

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

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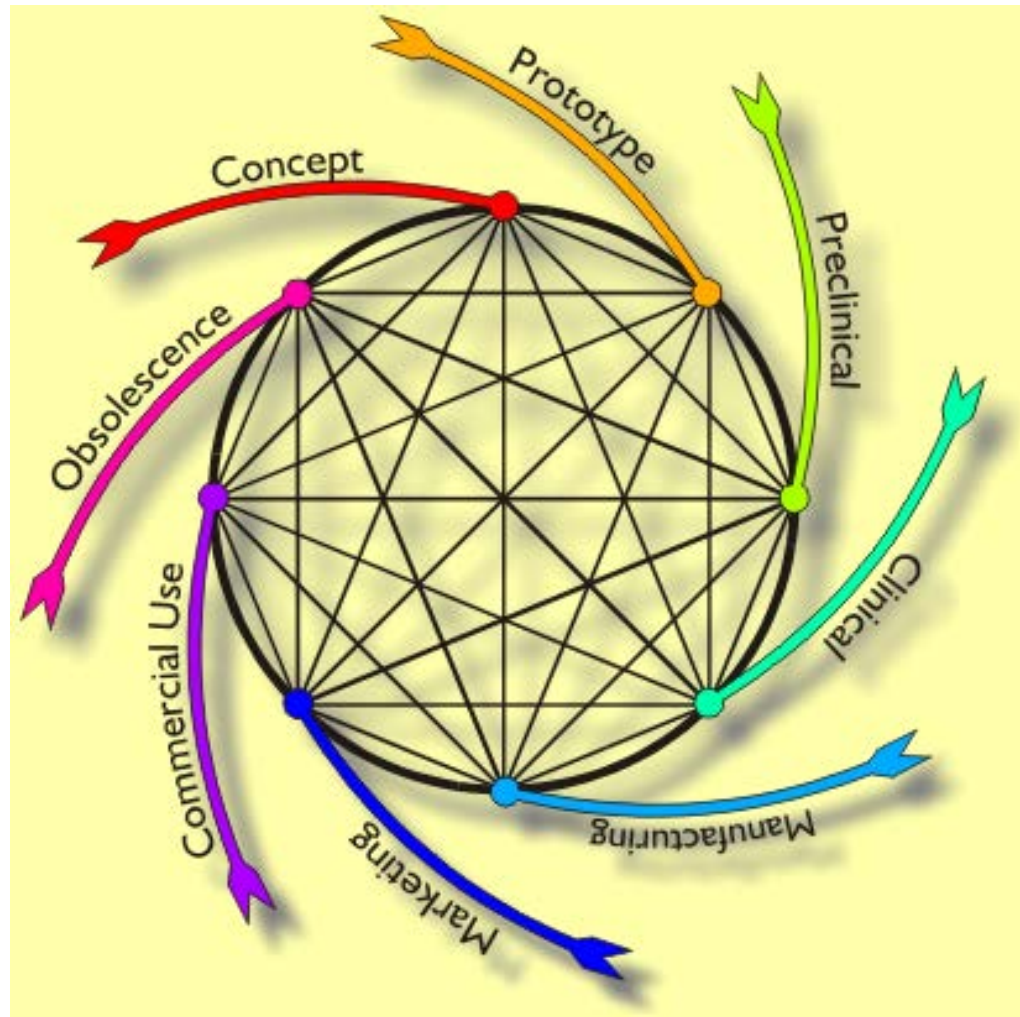
Acting Director
Division of Dental Devices

Assistant Director
Division of ENT, Sleep, Respiratory, Anesthesia Devices

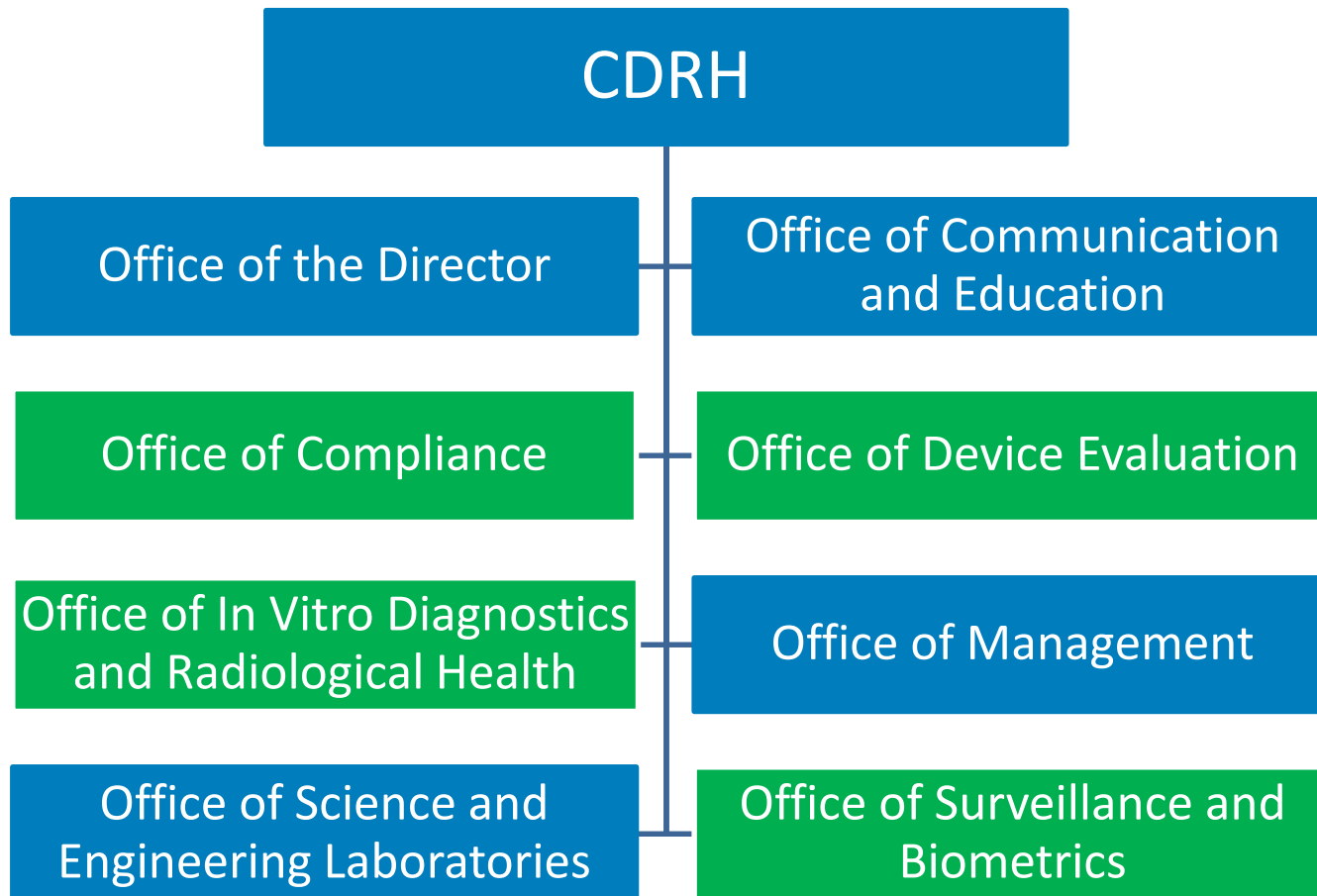
Center of Devices and Radiological Health
U.S. Food and Drug Administration



