Innovative, Safe and Effective Dental Medical Products

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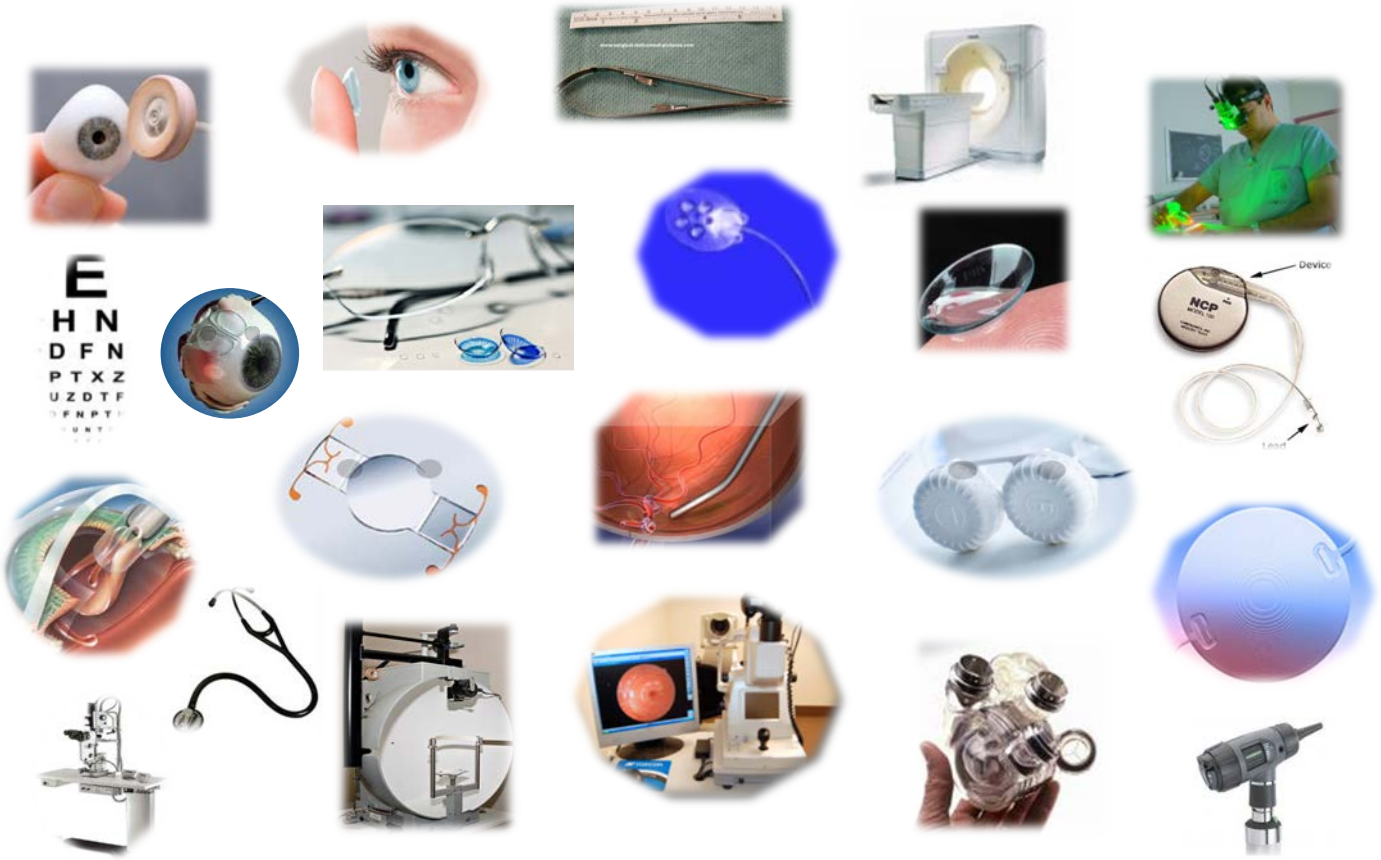
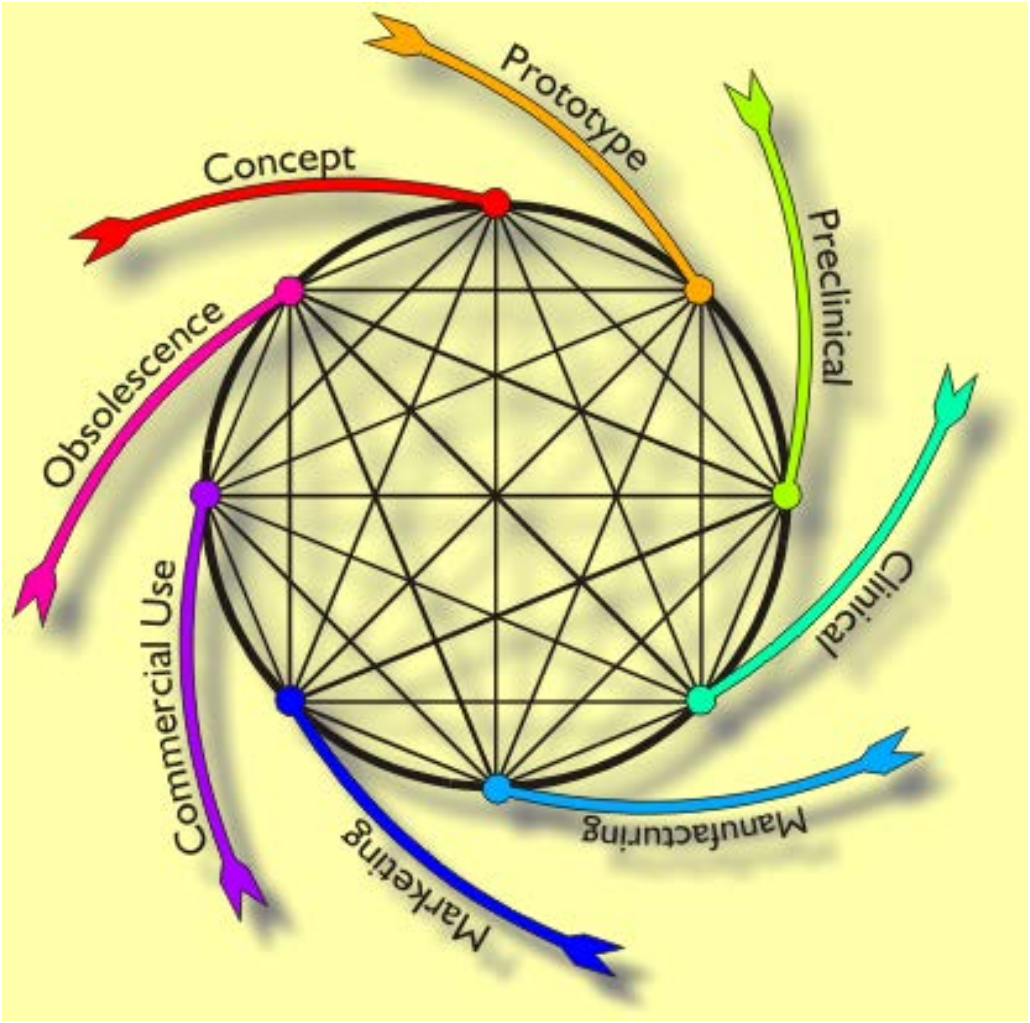
Center of Devices and Radiological Health
U.S. Food and Drug Administration

