FDA CDRH Office of Cardiovascular Devices Perspective on Medical Device Convergence and Cooperation

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Bram Zuckerman, MD has no conflicts of interest relevant to this talk

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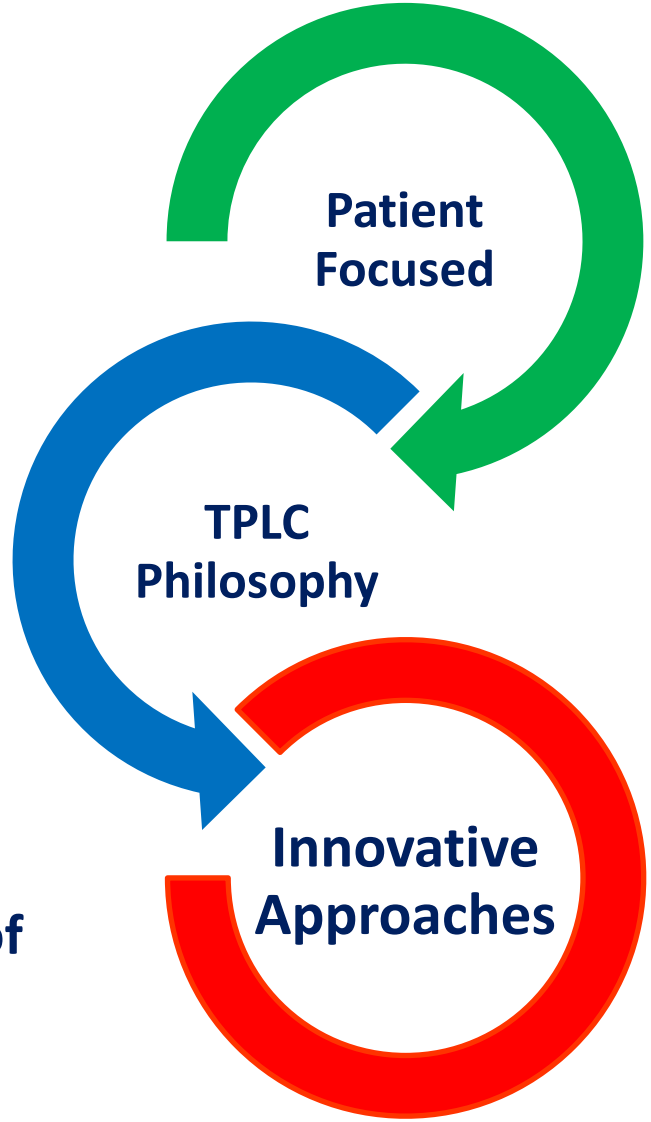
CDRH Vision



CDRH Vision

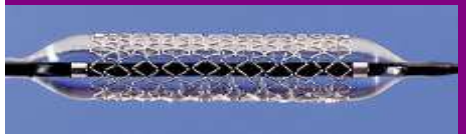
1. Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world.
2. Marketed devices remain safe, effective, and are of high quality.

Devices are not Drugs – Risk Based Device Paradigm

Medical Device Classes:

Class I
General Controls
Most exempt from premarket submission

Class II
Special Controls
Premarket Notification [510(k)]



Class III
Premarket Approval Application [PMA]

Additional Classification:

De Novo
Device "types" that have never been marketed in the U.S., but whose safety profile and technology are now reasonably well understood

Humanitarian Device Exemption (HDE)
Devices for orphan diseases intended to benefit patients in diagnosis and/or treatment of disease or condition affecting or manifested in fewer than 8,000 patients per year in the United States

PreMarket Approval Application (PMA)

Higher risk devices
Establish reasonable assurance of safety and effectiveness

Bench - Animal - Human

Similar to new drug approval process

Critical Issues in a Device Submission to Support Device Approval

1. **Pre-clinical Testing**
   Are bench and animal studies acceptable?

2. Pivotal Trial –
   Design: Minimize bias and confounding
   Design: Use sample size re-estimation or Bayesian design to get sample size right
   Execution: Minimize amount of missing data
   Analysis: Rule out chance (i.e., several prospectively chosen, clinically relevant hypotheses with plan for alpha allocation)
   Have clinically meaningful results been clearly demonstrated?