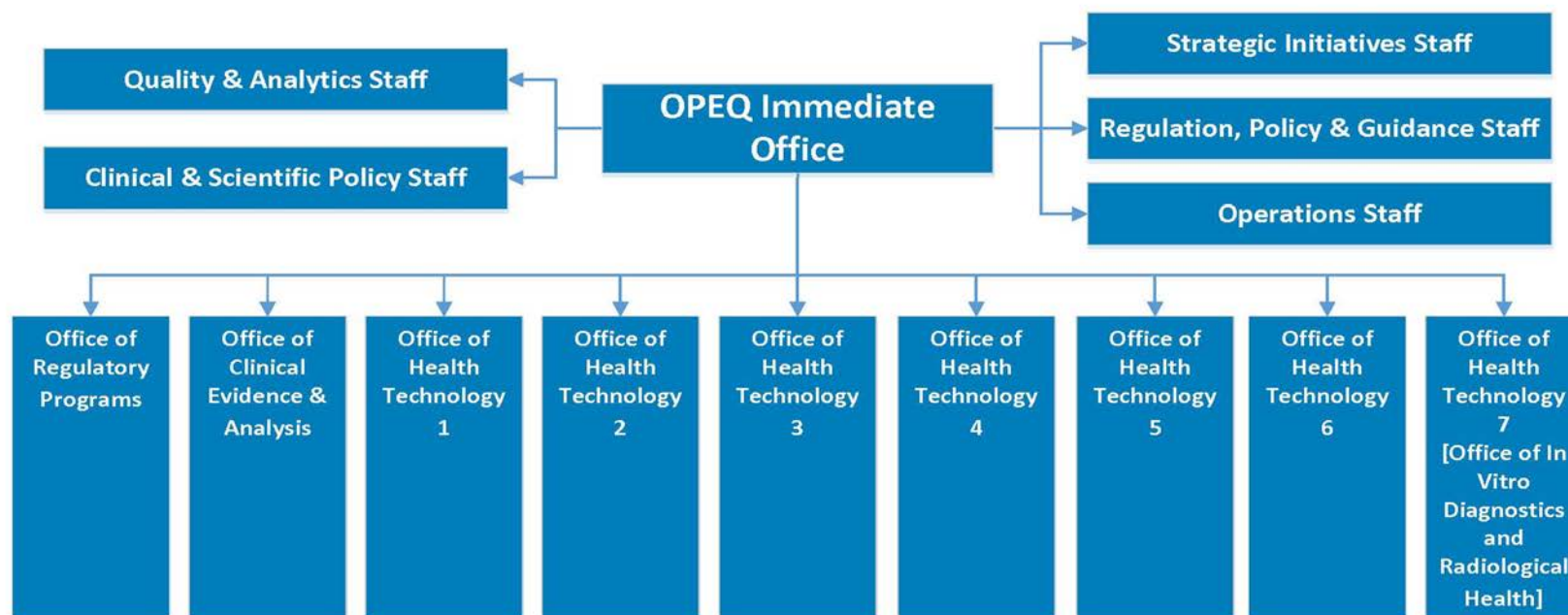
Total Product Lifecycle

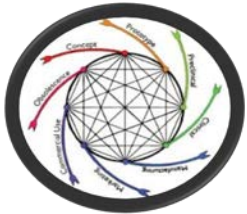


Total Product Lifecycle (TPLC) Reorganization

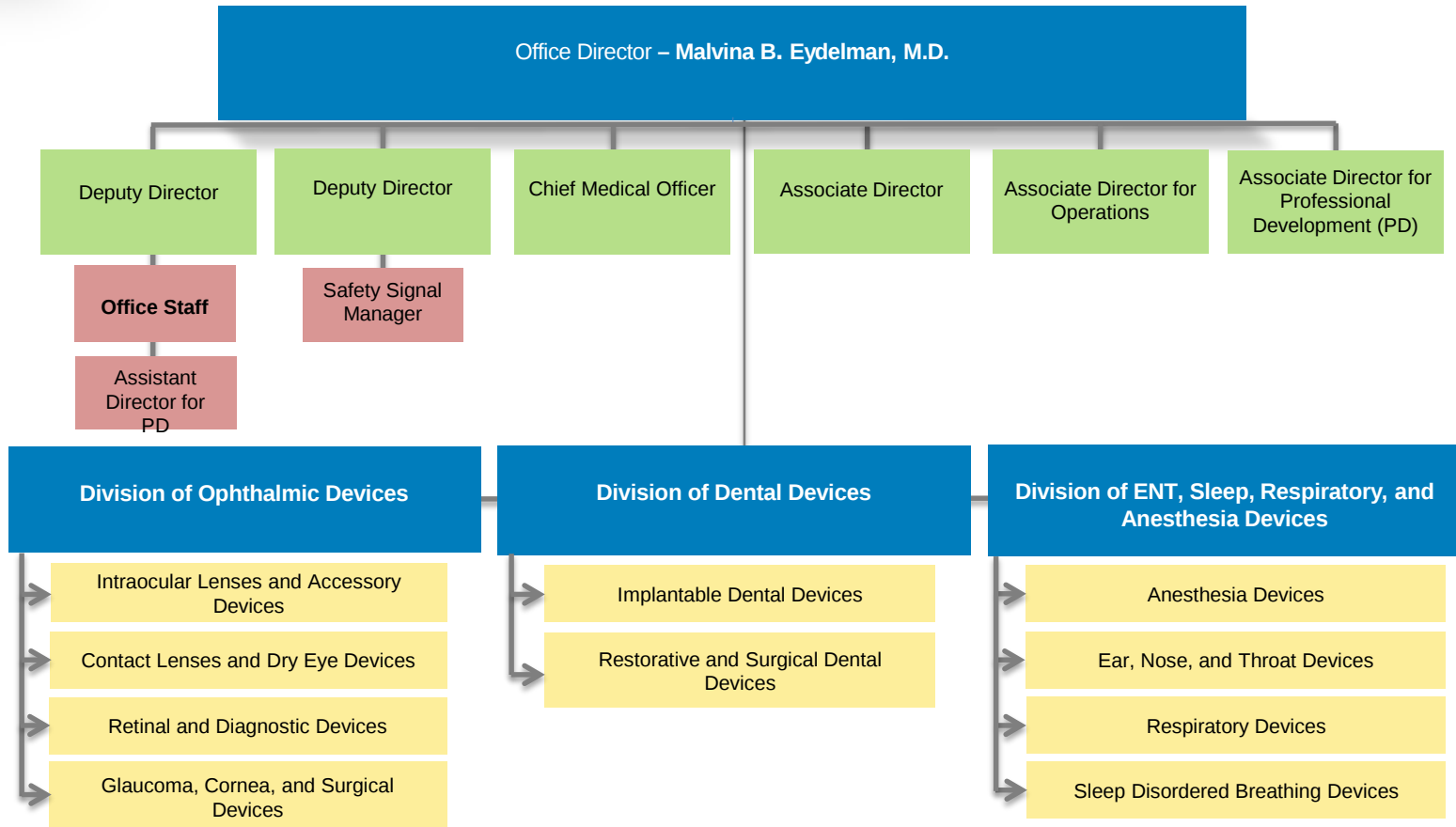


Office of Product Evaluation and Quality (OPEQ)

