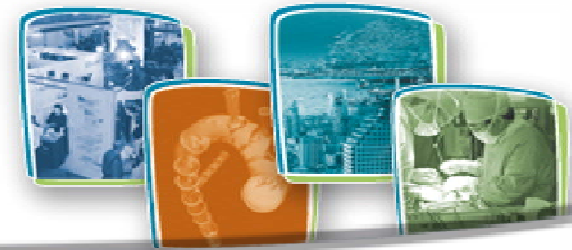


**ICI** Meeting  
**2008**

**Innovations  
in Cardiovascular  
Interventions**



**December 7-9, 2008 | Tel-Aviv, Israel**



## **The FDA Regulatory Process**

***Protecting Patient Safety and Balancing Risks and  
Benefits in a Least Burdensome Manner***

**Andrew Farb, MD  
Interventional Cardiology Devices Branch  
Office of Device Evaluation  
Center for Devices and Radiological Health  
U.S. FDA**

## Disclosures

- **Speaker's name: Andrew Farb**
- **None**

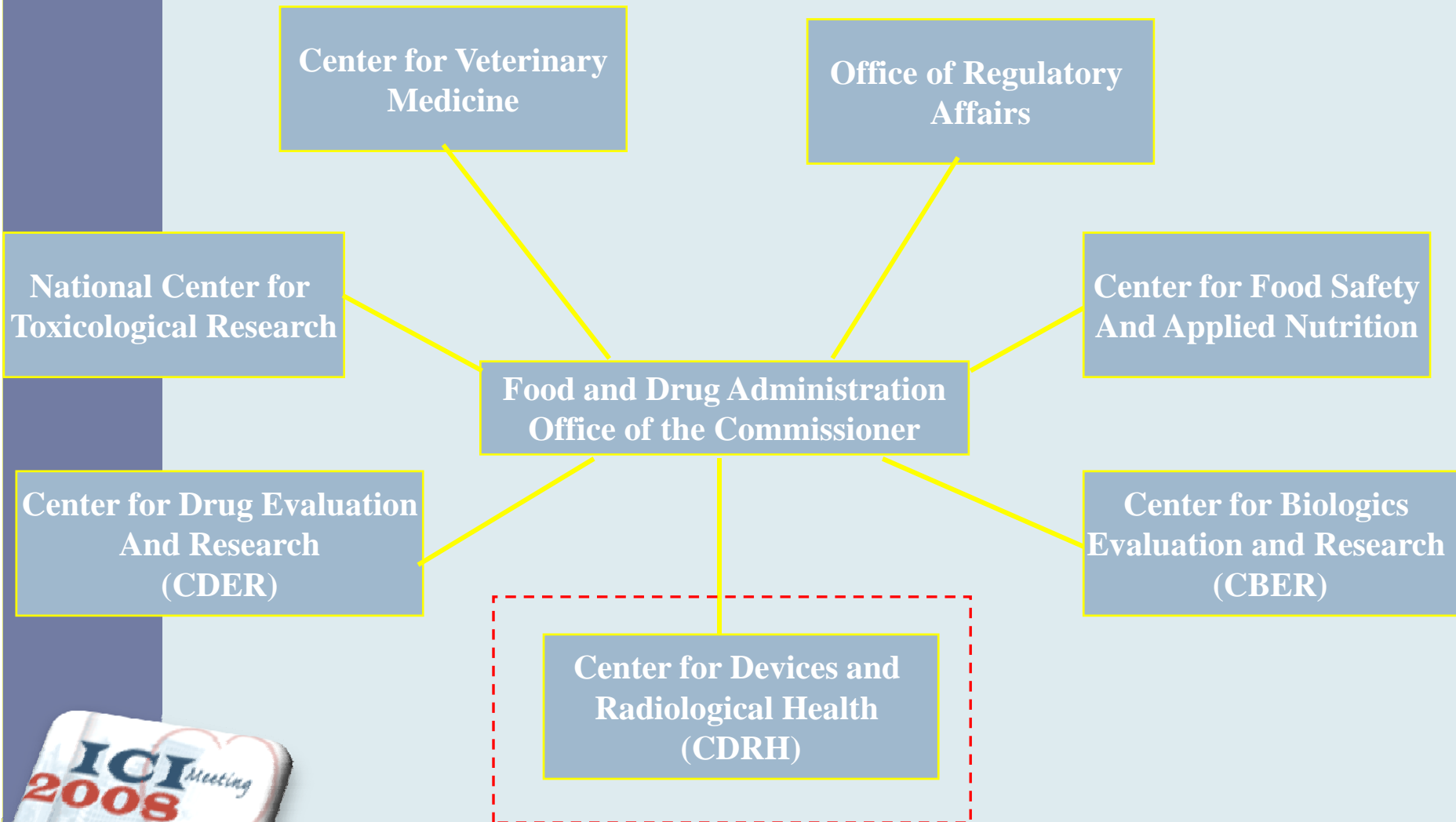


# FDA's Role

Establish reasonable  
assurance of the safety and  
effectiveness of medical products  
marketed in the U.S. using valid  
scientific evidence