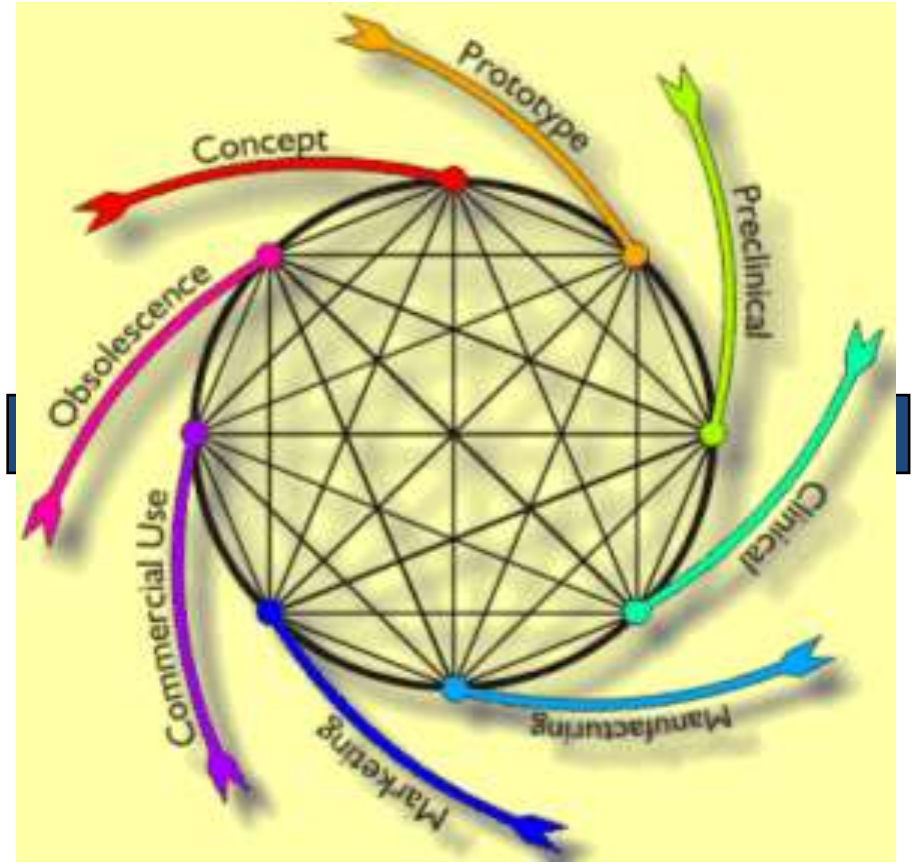
3. Manufacturing
   Can device be built safely in larger numbers for commercial distribution?

4. Is the Device Label truthful and accurate?

The Total Product Life Cycle

U.S. FOOD & DRUG ADMINISTRATION

- Regulation of device technologies requires a total product life cycle approach.



Estimated Cost of FDA Decisions on a 30 Employee Company

	Expense to Company
8 Week Delay in Scheduling a Meeting	$1.8 M
Additional 20 Animal Study (6 months)	$5.5 M
Extra Year in Negotiating an IDE	$10.8 M
Additional 100 patient study with 1 year Follow-up (24 months)	$24.1 M

Versant Ventures

Innovative Medical Device Evaluation in the US

The Past

Migration of initial clinical testing of novel devices overseas

Time lag in the access to beneficial medical devices for US patients

Delay in physician experience with new products

US was the 42nd nation to approve a transcatheter aortic valve replacement device

Many clinical trial ecosystem factors contributed to these trends including FDA's requirements for non-clinical testing prior to initiating clinical studies of new devices.

Regulatory Initiatives for Addressing Important New Device Technology and Innovation

- Breakthrough Devices Program
- Early Feasibility Studies (EFS) Program
- Reduction in Median IDE Review Times
- Safer Technologies (STEP)Program
- Digital Health Initiatives
- TAPS Program

Regulatory Initiatives for Addressing Important New Device Technology and Innovation

- These programs are helpful but do not address all challenges for making the system more scientific, efficient and cost effective

- **Global cooperation and convergence are important in this respect**

Advantages of Global Cooperation and Convergence

- Standardization of definitions to ensure data interpretability
- Best scientific thinking to address a complex and dynamic scientific environment – optimal use of “collaboratories”
- **Pediatric device development requires greater international collaboration**
- Improved Global surveillance of marketed devices and information sharing will enable early detection of safety signals
- Optimal development of clinical trials science and medical device development – valid clinical evidence has no borders

Thank you!

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