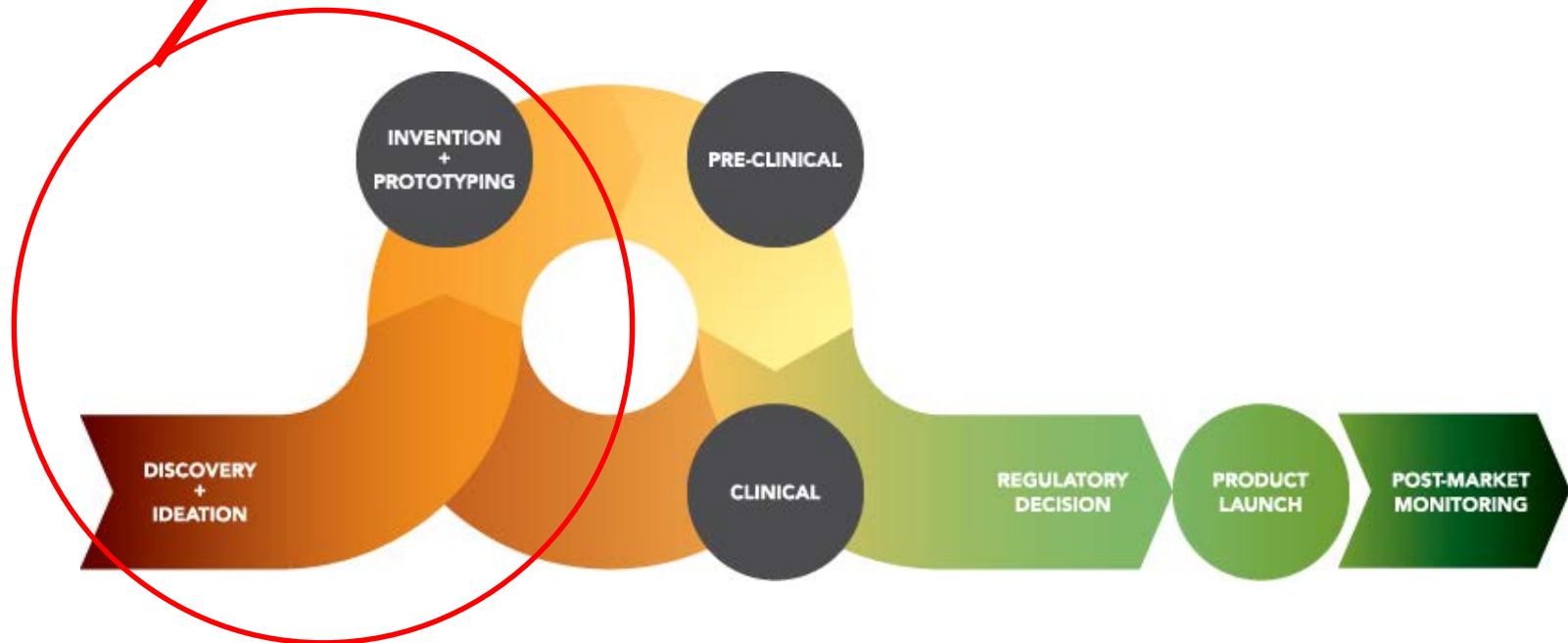




OFFICE OF OPHTHALMIC, DENTAL, ENT, SLEEP, RESPIRATORY AND ANESTHESIA DEVICES



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

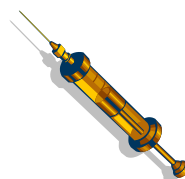


Dental Products

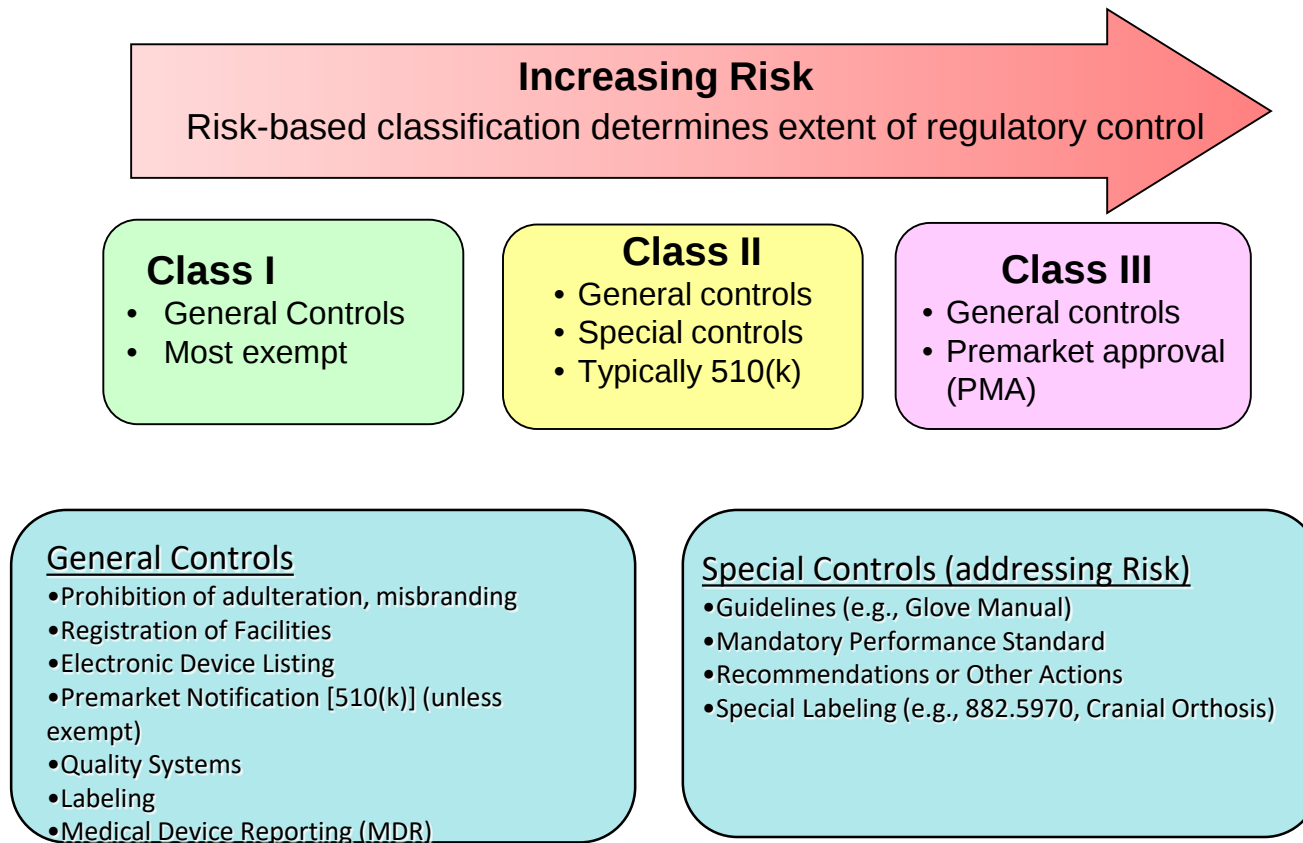
- Biological Product
- Drug
- Device
- Combination Product