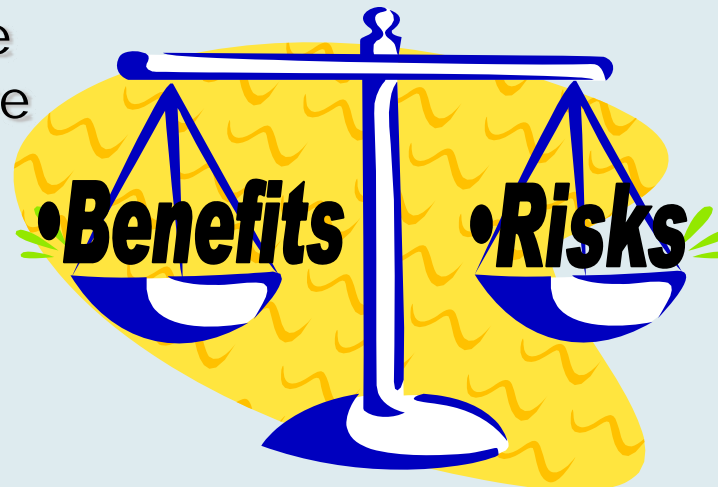


# FDA Organizational Structure



# CDRH's Mission

Getting safe and effective devices to market as quickly as possible...



... while ensuring that devices and radiological products currently on the market remain safe and effective.

Helping the public get **science-based** accurate information about medical devices and radiological products needed to improve health



**“...a reasonable assurance of safety and effectiveness”**

- **Safety:**

- **“...when it can be determined based on valid scientific evidence that the **probable benefits** to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, **outweigh the probable risks.**” (21 CFR 860.7)**



**“...a reasonable assurance of safety and effectiveness”**

• **Effectiveness:**

- **“...when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide **clinically significant results.**”**



(21 CFR 860.7)

## Valid Clinical Scientific Evidence

- ◆ Randomized Studies
- ◆ Partially Controlled Studies
- ◆ Objective Trials Without Matched Controls
  - Historical Controls
  - Optimal performance criteria
  - Performance goals
- ◆ Case Histories
- ◆ Well-Established Human Experience



# Medical Device Classification

## Risk-Based Paradigm

Medical devices are classified and regulated according to their degree of risk to the public



Class I



Class II



Class III



## Path to US Premarket Approval

- Studies to be conducted in the US require FDA-approved investigational device exemption (IDE) + IRB approval
- Data needed to support initiation of an IDE = evidence of adequate safety
  - Bench testing – full device characterization
  - Animal testing – use of preclinical models to evaluate safety and potential effectiveness
  - All previous clinical experience
  - Most disapprovals based on inadequate bench and/or animal testing



## Market Entry (Pivotal) Trial

- Select study design: Valid clinical data, select control group, & minimize bias
- Identify target population: Enroll patients similar to those treated in clinical practice
- Present clinically relevant hypotheses for safety and effectiveness endpoints with sample size justification
- Utilize objective evaluation methods
- Optimize trial execution: Minimize missing data
- Use same protocols for US and OUS patients
- Use independent CEC, DSMB and core labs



## Myths and Misperceptions About FDA

- **FDA actions stifle development**
  - FDA's mission is to get good products to patients who need them
  - FDA does not require absolute safety and effectiveness – our standard is a reasonable assurance
  - Balance between getting new treatments to patients and our mandate to protect the public health



## Myths and Misperceptions About FDA

- **FDA is a black box**

- FDA aims to make decisions transparent and public on multiple levels
  - Summary of Safety and Effectiveness Data
  - Advisory Panel meetings
  - Dispute Resolution
  - Guidance documents
- FDA encourages interaction
  - With manufacturers (pre-IDE meetings)
  - With professional societies
  - With academic clinicians
  - With regulatory agencies in other countries



## Myths and Misperceptions About FDA

- **FDA sees Europe and other OUS Regions as an incubator for US device development**
  - FDA seeks a global approach to device development
  - Efficient use of data collected both US and OUS for regulatory and reimbursement purposes
    - We can assist with approaches to data poolability
  - Global trials are often feasible and advantageous
  - Global approach moves good devices to patients more rapidly

