EUA & Breakthrough Device Designation Case Studies

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Disclaimer Statement

The views and opinions expressed or presented are my own and do not necessarily represent the views or official position of any firm or firms.

Agenda – EUA Case Study

Introduction

Who Should Care about EUAs?

Scenario

What Not to Do

Countdown – Top 10

Lessons Learned

Who Should Care about EUA's Anymore?

Answer: **YOU**

Why?

The FDA and many regulators world-wide have re-allocated staff for 1-2 years to manage the COVID -19 healthcare crisis.

The cross-functional learning by regulators within and between regulatory agencies has been phenomenal – particularly in the US of upstream development and knowledge of naïve manufacturers

This has been the greatest period of learning for regulators in our lifetime and will shape FDA and world-wide policy and regulations for years to come.

Scenario – EUA – ABC Diagnostics

Small, pre- IPO infectious disease firm suddenly changes course to pursue an EUA for COVID-19 in March of 2020. Only a handful of persons 5/60 has FDA regulated device experience. Only a limited paper QMS and training system has been established but not maintained and the firm has not had any projects initiated past concept in Design Control. The device is Point of Care and consists of an instrument and a COVID 19 assay with reagents, software, and controls. The instrument is not 510(k) cleared. Due to significant turn-over in QA/RA you have 1 headcount. Your mission as Head of QA/RA is to obtain an EUA as fast as possible – ideally within 1 year.

What 10 Things Do You Not Do?

What 10 Things Do You Do?

10. Establish & implement electronic eQMS and training system
9. Hire
8. Work Upstream with R&D – Analytical Studies
7. Define Deliverables (EUA + 510(k)) and Involve All Levels of Personnel
6. Test validated device to IEC 60601 per FDA EUA Guidance

What 10 Things Do You Do?

5. If Software - Follow 2005 FDA Guidance “Software Contained in Medical Devices” and Cybersecurity…

Table 3. Documentation Based on Level of Concern

SOFTWARE DOCUMENTATION	MINOR CONCERN	MODERATE CONCERN	MAJOR CONCERN
Level of Concern	A statement indicating the Level of Concern and a description of the rationale for that level.		
Software Description	A summary overview of the features and software operating environment.		
Device Hazard Analysis	Tabular description of identified hardware and software hazards, including severity assessment and mitigations.		
Software Requirements Specification (SRS)	Summary of functional requirements from SRS.	The complete SRS document.	
Architecture Design Chart	No documentation is necessary in the submission.	Detailed depiction of functional units and software modules. May include state diagrams as well as flow charts.	
Software Design Specification (SDS)	No documentation is necessary in the submission.	Software design specification document.	
Traceability Analysis	Traceability among requirements, specifications, identified hazards and mitigations, and Verification and Validation testing.		
Software Development Environment Description	No documentation is necessary in the submission.	Summary of software life cycle development plan, including a summary of the configuration	Summary of software life cycle development plan. Annotated list of control documents generated during development
		maintenance activities.	configuration management and maintenance plan documents.
Verification and Validation Documentation	Software functional test plan, pass / fail criteria, and results.	Description of V&V activities at the unit, integration, and system level. System level test protocol, including pass/fail criteria, and tests results.	Description of V&V activities at the unit, integration, and system level. Unit, integration and system level test protocols, including pass/fail criteria, test report, summary, and tests results.
Revision Level History	Revision history log, including release version number and date.		
Unresolved Anomalies (Bugs or Defects)	No documentation is necessary in the submission.	List of remaining software anomalies, annotated with an explanation of the impact on safety or effectiveness, including operator usage and human factors.	

What 10 Things Do You Do?

4. Human Factor Studies and re-integrate learning into R&D/Design Control
3. Hazard Analysis
2. Create Executive Summaries for Every Report
   - Restate Study Design and Objective
   - Include sample type, lot #'s
   - Summarize Key Results and Acceptance Criteria
   - State any specifications established
   - Explain any outliers
1. Cover Letter – as Marketing tool

Lessons Learned

1. Take advantage of pre-EUA if time permits
2. Create/Obtain FDA Screening Checklist for EUA's
3. Cross-functional internal/external review w/ naïve reviewers
4. Attend FDA weekly/biweekly Town Halls
5. Hire consultants for specific expertise (cybersecurity, Human Factors etc.), as needed

Agenda – Breakthrough Designation Case Study

Goal

Metrics

Breakthrough Requirements

Scenario

Countdown – Top 10

Lessons Learned

Goal of Breakthrough Program

is to create “a more agile process for developers of breakthrough devices to obtain feedback from the FDA on their innovations,”