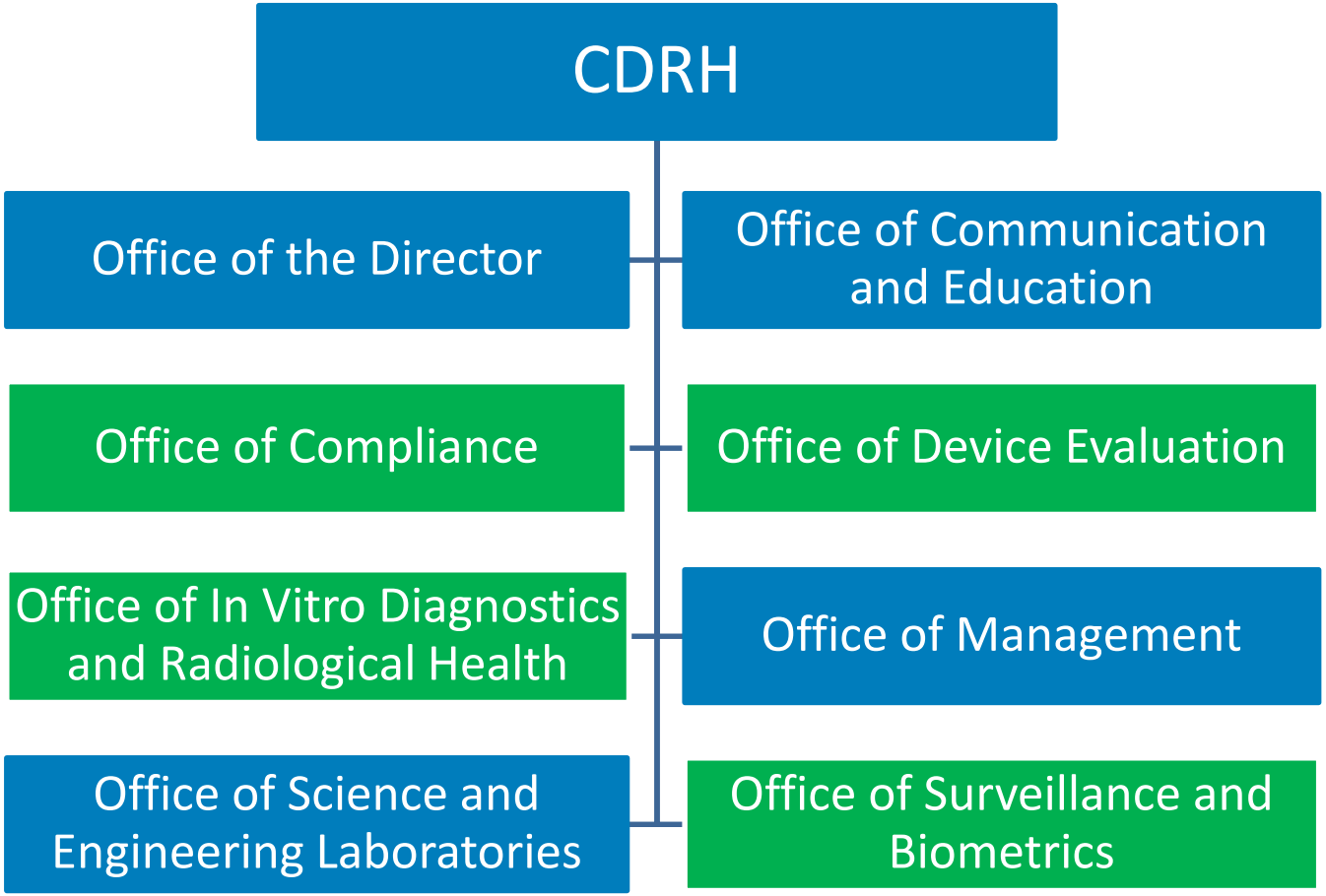
# Center for Devices and Radiological Health (CDRH) Regulates All Medical Devices