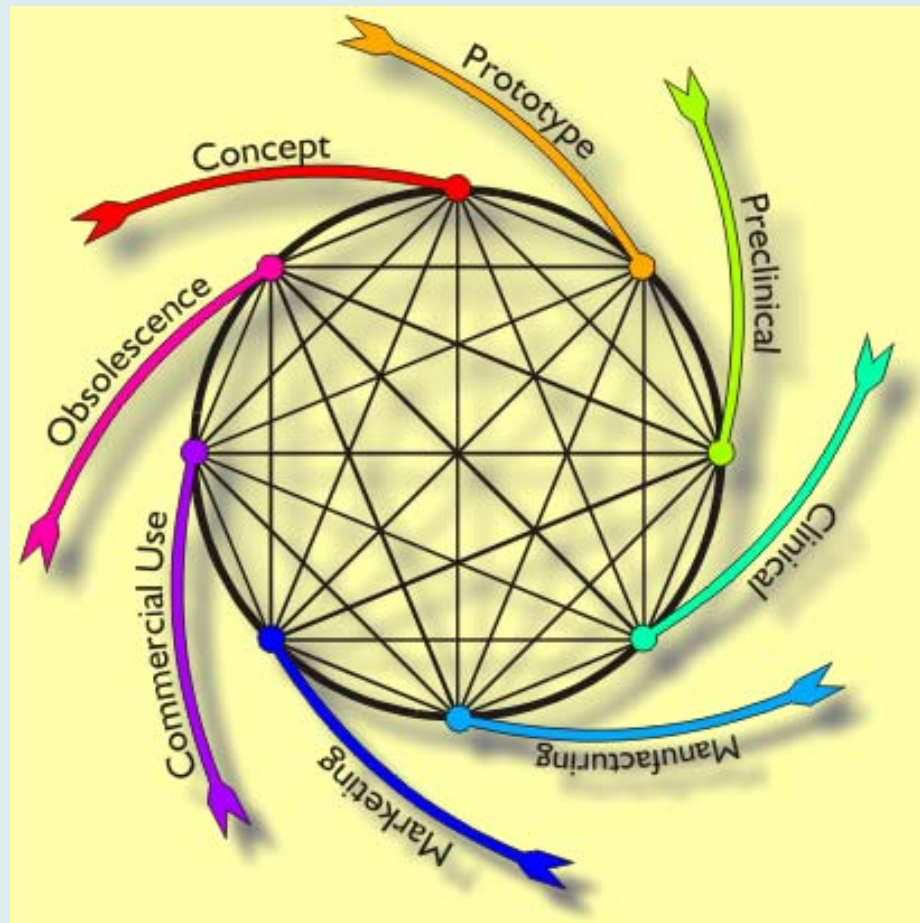


# Going Forward

- Focus on postmarket issues
- **FDA's responsibility does not end at market introduction**
- **Postmarket transformation in process**
  - Anticipate and proactively seek out potential safety signals
  - Apply lessons from postmarket to premarket evaluation
- **Move toward a continuum of data collection across pre- and postmarket**
  - e.g., pooling of death, MI, stent thrombosis rates in pre & post-approval studies in next generation DES trials



## CDRH's Total Product Life Cycle Approach



## Least Burdensome Principles

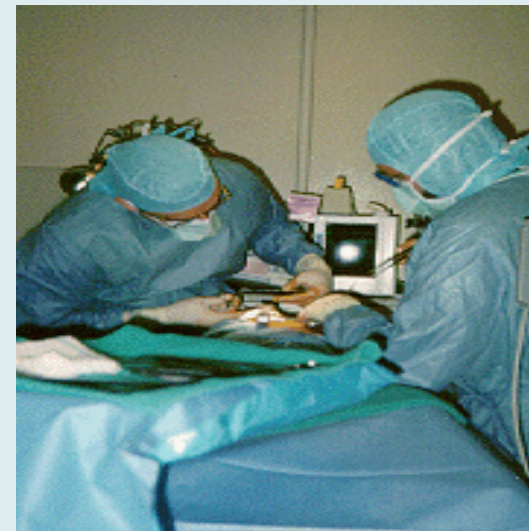
- **What it is:**
  - Leverage publicly available information and data from earlier generations
  - Consider alternatives to RCTs when potential bias associated with alternative controls can be addressed
  - Rely on post-approval studies when appropriate
- **What it is not:**
  - Clinical studies that will not likely produce interpretable data
  - “Lowering the bar” for safety and effectiveness



## And one more point:

FDA regulates Medical Devices...

- ... FDA does not regulate medical procedures or the physician – patient relationship
- (aka “practice of medicine”)



## How can requested data be obtained without slowing innovation?

- Multiple approaches likely acceptable to meet suggested objectives
- Utilize both premarket and postmarket data collection
- Incorporate US, OUS, and global studies
- Global Harmonization effort
- Early interactions to with FDA to discuss the full clinical trial program (as well as nonclinical issues)



## Thank you!

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# Postmarket Studies

## Adverse event reporting

- Historically passive system
- Manufacturers required to report
- Hospitals, providers - voluntary reporting

## Active data collection

- Continued follow-up of premarket trial cohorts
- Enrollment of additional cohorts
  - "Real-world" cohorts

