



Regulatory Considerations

“All too often, regulatory due diligence gets short shrift...the biomedical investment landscape is littered with the wrecks of many early stage companies who have failed to successfully navigate through the FDA/EU regulatory regimes, and to develop a program to anticipate and satisfy reasonably foreseeable regulatory issues’

BF Mackler, PhD, JD, Heller Erhman

BioTechnology Transfer, LLC

'Evaluate an Innovation'

- Business Model
 - Markets
 - Competition
 - Technology
 - Intellectual Property
 - Team
 - Risks
 - Financial
- Regulations
-
- ```
graph LR; Team --> Regulations; Risks --> Regulations; Financial --> Regulations;
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# Major Regulatory Bodies

- US
  - FDA
  - CMS
- EU
  - CE mark
  - ISO
- TGA [Australasia]
- Japan
- DCGI [India]

# What does FDA regulate?

- **Devices, diagnostics**
- Biologics [vaccine, blood product, cell, tissue]
- Drugs [human, animal]
- Foods [human, animal]
- Dietary supplements
- Cosmetics
- Color additives [food, drugs, cosmetics, devices]
- Radiation-emitting Electronic Products
- Combination products
  - Drug-device
  - Drug-biologic
  - Device-biologic

# How does FDA regulate products?

- Based on classification
  - Product type
  - Intended use
    - Labeling claims
    - Point of use [hospital, office, OTC]
    - End user [consumer, physician, lab]
  - Product risk
- Not based on technology

# Which FDA division will regulate the product?

- Based on product type

CDRH [devices, diagnostics]

CBER [biologics]

CDER [drugs]

OCP [combination products]

CFSAN [food, supplements]

CVM [vet medicine]

# What level of regulation will FDA require?

- Based on product risk classification
  - Research use only
  - Analyte specific reagent
  - Class I
  - Class II
  - Class III

# FDA Product Classification

## Class I, low risk

- General controls
  - Registration of product and company
  - GMP
  - Accurate labeling
  - Record keeping requirements
  - Repair, replace, refund

# FDA Product Classification

## Class II, moderate risk

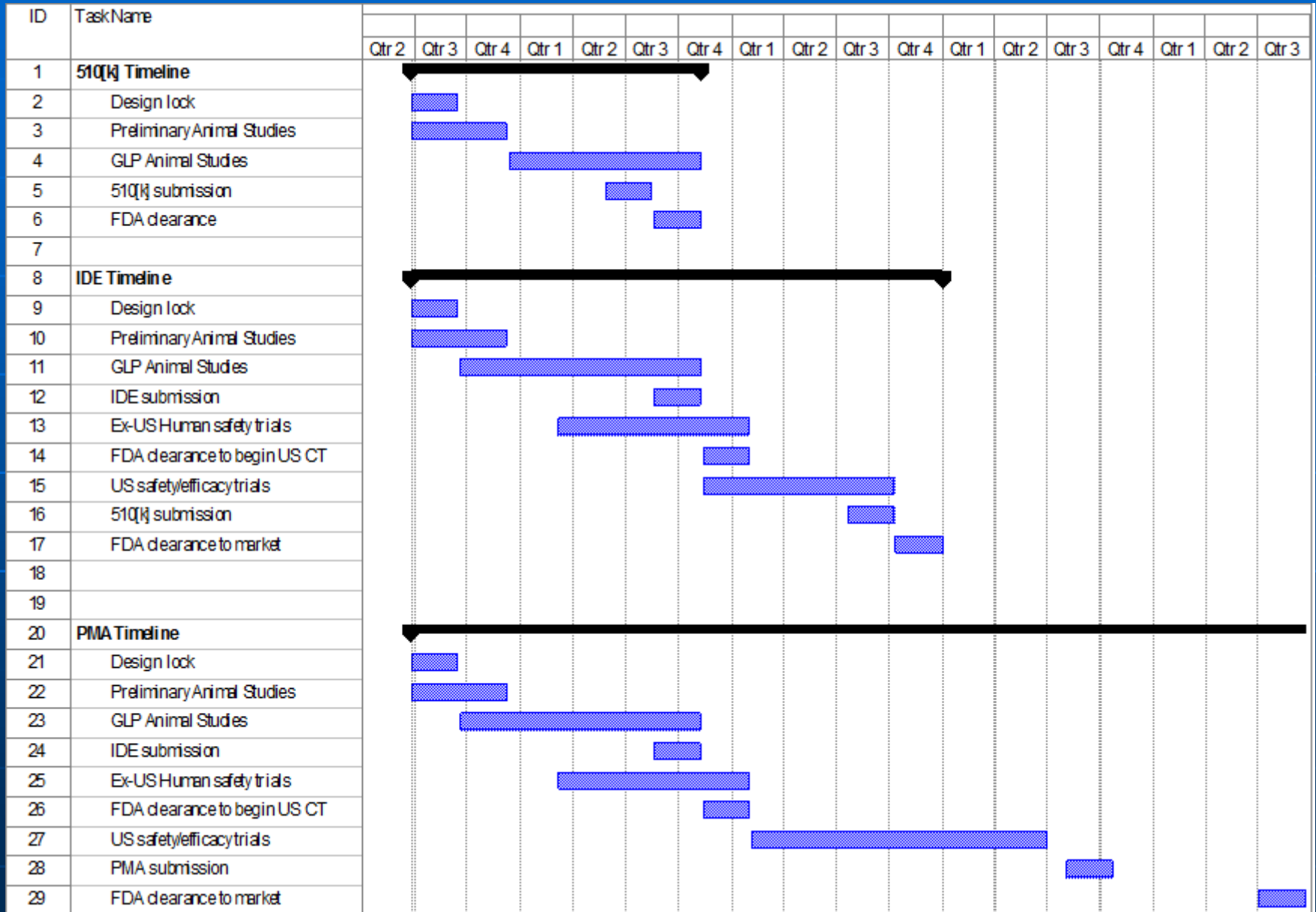
- Special controls
  - Performance standards
  - Guidance documents