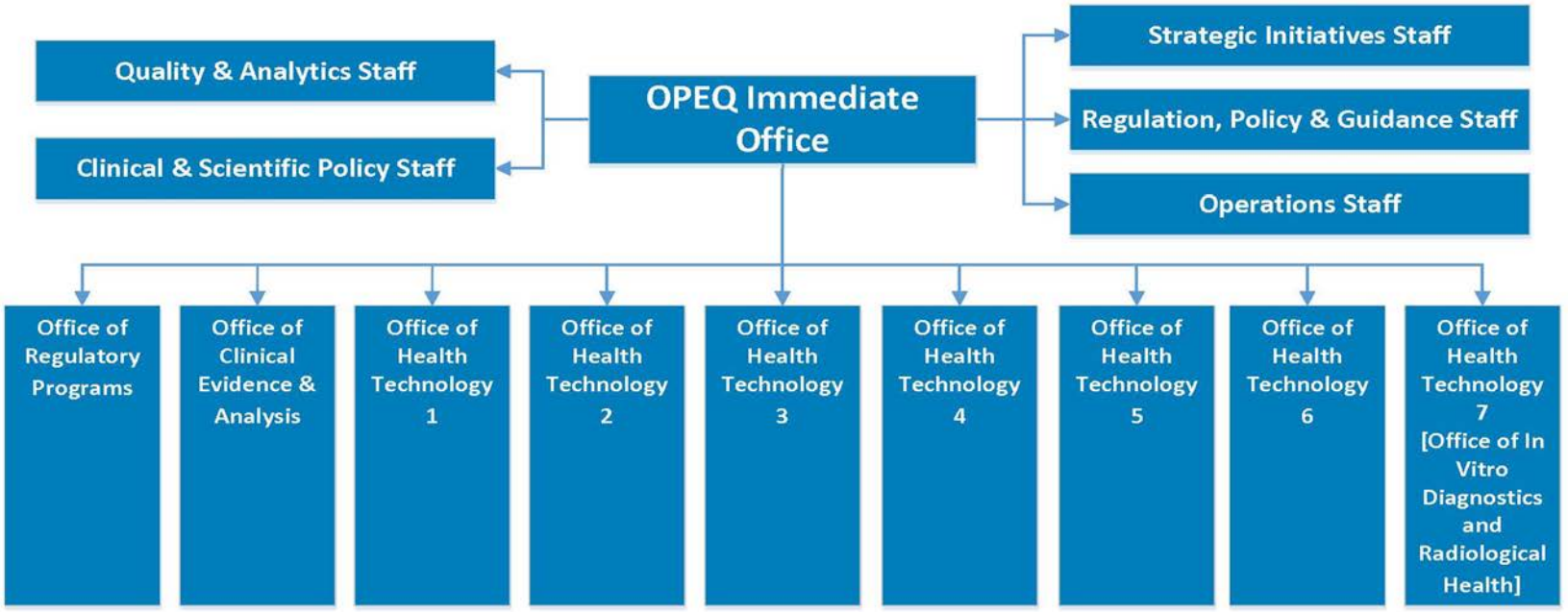
# Total Product Lifecycle



# Total Product Lifecycle (TPLC) Reorganization

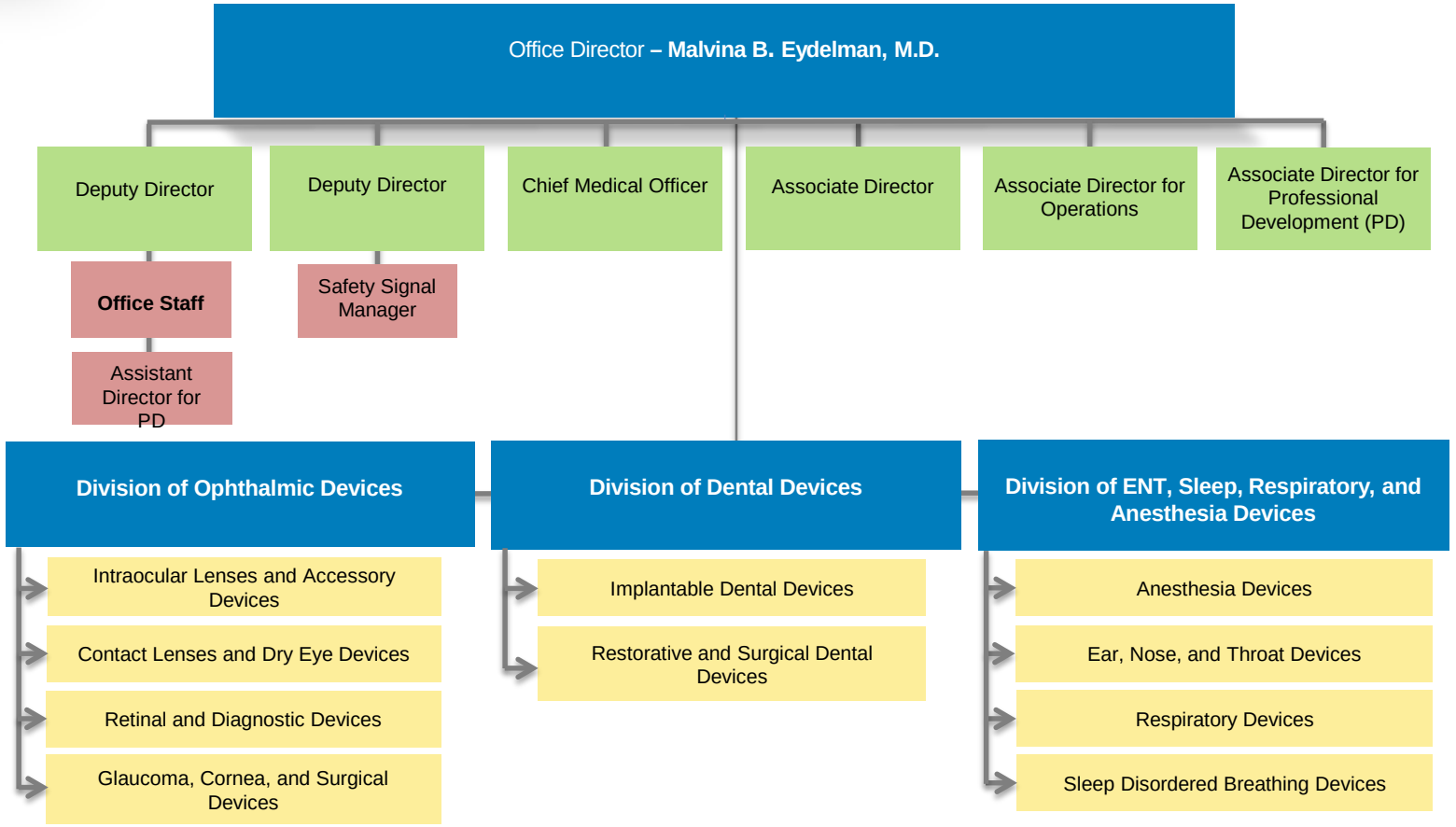


# Office of Product Evaluation and Quality (OPEQ)

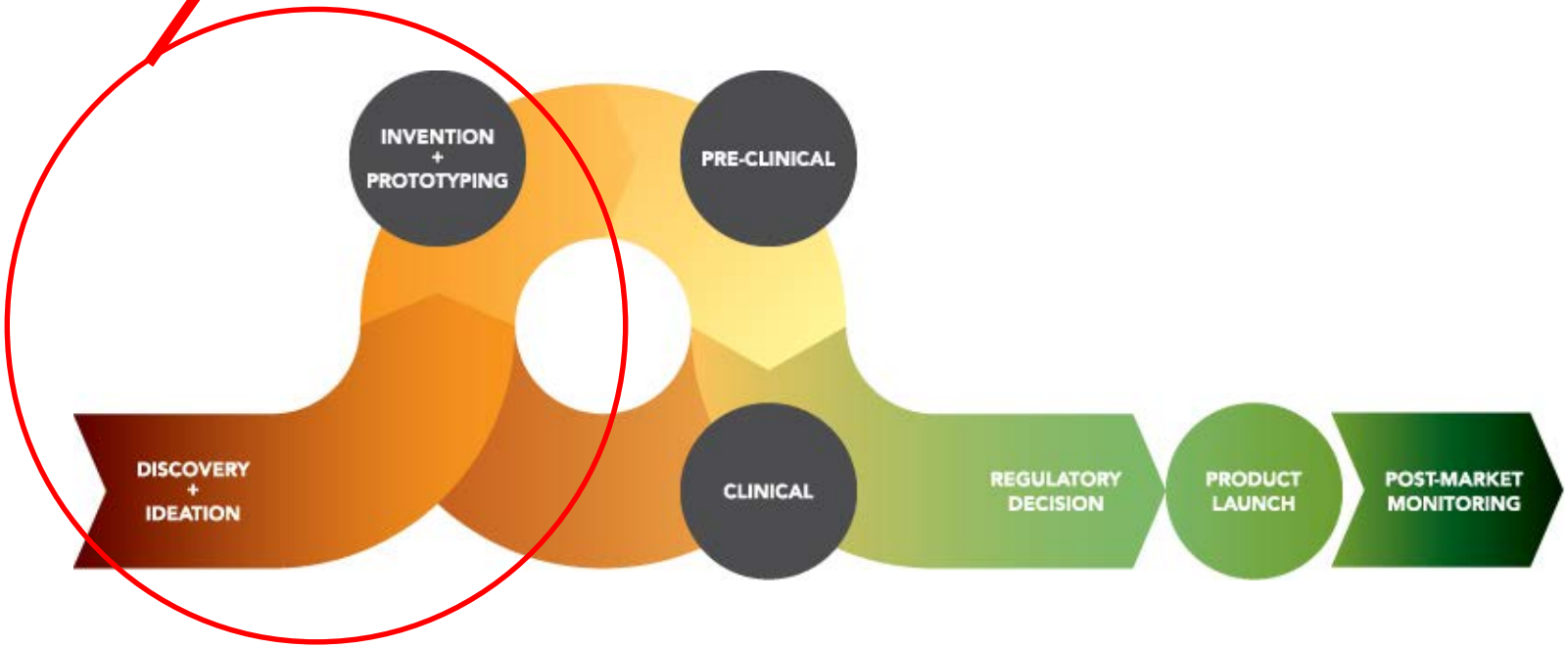


TPLC Pilot

# OFFICE OF OPHTHALMIC, DENTAL, ENT, SLEEP, RESPIRATORY AND ANESTHESIA DEVICES



- **Product Type /Classification (RFD)**
- **IFU (HUD)**
- **Summaries of Approvals/Clearances**
- **FDA Meeting / Q - sub**



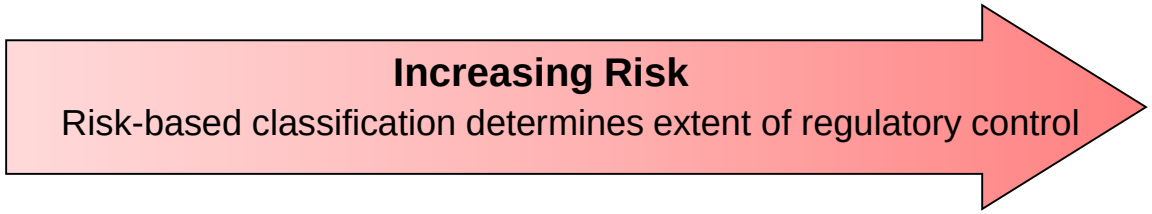
# Dental Products

- Biological Product
- Drug
- Device
- Combination Product

# It is a Medical Device if it:

- Diagnoses, Cures, Mitigates, Treats or Prevents a Disease or Condition, or
- Affects the Function or Structure or the Body, and
- Does Not Achieve Intended Use Through Chemical Action, and
- Is Not Metabolized

# Risk-Based Oversight of Medical Devices




**Class I**
- General Controls
- Most exempt

**Class II**
- General controls
- Special controls
- Typically 510(k)

**Class III**
- General controls
- Premarket approval (PMA)

General Controls
- Prohibition of adulteration, misbranding
- Registration of Facilities
- Electronic Device Listing
- Premarket Notification [510(k)] (unless exempt)
- Quality Systems
- Labeling
- Medical Device Reporting (MDR)

Special Controls (addressing Risk)
- Guidelines (e.g., Glove Manual)
- Mandatory Performance Standard
- Recommendations or Other Actions
- Special Labeling (e.g., 882.5970, Cranial Orthosis)

# FDA Resources

- Device Classification

  www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/default.htm

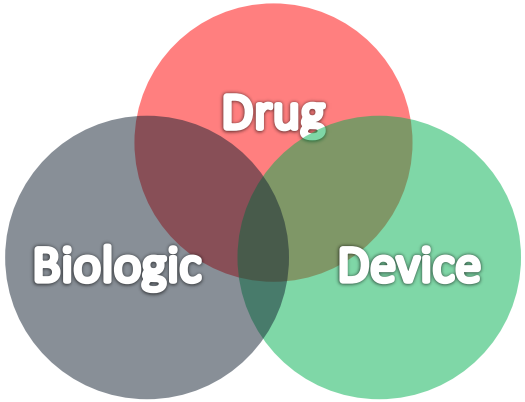
- Request for Information (513(g))
  - Means for obtaining the agency's views about the classification/regulatory requirements that may be applicable to a particular device

  http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm209841.htm

# What is a Combination Product?

Combinations of 2 or more DIFFERENT products:

- Drug + Device
- Device + Biologic
- Drug + Biologic
- Drug + Device + Biologic



# How do I get a Classification / Jurisdiction Assignment?

- Informal guidance:
  - Email: combination@fda.gov
  - Simple issues, uncertainty, process concerns
  - Determine whether an RFD is needed
  - Non-binding; can submit RFD if disagree with informal guidance
- Formal process:
  - Submit a Request for Designation (RFD)
  - Formal, binding determination – **60** days
  - Complex issues or dispute / uncertainty
  - Requirements in 21 CFR 3.7

# When to submit an RFD or informal inquiry?

Submit an RFD or informal inquiry **BEFORE** any submission (i.e., pre-submission / marketing submission)

<u>Why?</u>

FDA may stop the review clock while a determination is being made (21 CFR 3.10)