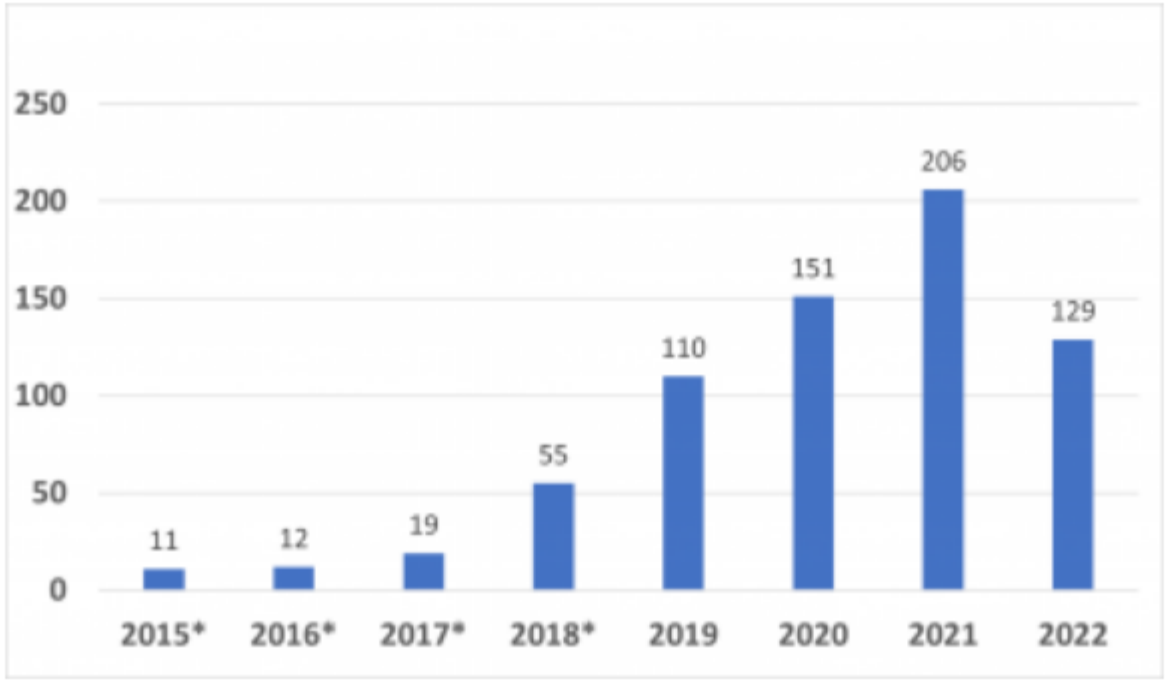
FDA Commissioner Scott Gottlieb and device center chief Jeff Shuren – December 18, 2018.

Breakthrough Device Program Metrics

June 30, 2022

As of June 20, 2022, CDRH and CBER have granted 693 BTD- including those designated under the Expedited Authorization Pathway (EAP) program. (687 - CDRH, 6- CBER)

Graph 1: Number of Granted Breakthrough Device Designations by Fiscal Year[1]



Breakthrough Device Program Metrics

June 30, 2022

Program Effectiveness: TBD

CDRH and CBER Breakthrough Device Marketing Authorizations
Data as of June 30, 2022
Total of 54 Marketing Authorizations, including 52 CDRH devices and 2 CBER devices out of the 693 potential contenders…

BUT

US has re-gained #1 Country for innovative products

How to Apply

- Must apply for breakthrough designation before submitting for marketing authorization.
- Sponsor needs to show a reasonable expectation that the device can function as intended, and the functioning device can more effectively treat or diagnose the identified disease or condition. While it may be possible to accomplish this with bench or animal data, clinical data is recommended..
- Request before starting the pivotal clinical trial to take advantage of flexible study design opportunities.

Requirements of Application

- Cover letter indicating “Designation Request for Breakthrough Device”
- Background on disease/clinical need • Device description • Indications for use (clearly outline patient population meeting breakthrough criteria)
- Regulatory history (prior FDA interactions)
- How your product meets breakthrough criteria
- Planned marketing application type (i.e., PMA, 510(k), De Novo) and rationale

Breakthrough Criteria Eligibility

Two important criteria must be met:

A. The device provides for more effective treatment or diagnosis of life-threatening OR irreversibly debilitating human disease or conditions.

B. The device meets at least one of the following:
   1. Represents breakthrough technology – No FDA approved/cleared alternatives exist
   2. Offers significant advantages over existing FDA approved/cleared alternatives
   3. Device availability is in the best interest of patients

Scenario – Breakthrough Designation – LDT Supergreat Diagnostics

Medium sized, LDT firm – Supergreat Diagnostics - changes course to pursue an IVD test using a Breakthrough Designation Pathway in December of 2018 prior to initiation of marketing application project. Only a handful of persons have FDA regulated device experience in the firm and none are department heads or higher. One project has gone through design control – but as this new project is in concept phase no product requirements have been established. You have the stealth BTD designation project, 3 QMS's (an LDT CLIA QMS, an IVD QMS and a US biologics QMS) i.e.. 3 sites in 3 different states and IVD's in 80 countries. Your mission as Head of QA/RA is to obtain an BTD as quickly as possible. The project is not formally sanctioned (stealth) and your staff is fully committed.

What 10 Things Do You Do?

5. Gather as much information as possible on BTD, conferences, guidance etc.
4. Define intended use
3. Educate firm on guidance document
2. Hire FDA Consultant (to educate self, firm, review submission)
1. Develop FDA Relationship w/ Reviewer

Lessons Learned

1. Very intense FDA Review
2. Screening for removal from program
3. IF intended use is similar/same as previous intended use with similar technology, then may not qualify for program (based on internal FDA policy)
4. Intense amount of data is required. Circular reference. Wanted input on Data Development Plan (DDP) BUT needed to provide DDP data to achieve BTD
5. Benefit to business to build/achieve investor confidence in new technology
6. Familiarizes FDA leadership and staff in new technology

Summary of BTD Designation

Great program to encourage device innovation remains in the US and involves high-level FDA Management. Great confidence builder for investors. Tangible regulatory advantages TBD.

Thank you

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1. Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, 2005
2. Template for EUA Molecular (or Serological or Antibody), dates subject to change without notice
3. IEC 60601-1 Medical electrical equipment – Part 1: General requirements for basic safety and essential performance
4. Emergency Use Authorization of Medical Products and Related Authorities, 2017
5. Breakthrough Devices Program Guidance for Industry and Food and Drug Administration Staff, 2018
6. Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program

Resources