YOU DRIVE INNOVATION, WE'LL NAVIGATE

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September 12, 2014

Innovating Within Regulation

Technologies of the Heart – September 12, 2014
2014 Frontiers of Engineering Symposium - Irvine, CA

515i

PMA

513g

CEC

IDE

DSMB

PI

FDA

FEA

510k

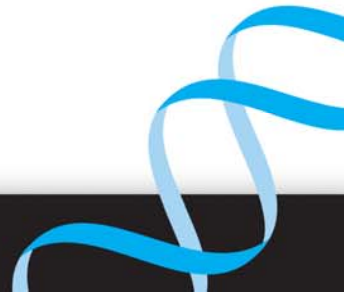
IND

AWT

ODE

CDRH

Pre-Sub

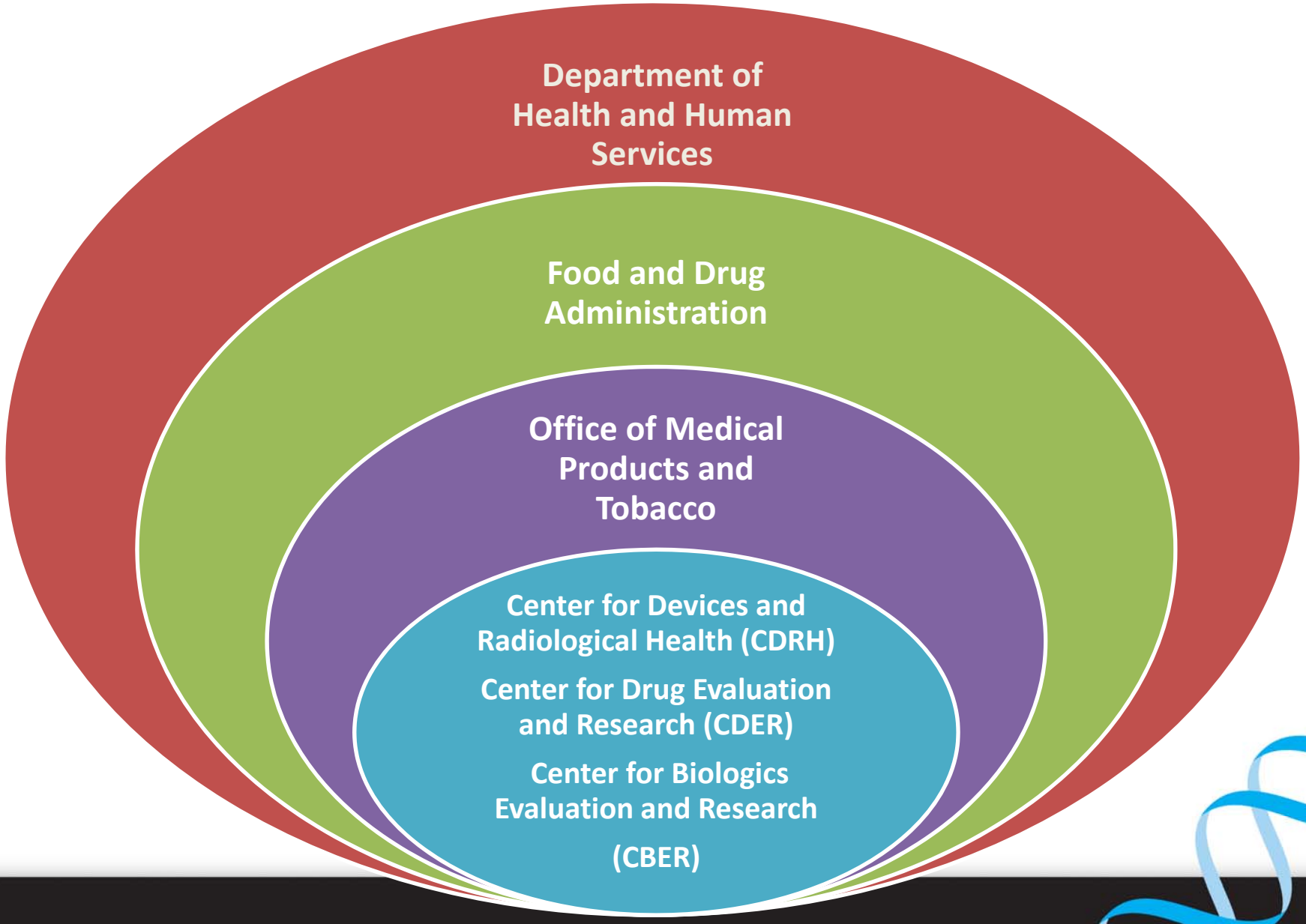