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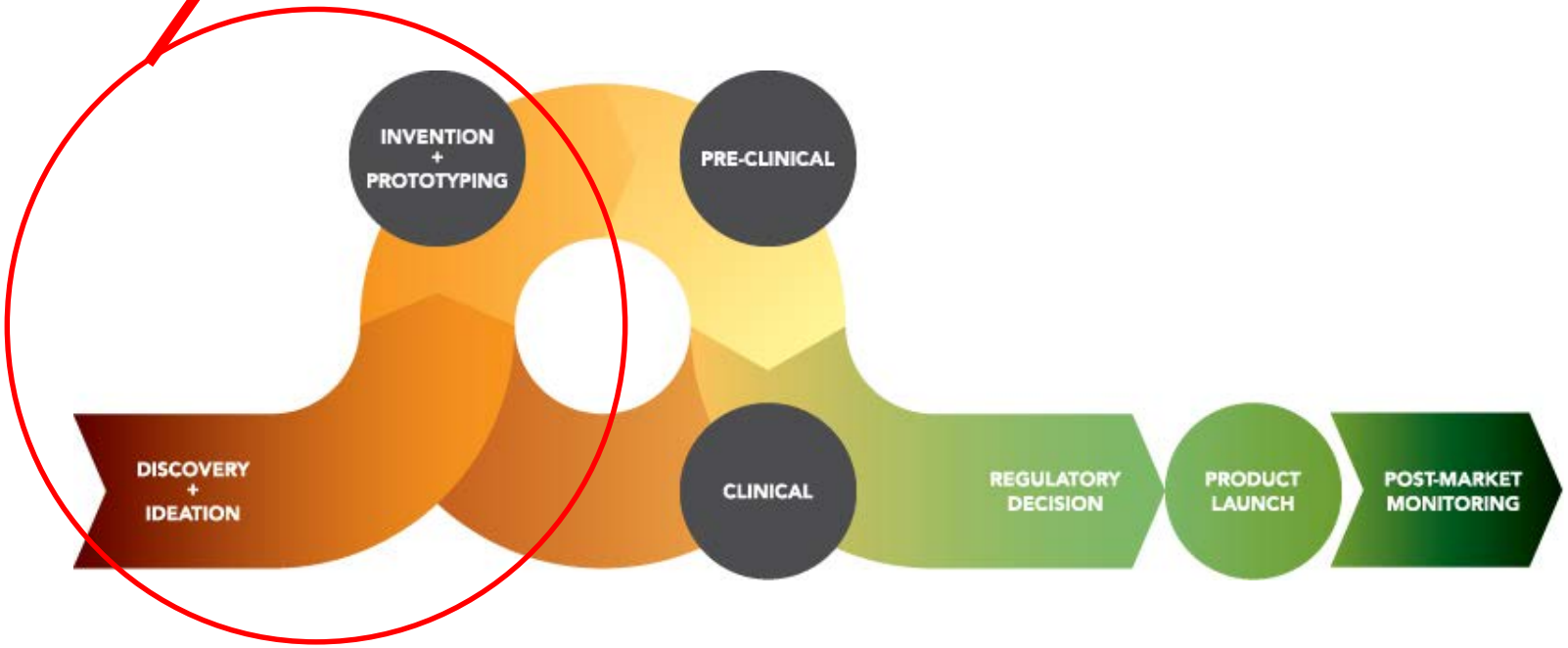


# Indication for Use (IFU)

- General description of the disease or condition the device will diagnose, treat, prevent, cure or mitigate, including a description of the patient population for which the device is intended [21 CFR 814.20]
  - Clinical study design depends on the IFU

# HUD Definition

A Humanitarian Use Device (HUD) is a medical device intended to benefit patients in treatment or diagnosis of a disease or condition that affects or is ~~manifested in fewer than 4,000~~ individuals per year in the United States. **not more than 8,000**

**21st Century Cures Act**

**Amendment to regulation published June 7, 2017**

# HDE Approval

- **Safety**
  - does not pose unreasonable risk of illness or injury
  - same threshold as PMA devices

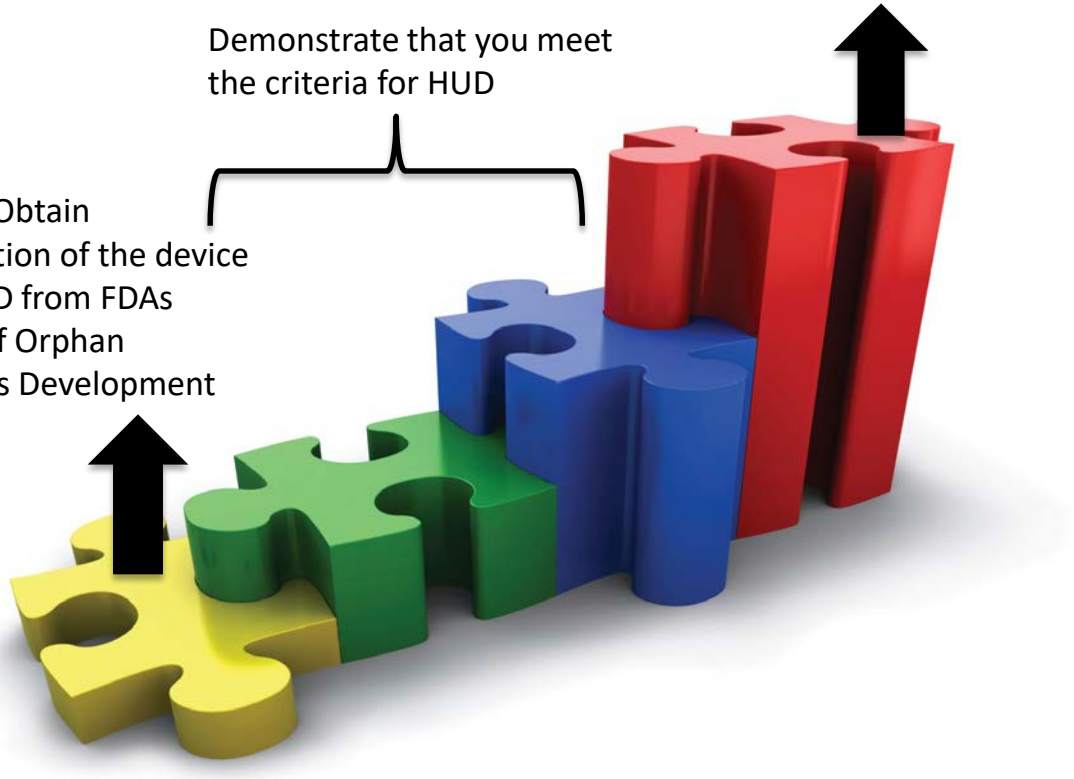
- **Probable benefit**
  - outweighs the risks of using the device, taking into account the probable risks and benefits of alternative therapies
  - exempt from effectiveness
  - different from PMA devices (reasonable assurance of effectiveness)

# HDE Application Process

**Step 2**: After HUD is granted, submit an HDE application to CDRH/CBER

Demonstrate that you meet the criteria for HUD

**Step 1**: Obtain designation of the device as a HUD from FDAs Office of Orphan Products Development (OOPD)



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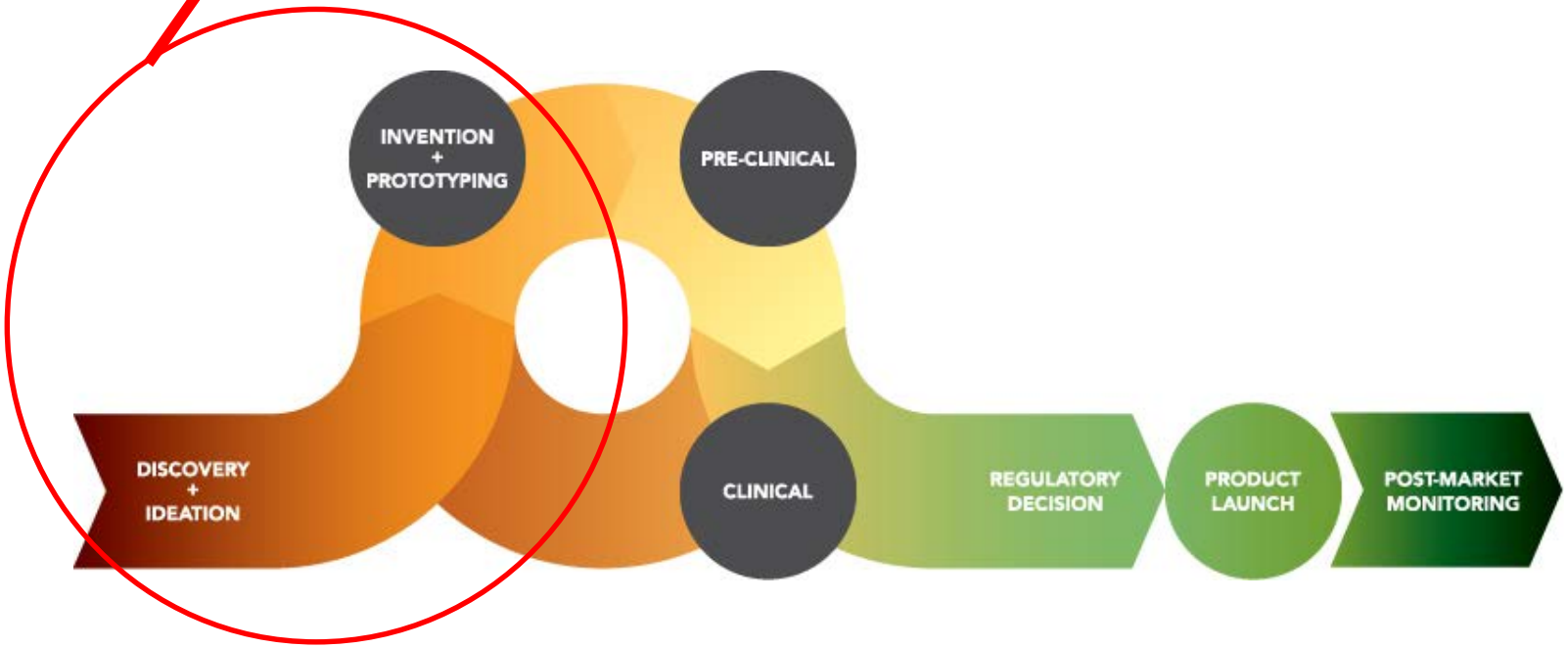