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



FDA Resources

- Device Classification

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

- Request for Information (513(g))

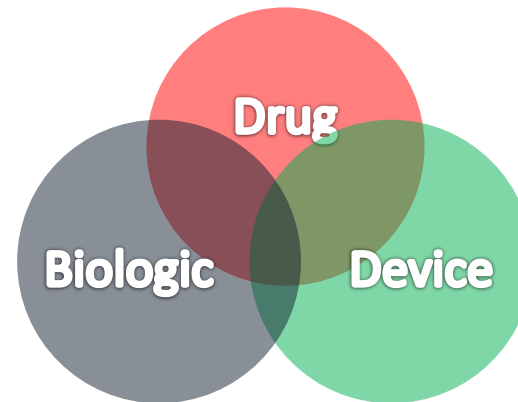
➤ Means for obtaining the agency's views about the classification/regulatory requirements that may be applicable to a particular device

<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?

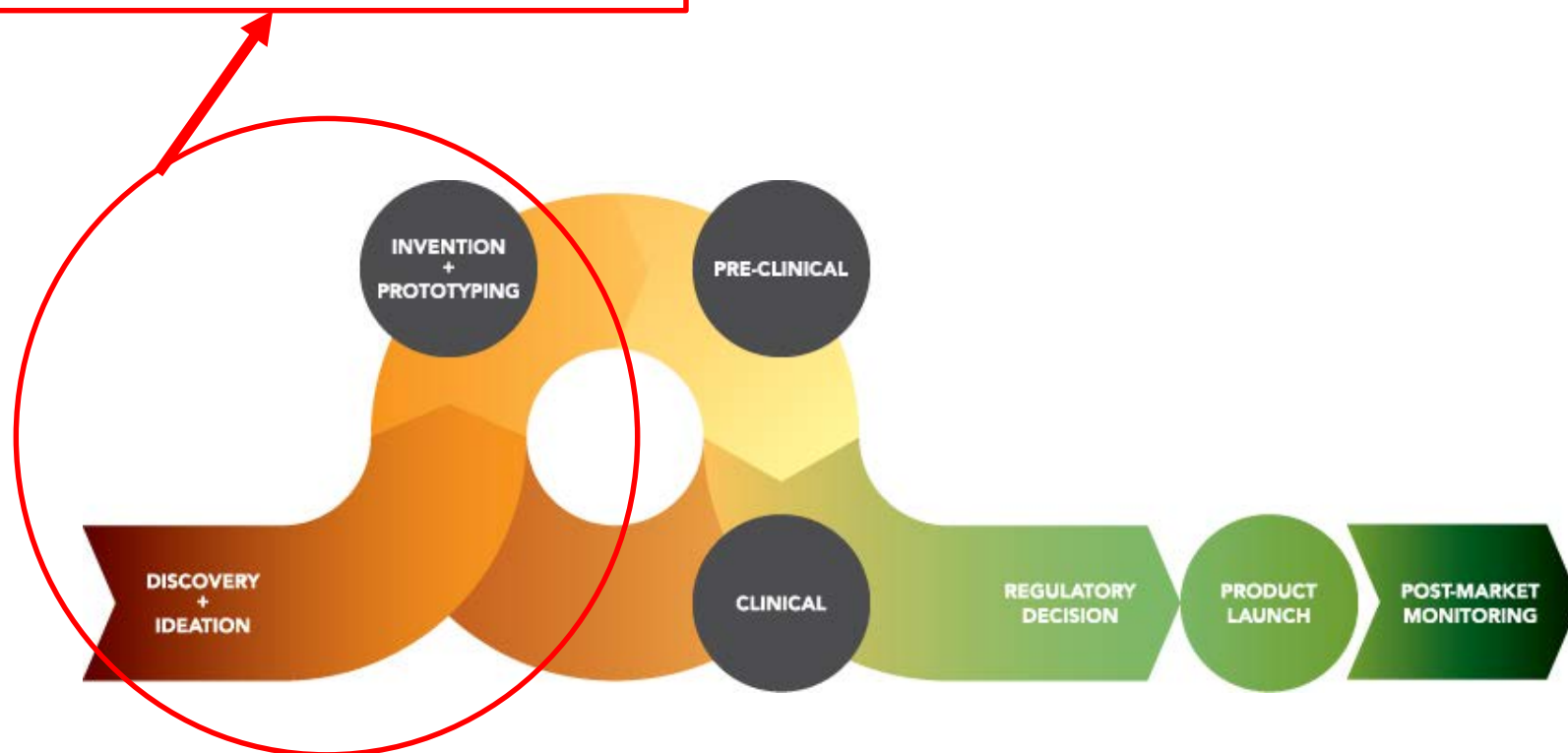
Submit an RFD or informal inquiry **BEFORE** any submission (i.e., pre-submission / marketing submission)

Why?

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



- Product Type /Classification (RFD)
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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**