OVERVIEW

- Regulations – Why do they exist?
- FDA – What do they do?
- Bench to Bedside – How do I get there?
- Innovation in Regulation – Can I get there faster?
- Speed Bumps - What will slow me down?
- The Medical Device Ecosystem
- The Future

REGULATIONS

THE REGULATORS



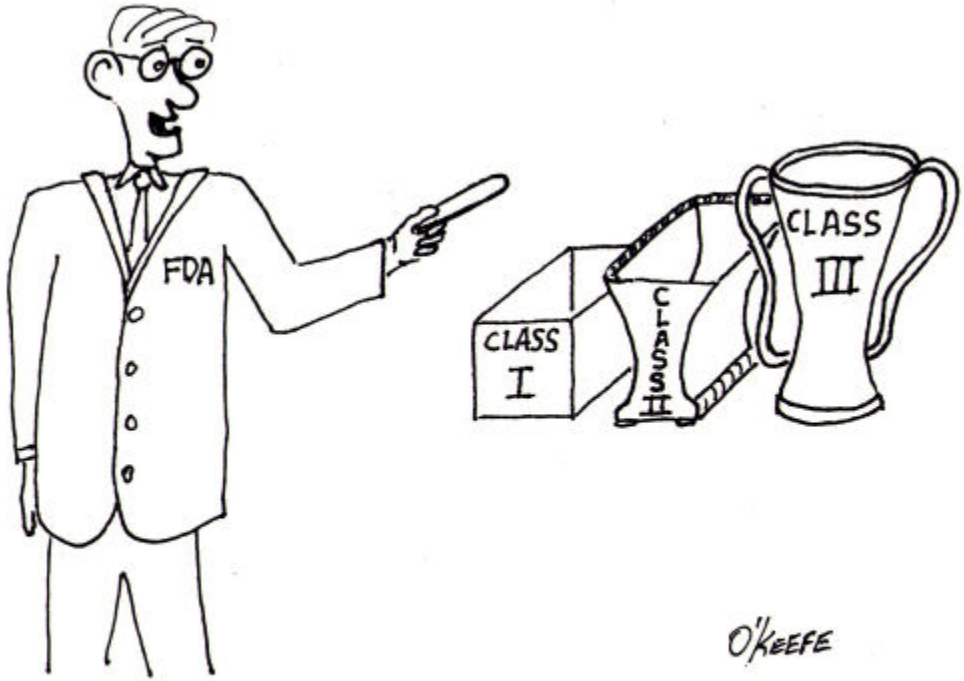
WHAT DO THEY DO?

NO, REALLY. WHAT DO THEY DO?