# FDA Resources: Summaries

- Summary of Safety and Effectiveness
  - http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm
- Summary of Safety and Probable Benefit
  - http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm
- 510(k) Summaries
  - http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/510kClearances/default.htm

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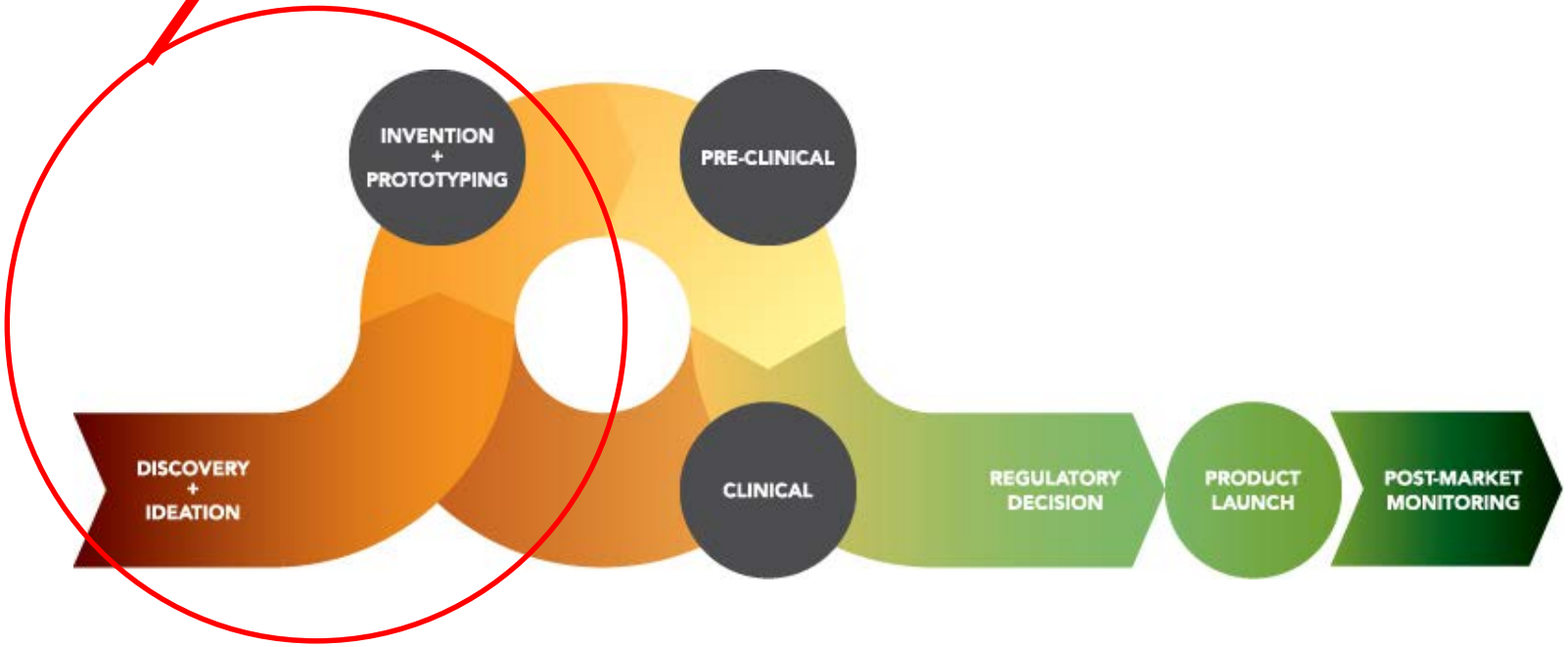


# Q-submission Program

- The Q-Submission Program provides a mechanism to request interactions with the FDA related to medical device submissions
- Q-sub guidance: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf.
- Feedback mechanisms addressed in guidance:
  - Pre-Submissions
  - Informational Meetings
  - Study Risk Determinations
  - Formal Early Collaboration Meetings
  - Submission Issue Requests
  - Day 100 Meetings for PMA Applicants

# Q-Sub type: Pre-Submissions

- Facilitates device development / innovation by providing FDA feedback on proposed:
  - Preclinical testing plan
  - Animal Study design
  - Clinical trial design (e.g., control group, endpoints, inclusion/exclusion criteria, statistical analysis plan)
  - Proposed indications for use
- Provides an opportunity for a meeting/teleconference with the FDA
  - Within 75-90 calendar days
  - No user fee
  - Written email feedback is also an option