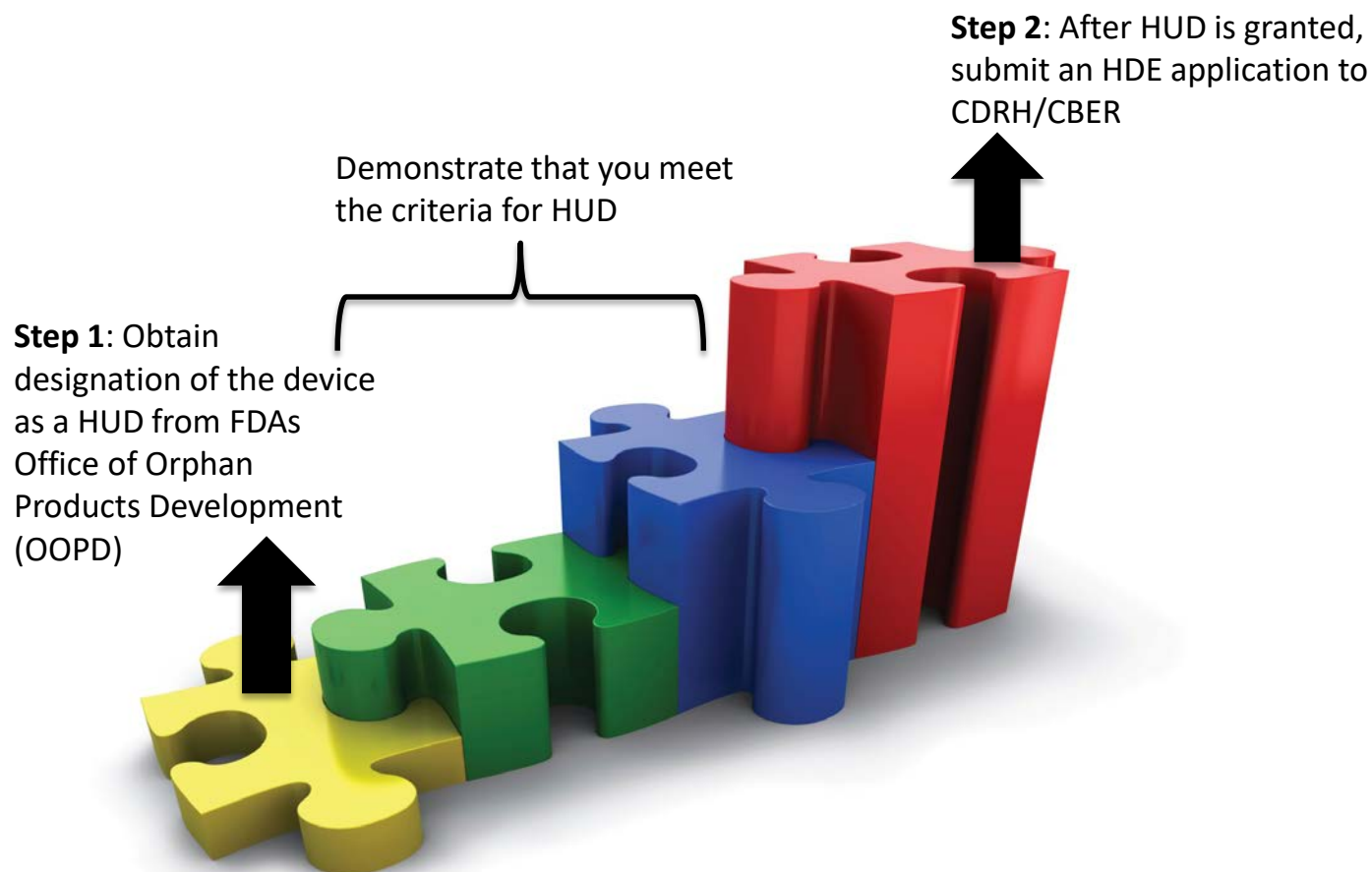
21st Century Cures Act

Amendment to regulation published June 7, 2017

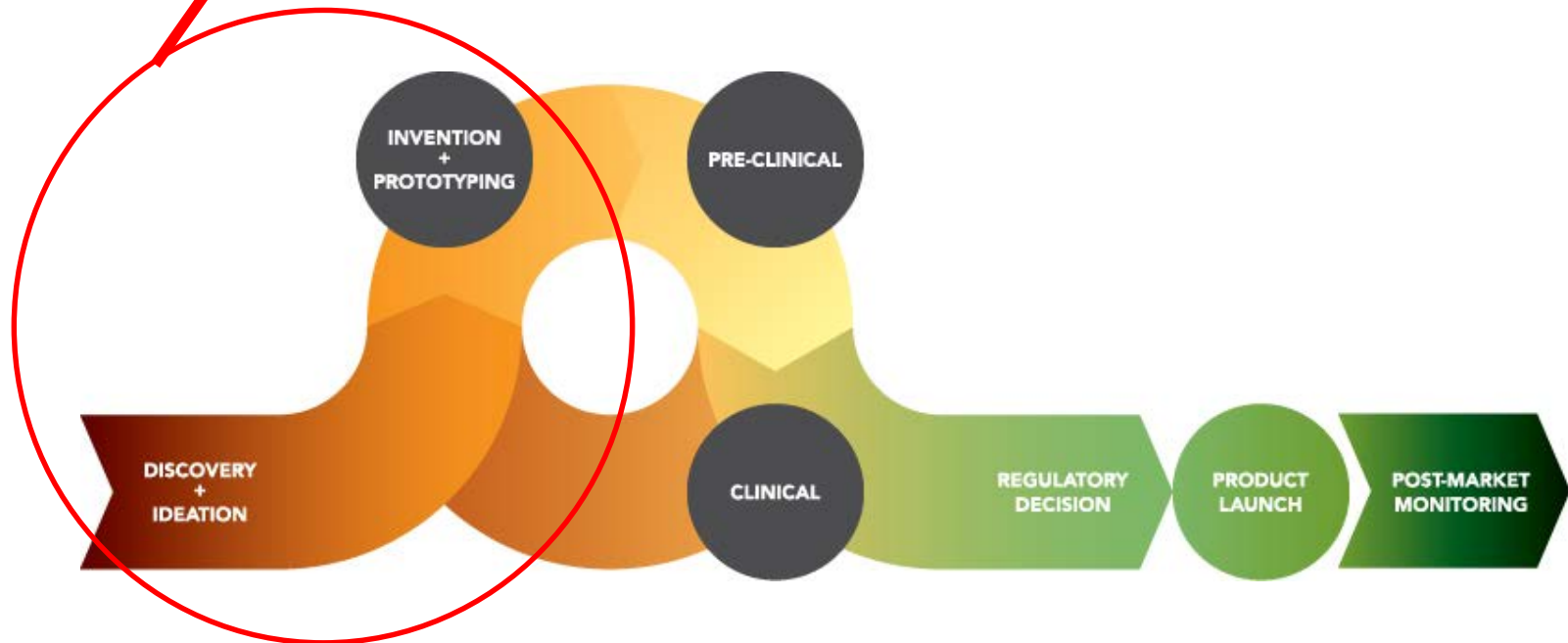
HDE Approval

- **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



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



FDA Resources: Summaries

- Summary of Safety and Effectiveness

- <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm>

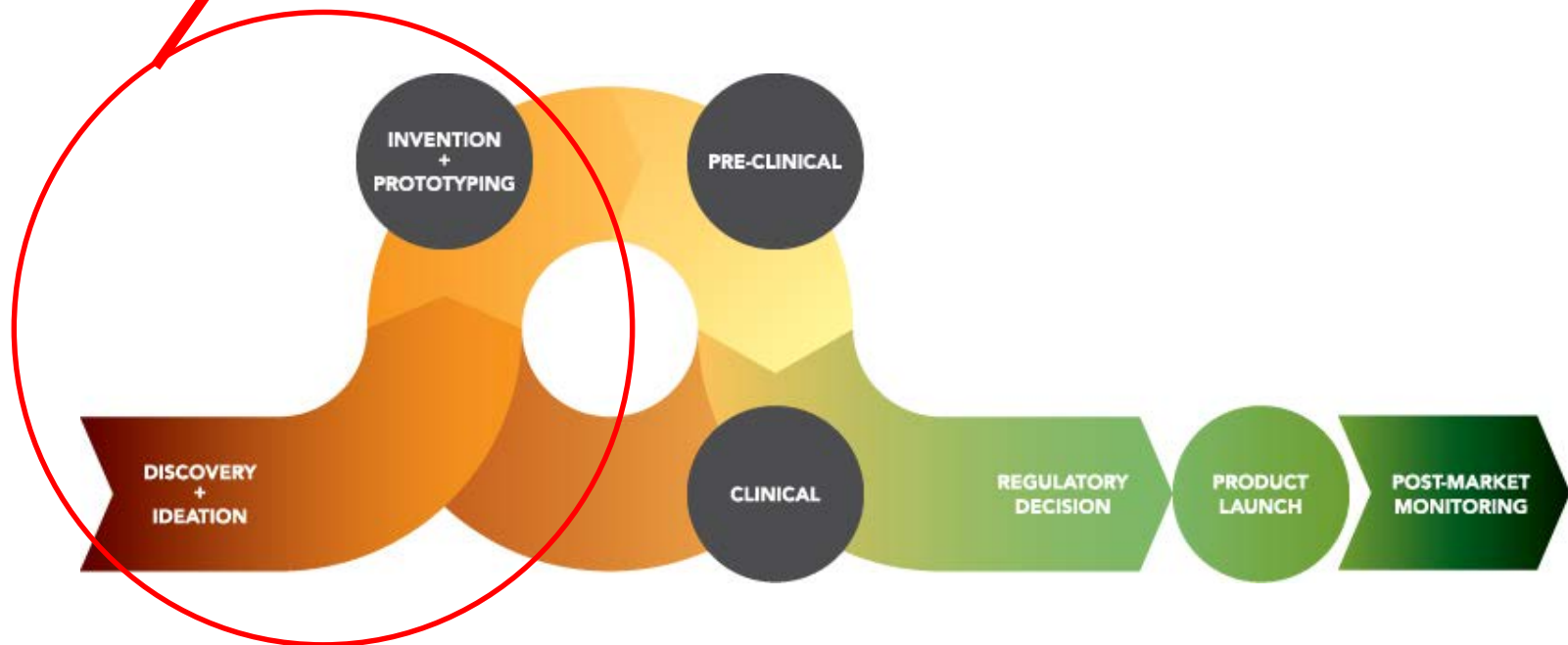
- Summary of Safety and Probable Benefit

- <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm>

- 510(k) Summaries

- <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/510kClearances/default.htm>

- Product Type /Classification (RFD)
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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