  - [Clinical Trials]
  - Premarket Notification - 510[k]
  - [De novo submission]

# FDA Product Classification

Class III, significant risk

- IDE
- Clinical Trials – Phase 1, 2, 3
- Premarket Approval [PMA]

# Comparative Timelines



# How do I determine product class?

- Request to FDA for Classification
  - 513[g], fee
  - Nonbinding
- Request to FDA for Designation
  - 21 CFR Part 3, no fee
  - Binding
- Formal, written regulatory assessment

# Formal Regulatory Assessment

- Product classification
  - Agency, division, office, panel
  - 21 CFR, product code, class
- Submission type
  - None
  - 510[k]
  - De novo
  - IDE
  - BLA/PMA
  - MAF

# Formal Regulatory Assessment

- Staged regulatory pathway, e.g.:
  - Single → combination product
  - Indication [soft tissue → cardiac → minimally invasive]
  - Sample type [blood → marrow → UCB]
  - Patient population [adult → pediatric]
  - Competitor predicate → your device as predicate

# Formal Regulatory Assessment

- Data required
  - Consensus standards [ISO, ASTM, CLSI]
  - Guidance documents [FDA]
- Study design
  - Biocompatibility
  - Animal
  - Human
- Submission elements, format
- Postmarket requirements

# What must be done to satisfy FDA?

## Basic FDA requirements

- Product must be safe and effective
- Labeling must be accurate and complete
- Design must be controlled, documented
- Systems must be functioning

# What must be done to satisfy FDA?

## FDA-mandated Systems [QSR]

- Design Control [Project Mgmt]
- Document Control
- GLP
- GCP
- GMP

# How do we implement the systems?

## ■ The Process

Research → Development →  
Prototype Mfg → [Animal Studies →  
IDE → Clinical Trials] → FDA  
Submission → FDA Clearance →  
Manufacturing → Market

# How do we implement the systems?

- The Process + **Systems [QSR]**

**Design, Doc Control** → Research →  
**GLP** → Development → Prototype Mfg →  
Animal Studies →  
**GCP** → IDE → Clinical Trials  
→ FDA Submission → FDA Clearance →  
**GMP** → Manufacturing → Market

# Device Master File

- Protects proprietary information
- Referenced by other companies
- Allows methods/devices to be used for additional applications
- A few elements more than 510[k]; no filing fee