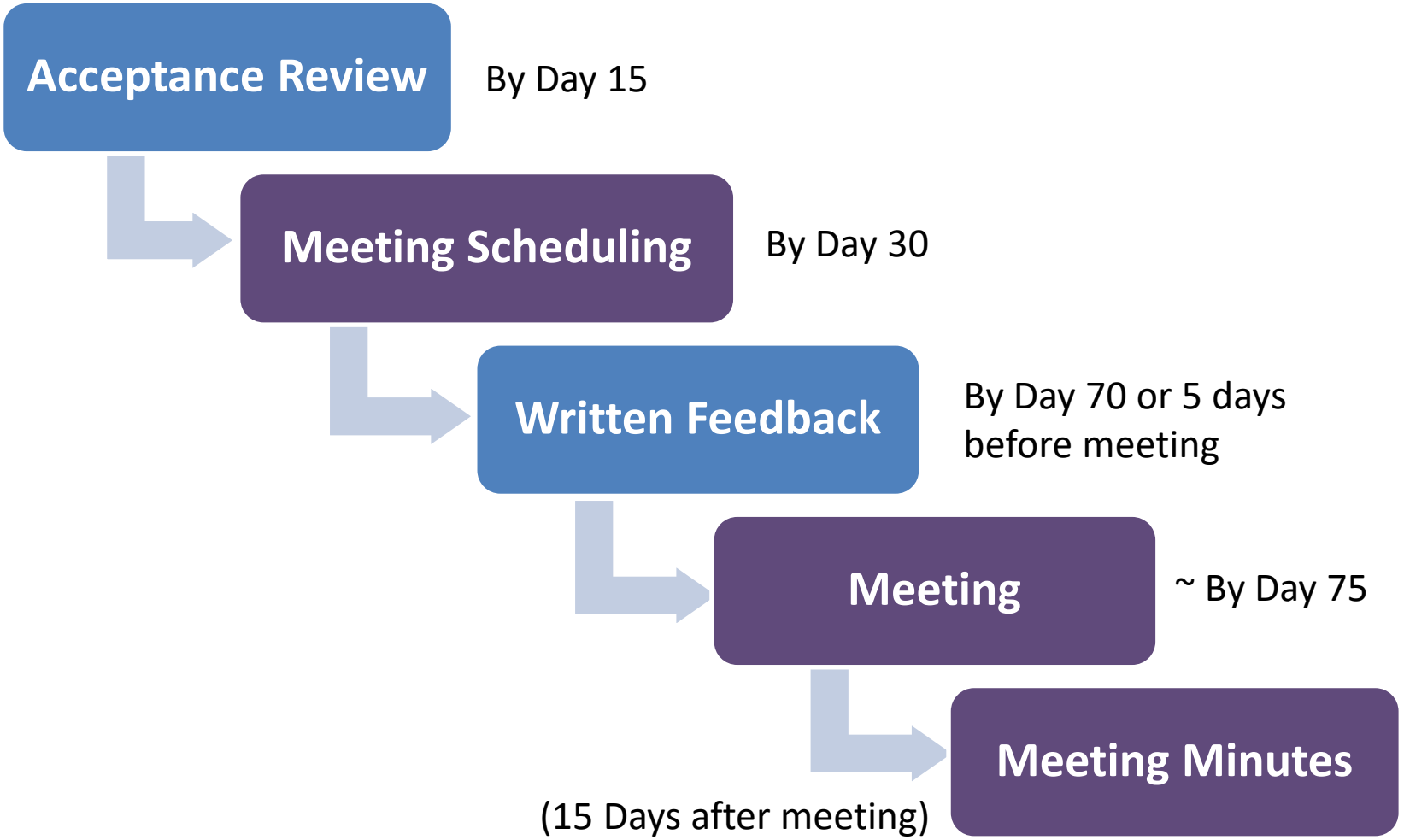
# Key Information in a Pre-submission

- Detailed Device Description
- Proposed Intended Use/Indications for Use
- Summary of Previous Discussions or Pre-Submissions or Submissions Regarding the Same Device
- Specific Questions for FDA Feedback
- Preferred method to receive FDA Feedback
- *Meeting Format, Preferred Dates and Times, Planned Attendees, and Audiovisual Equipment Needs, if meeting or teleconference is requested*

# Pre-Submission Reminders

- FDA review of a Pre-Sub does not guarantee approval or clearance of future premarket submissions
- FDA intends to stand behind their feedback
- Sponsors should reference Pre-Sub feedback received in subsequent submissions

# Pre-Submission Process



# Preparing your Pre-Submission

**Do**

- While conducting research consider when initial interactions with FDA would be helpful
- Include only relevant information in your package
- Include specific questions you wish to ask the FDA

**Don't**

- Have broad questions
- Have too many questions
- Expect a pre-review

# The Meeting

**Do**

- Use written feedback to refine your agenda
- Use the meeting time wisely
- Ensure the right people are at the meeting

**Don't**

- Feel obligated to hold meeting if written feedback meets needs
- Don't provide significant new information after written feedback is sent

# After the Meeting

**Do**

- Do submit meeting minutes within 15 days
- Check in if significant time has elapsed since receiving feedback
- Include summary of Pre-Sub discussions in subsequent pre-market submissions and how you addressed feedback

**Don't**

- Include new discussion topics in the meeting minutes

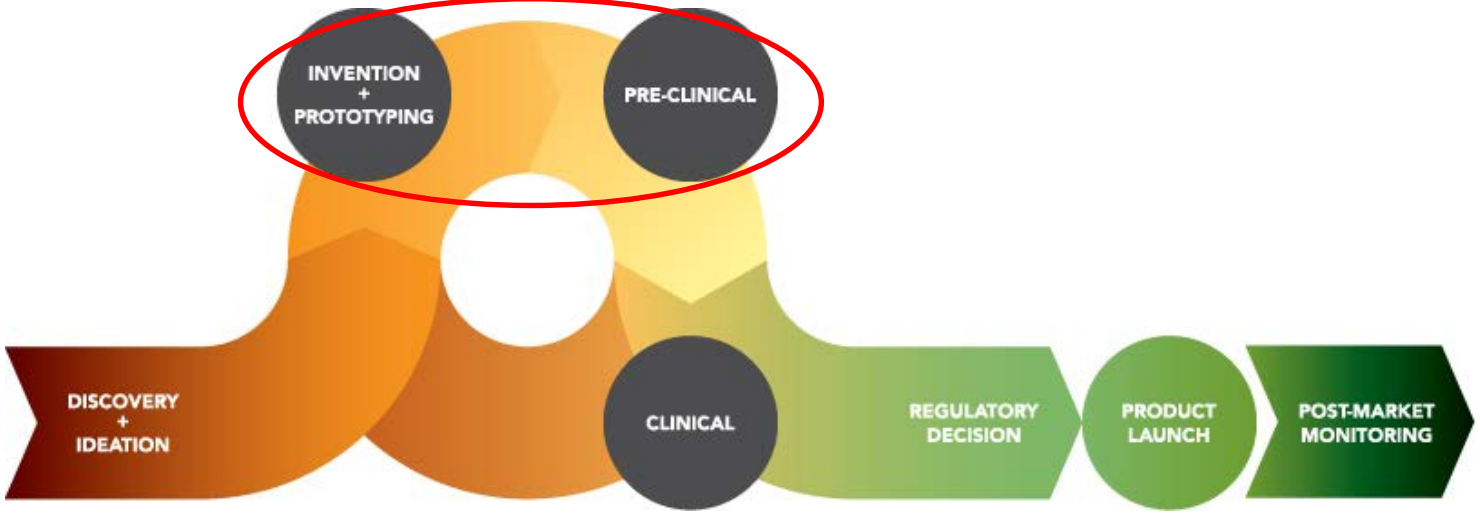
# Q-Sub Type: Informational Meeting

- A meeting with the intent to share information with FDA without the expectation of receiving feedback
- FDA is in listening mode
- Timeframe: 90 days, resource permitting
- Provide an overview of ongoing device development
- Familiarize reviewers about new device with significant differences in technology from currently available devices

# Q-Sub Type: Study Risk Determination

- FDA will help sponsors, clinical investigators, or institutional review boards (IRB) make a study risk determination for not exempt studies
- FDA will provide a study determination letter
- Detailed Device Description and how it will be used in the study
- Clinical Study Protocol
- Description of the study population

- Q-Sub
- Guidance / Standards
- EFS
- MDDT



# FDA Guidance

- Guidance describes FDA's interpretation of, or policy on, a regulatory issue
  - Submissions
  - Labeling
  - Manufacturing
- Guidance for Clinical Studies
  - Regulatory Pathway
  - Study Design
  - Data Analysis
- Check availability of FDA Guidance