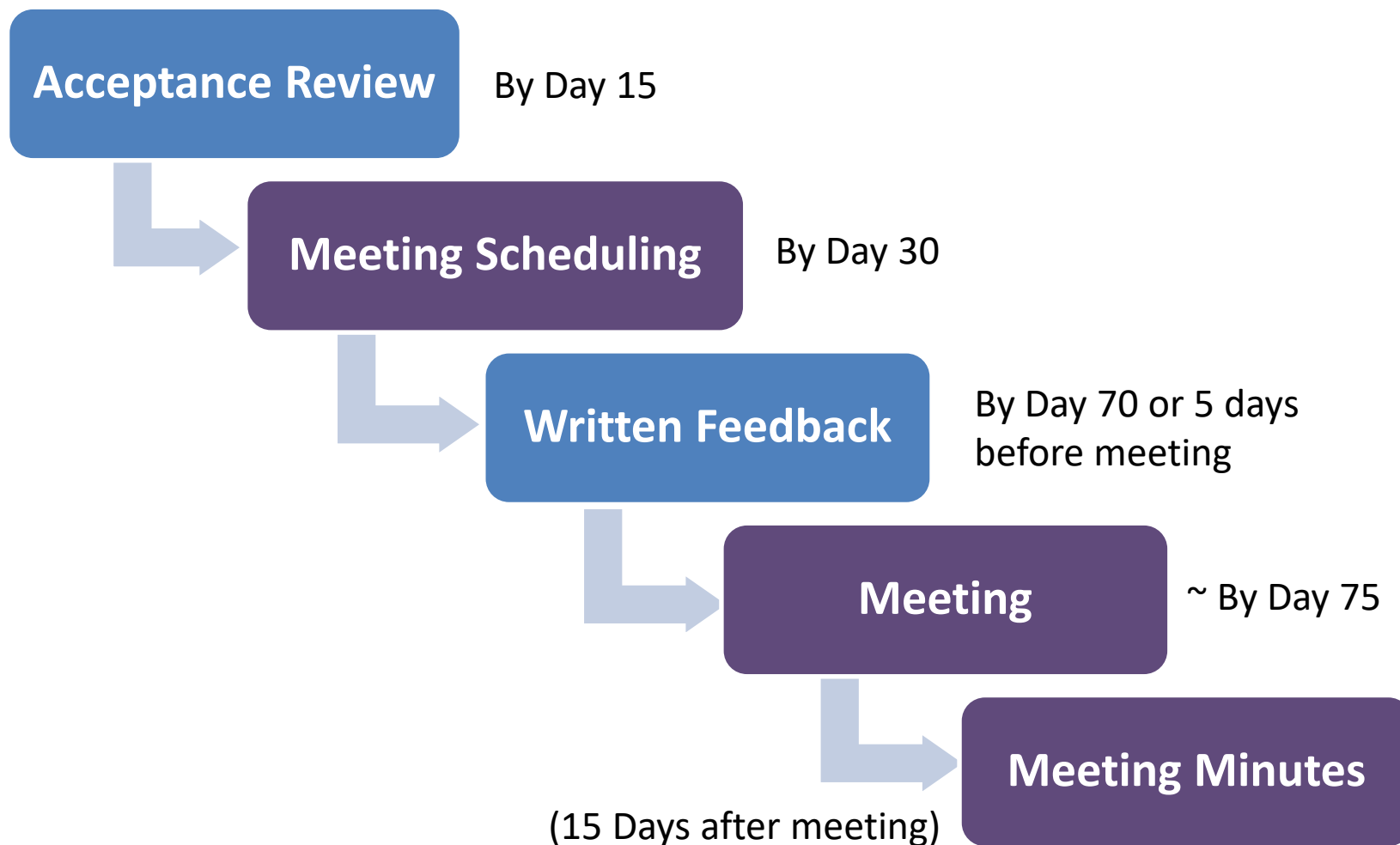
Key Information in a Pre-submission

- 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

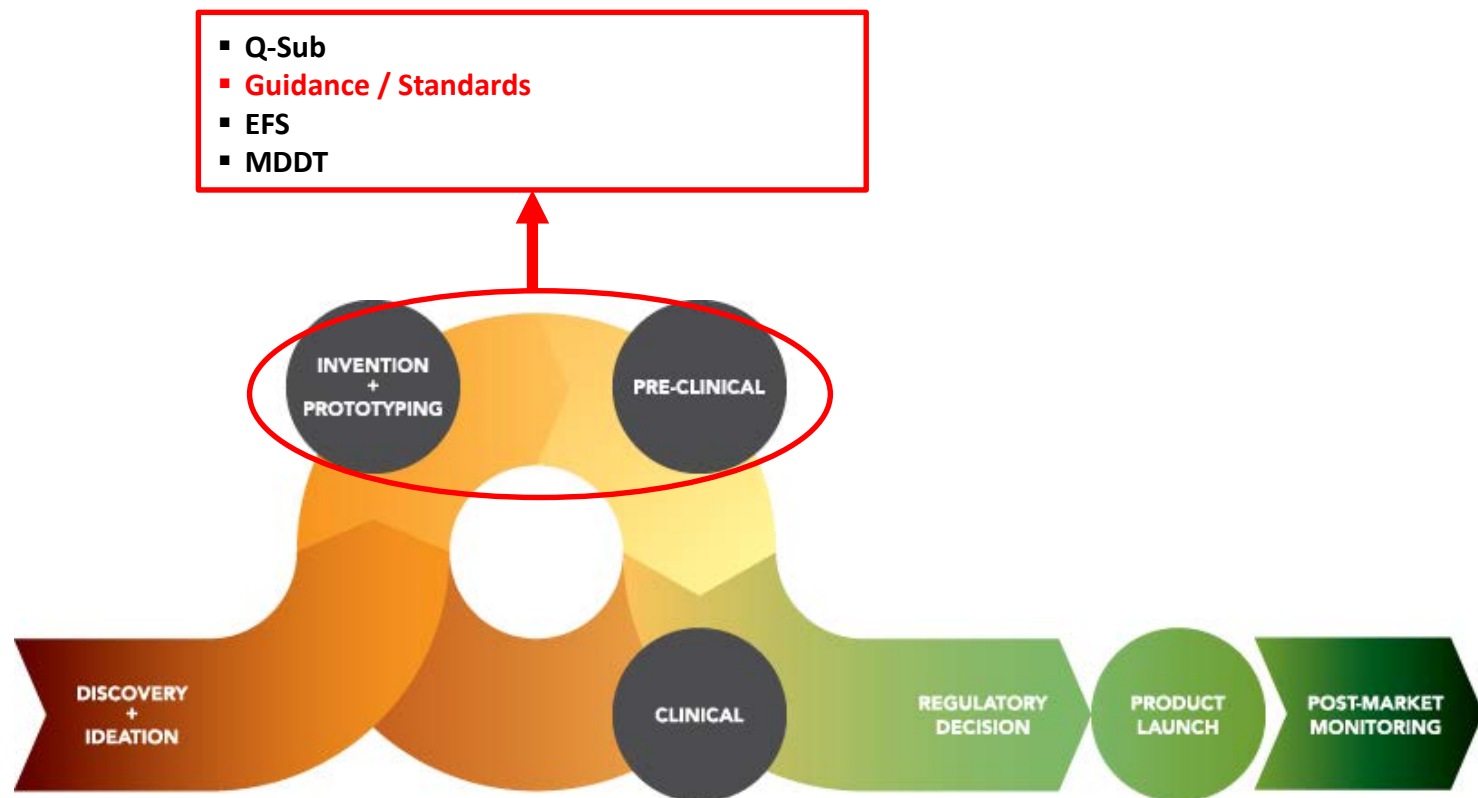
- Include new discussion topics in the meeting minutes

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



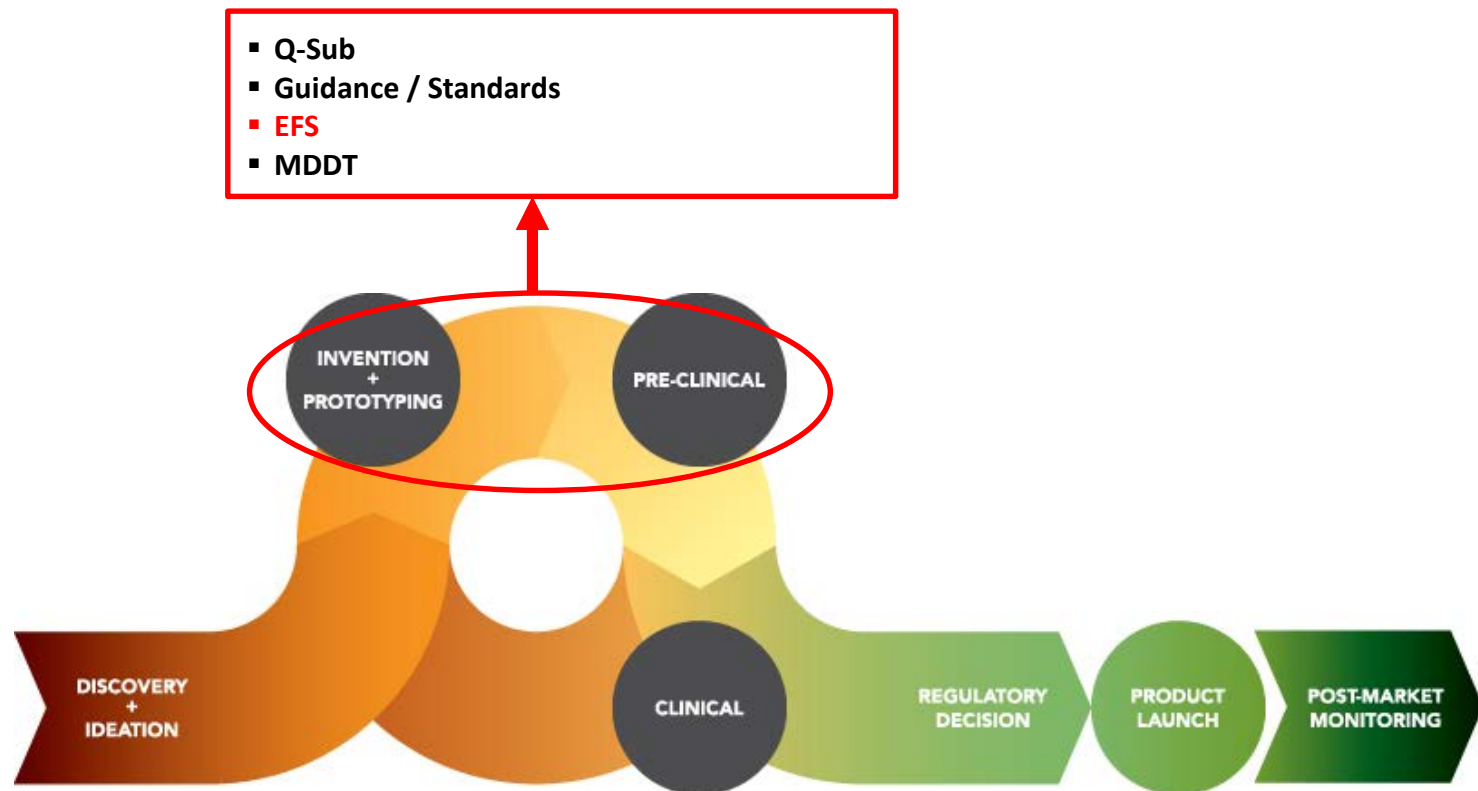
FDA Guidance

- 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



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

EFS

- Device design may not be final, with changes anticipated
- Less nonclinical data available for the study device with potentially more reliance on device design and leveraged information
- Intended to provide initial insights

Traditional Feasibility

- Device design may be final or near-final
- Generally supported by more nonclinical or prior clinical data
- Intended to capture preliminary safety and effectiveness information and to adequately plan an appropriate pivotal study

Pivotal

- Final device design
- Clinical feasibility established and all IDE-level nonclinical data completed
- Intended to capture safety and effectiveness data to support a marketing application

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

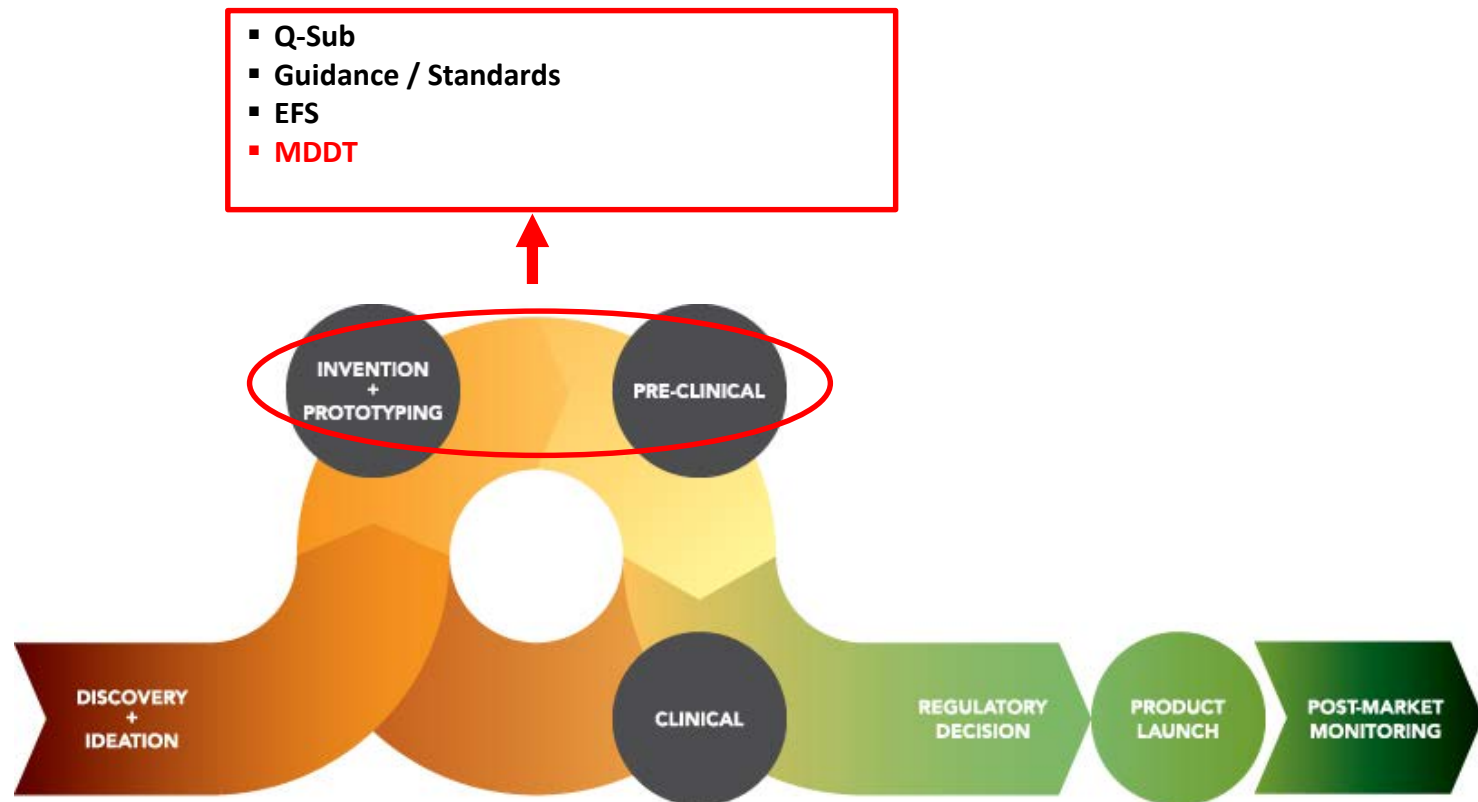
After...

- 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

Communication with FDA throughout the development process is recommended to optimize submission efficiency



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

Research

Development

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

**MDDT
reduces
regulatory
burden**

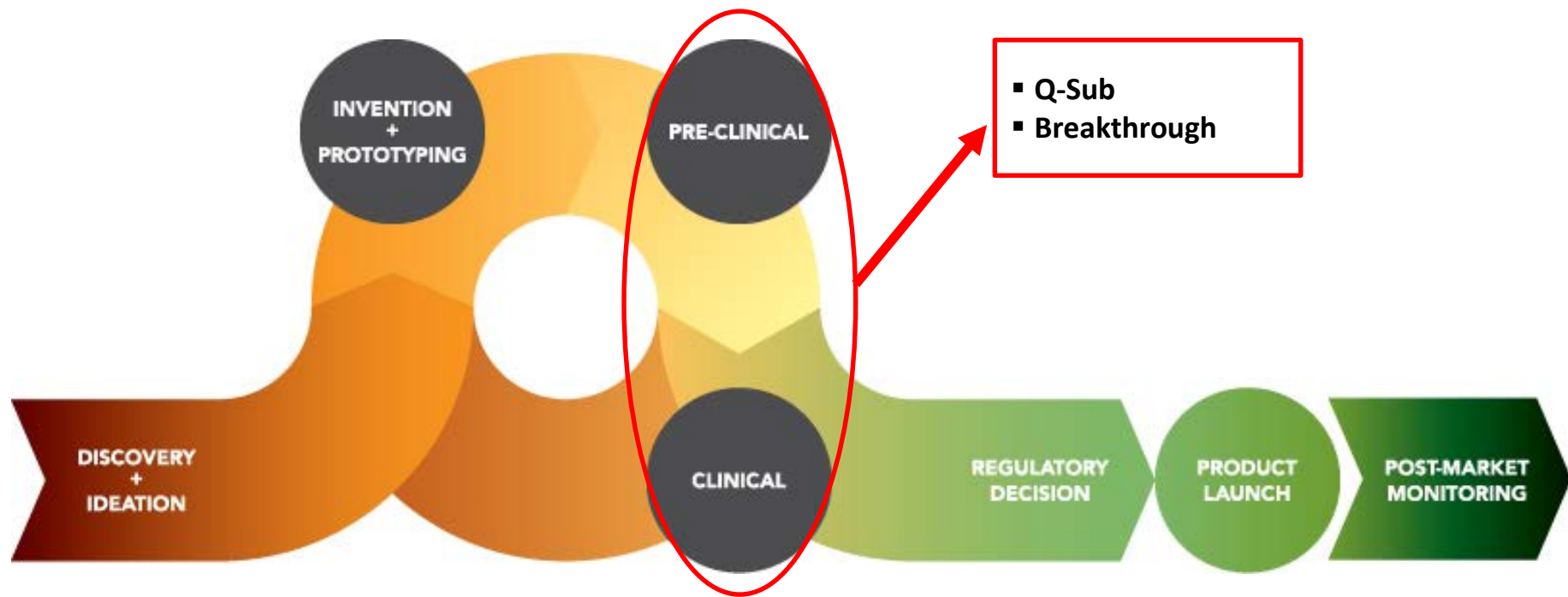
Tool
Developer

FDA-
Regulatory
Scientists

Device
Industry

FDA-
Product
Evaluators

Patients



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

+

At least one of the following:



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