  www.fda.gov/cdrh/guidance.html

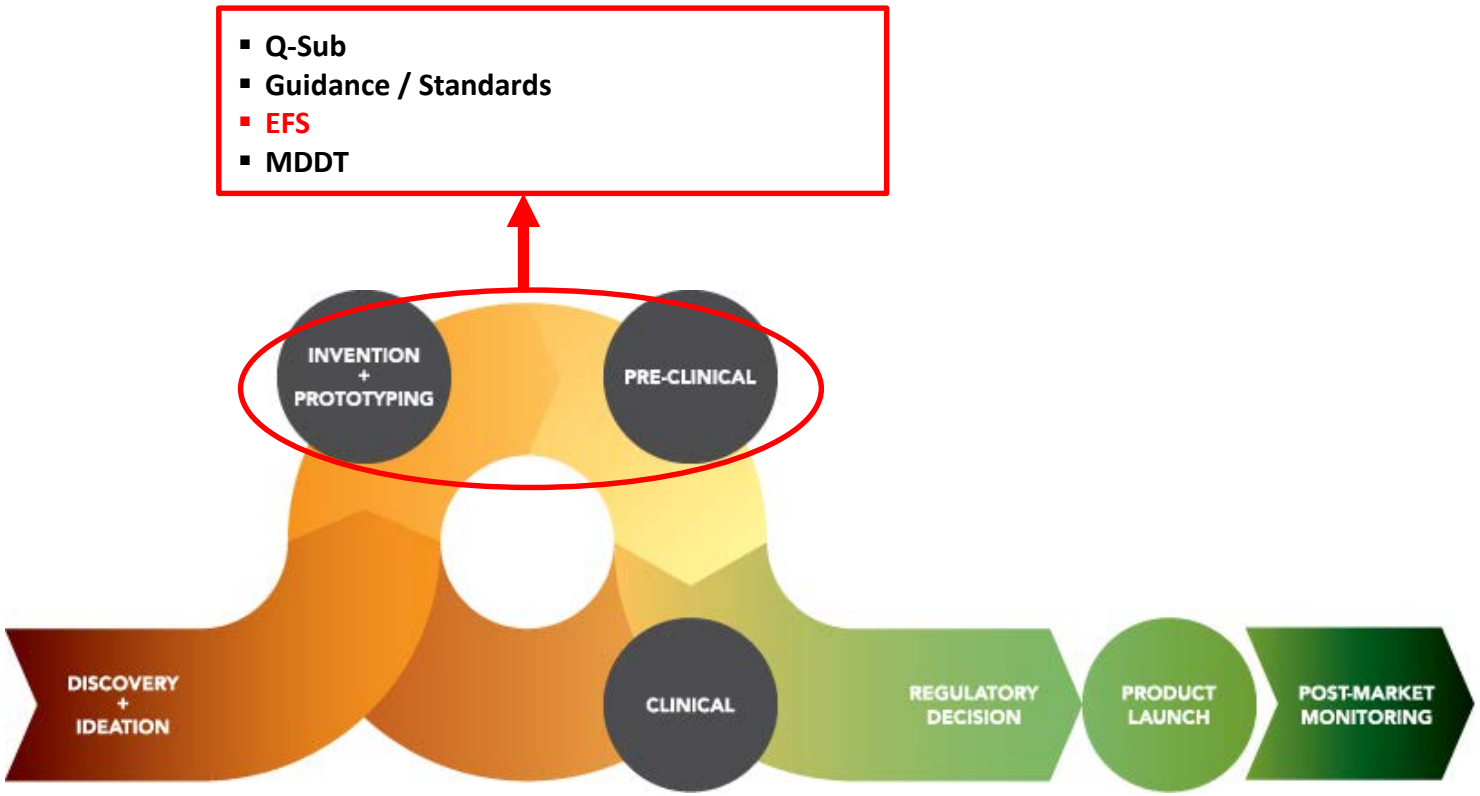
# Recognized Standards

- A consensus standard which FDA has recognized for use in satisfying a premarket submission requirement

- Outlines:
  - Parameters needed for evaluation of a specific device
  - Pre-clinical testing needed prior to human testing
  - Recommended clinical trial

- Check recognized Standards

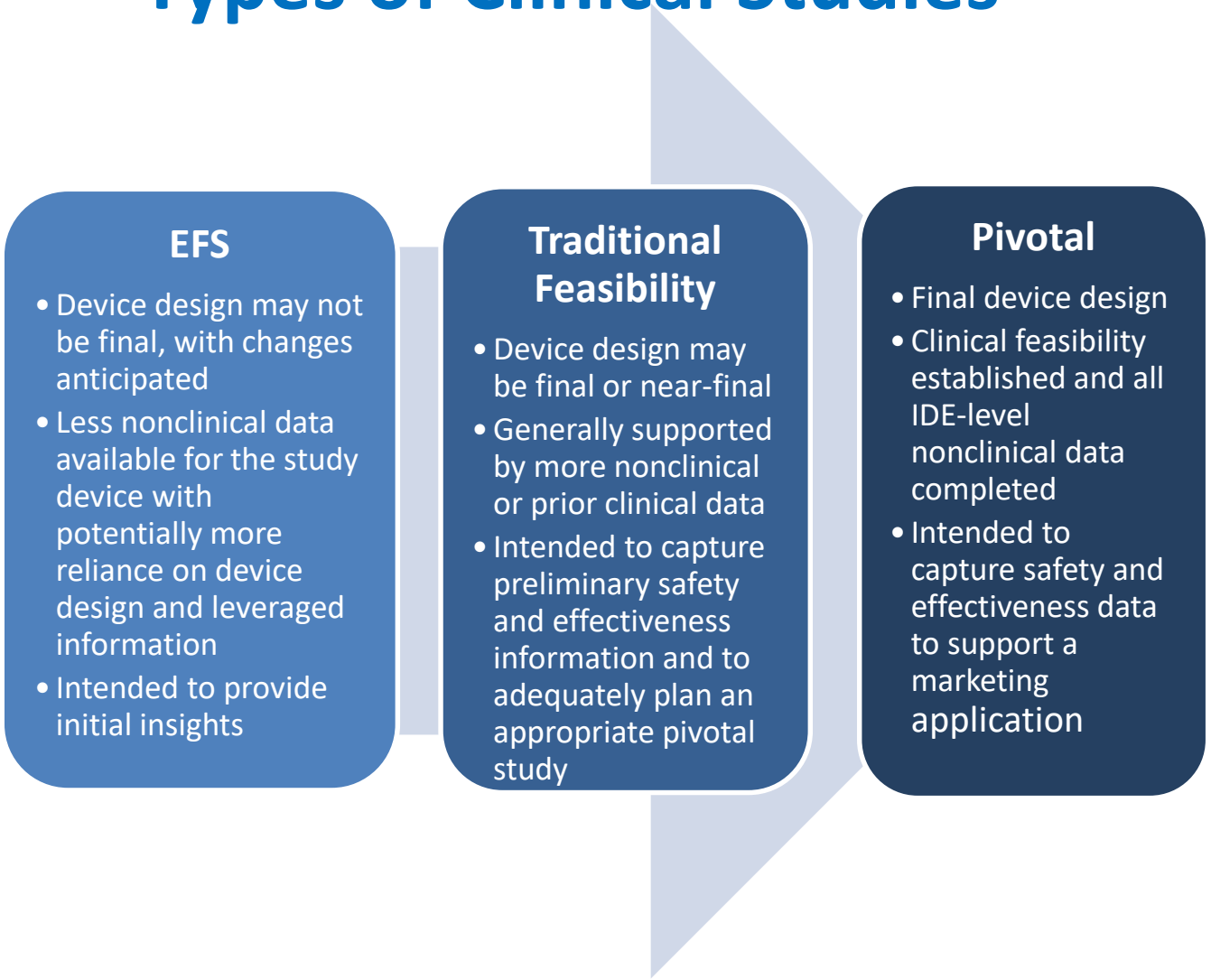
www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm


Q-Sub
Guidance / Standards
EFS
MDDT
INVENTION + PROTOTYPING
PRE-CLINICAL
DISCOVERY + IDEATION
CLINICAL
REGULATORY DECISION
PRODUCT LAUNCH
POST-MARKET MONITORING

# Early Feasibility Study Program

- Goal
  - Encouraging innovation in the US by supporting the study of new technology
- Guidance
  - http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM279103.pdf
- Key Principle
  - Approval of an early feasibility study may be based on less nonclinical data than would be needed to support the initiation of a larger clinical study on a more final device design

# Types of Clinical Studies



# When is a Good Time to Talk to FDA About an EFS?

After…

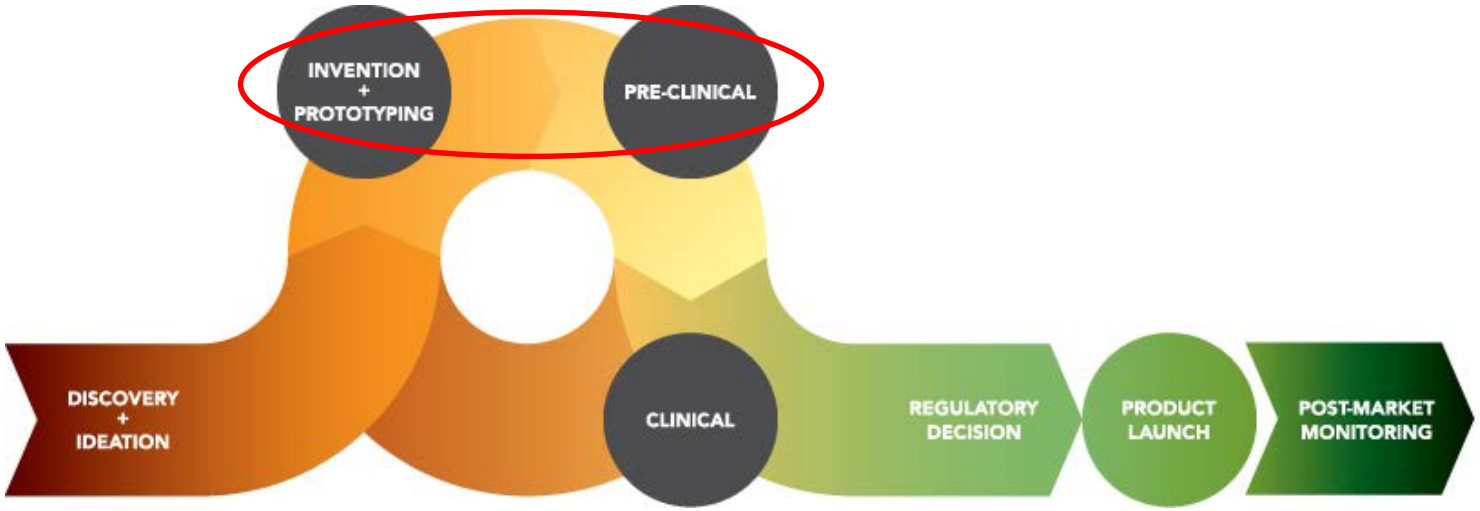
- You have established your general device design, intended use and what information you would like to gather from the EFS

Before…

- Expensive and time consuming nonclinical testing has been started

<u>Communication with FDA throughout the development process is recommended to optimize submission efficiency</u>

- Q-Sub
- Guidance / Standards
- EFS
- MDDT



# Medical Device Development Tool (MDDT)

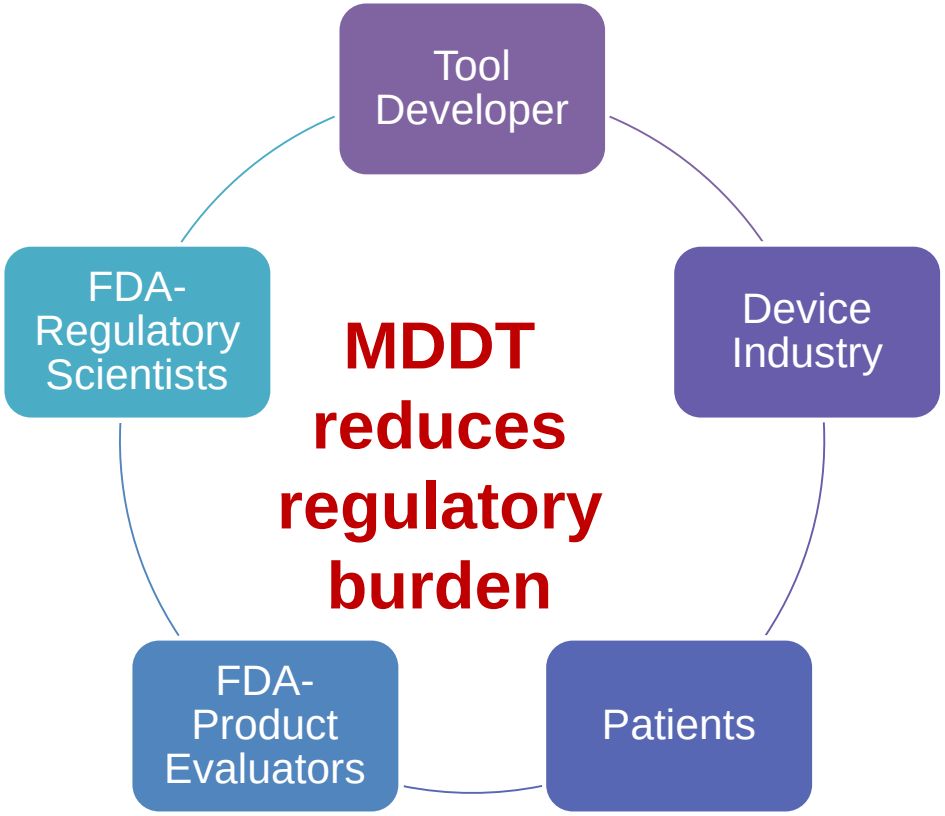
- **Medical Device Development Tool (MDDT)** is a method, material, or measurement used to assess effectiveness, safety, or performance of a medical device
  - MDDT Categories: Clinical Outcome Assessment (COA), Biomarker Test (BT), Nonclinical Assessment Model (NAM)
  - A MDDT is scientifically validated and qualified for a specific ***Context Of Use*** (COU) on the way the MDDT should be used
  - Qualification is a FDA conclusion that within the COU a MDDT has a specific interpretation and application in medical device development and regulatory review

Website:
http://www.fda.gov/MedicalDevices/ScienceandResearch/MedicalDeviceDevelopmentToolsMDDT/default.htm

Questions? email: MDDT@fda.hhs.gov

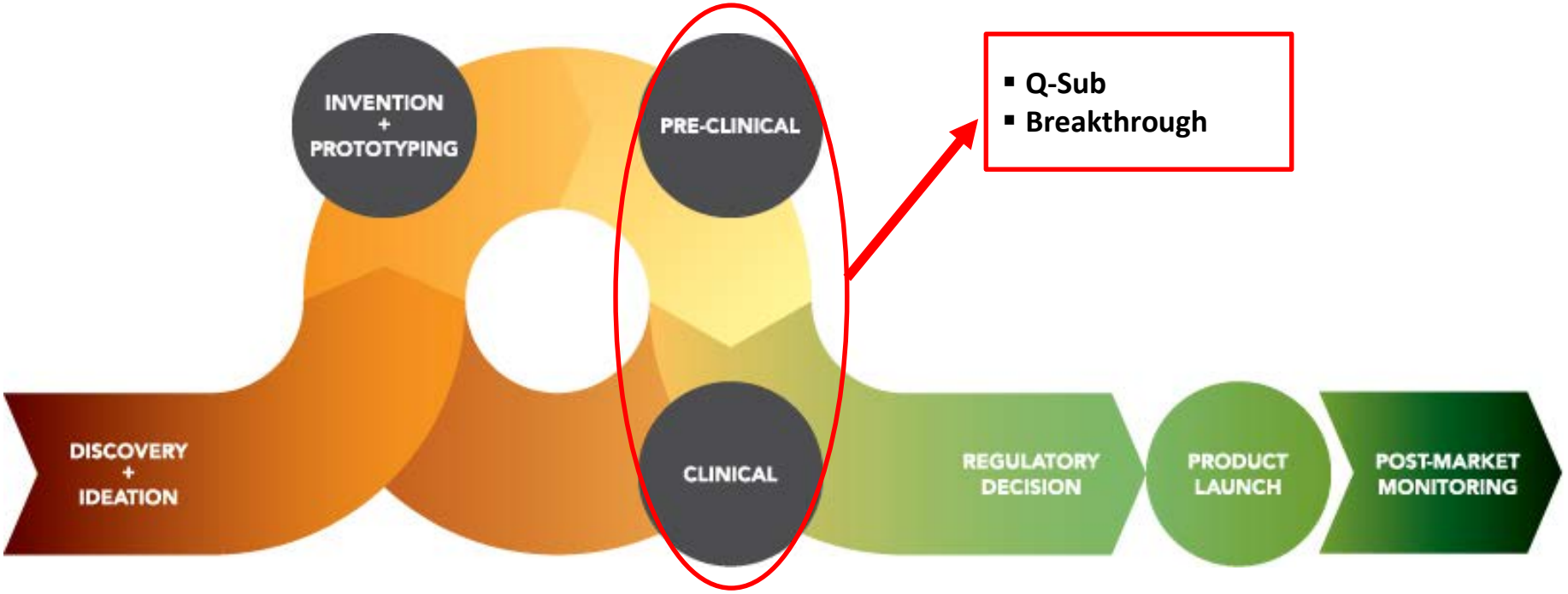
# Medical Device Development Tool Program


***Promotes Efficient Medical Device Development***




## *Benefit of Qualifying Tools*

- Fosters innovation
- Encourages collaboration
- Reduces resource expenditure
- Qualified MDDT applied in multiple device submissions
- Promotes efficiency in CDRH regulatory review resources
- Minimizes uncertainty in regulatory review process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POST-MARKET MONITORING
Q-Sub
Breakthrough

# Breakthrough Device Pathway (Formerly Expedited Access Pathway)

**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.**

- Interactive & Timely Communication
- Pre-Postmarket Balance
- Flexible Clinical Study Design
- Senior Management Engagement
- Priority Review
- https://www.fda.gov/media/108135/download

# Criteria for Breakthrough Devices

- More effective treatment or diagnosis of life threatening or irreversibly debilitating disease

+

<u>At least one of the following:</u>

- Represents breakthrough technology
- No approved or cleared alternatives exist
- Offers significant advantages over existing approved/cleared alternatives
- Availability is in the best interest of patients (e.g., addresses an unmet medical need)

# Benefits of Breakthrough Device Designation

- Interactive and timely communication during development & review
  - Between submissions and during open submission review
  - Review team support
  - Senior management engagement
- Prioritized review design
- Efficient and flexible clinical study
- Enhanced opportunity for pre/ post-market balance of data collection for PMA devices
- Opportunity for reduced manufacturing information in a PMA

# Breakthrough Device Process

**Designation Request Q-Submission**

- Applicant provides device description, proposed indication, rationale for meeting statutory eligibility criteria
- 60 day review clock

**Follow On Q-Submissions**

- Data Development Plan collaboration (optional)
- Requests for feedback similar to Pre-Submissions (highly interactive, prioritized review)
- Regular status updates in between submissions

**IDEs and Marketing Submissions for Granted Breakthrough Devices**

- Prioritized review, senior management involvement
- Potential to accept greater uncertainty for approval with the possibility of post-market data component


Questions?


THANK
YOU