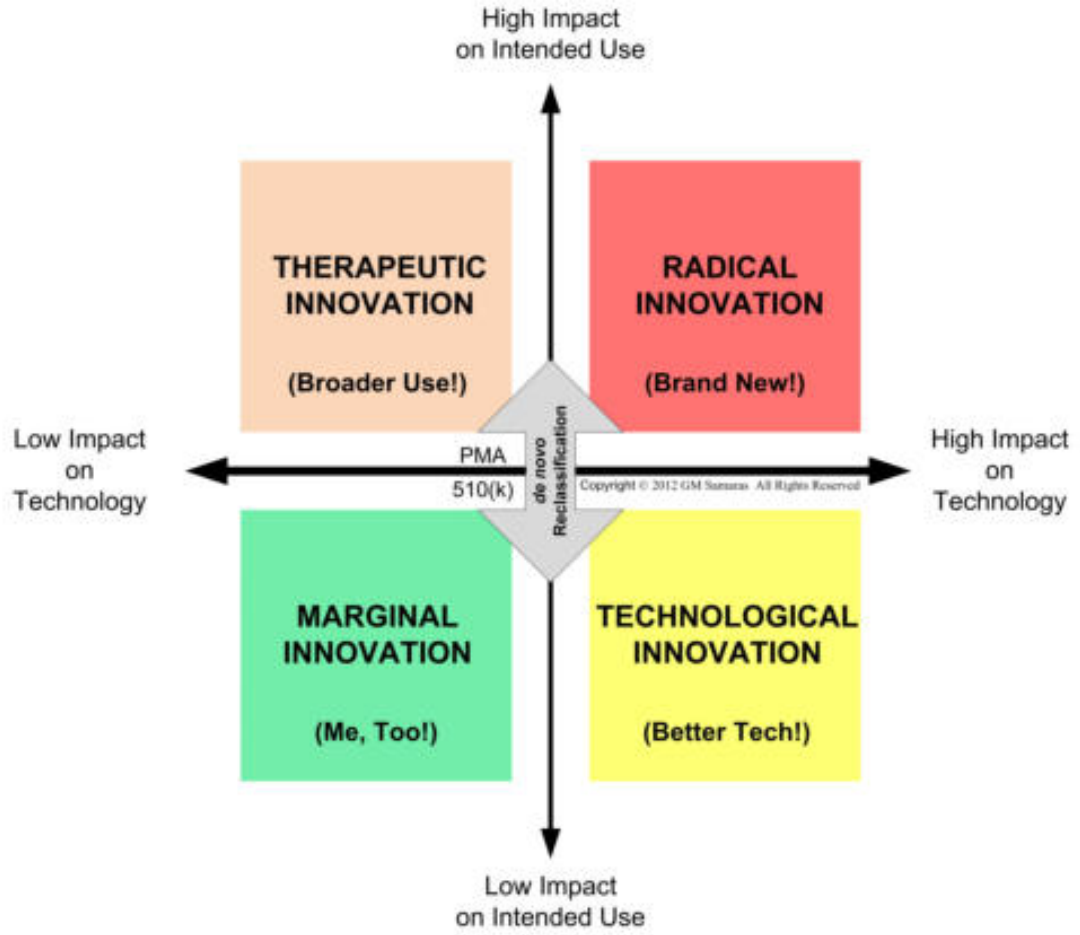
FDA Mission:

To protect and promote the public health.

DEVICE RISK



Eenie, meenie, mynie, moe, in which bin should the tongue depressor go?

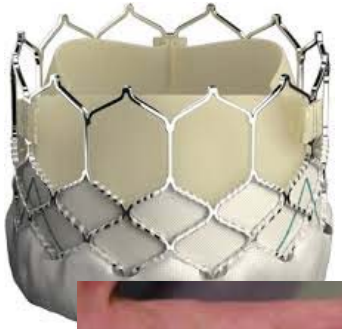


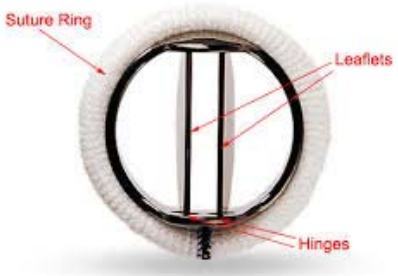
Class I and II

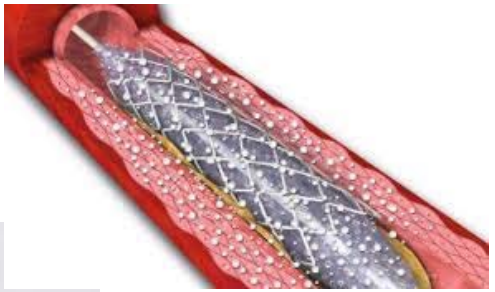
Class III

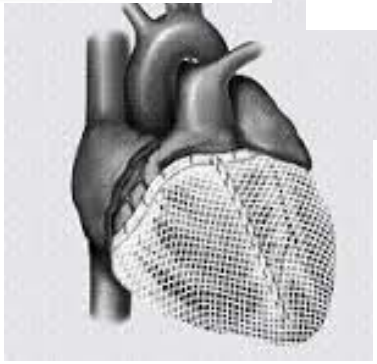
LEVEL OF INNOVATION	REGULATORY APPROACH	UNCERTAINTY ABOUT SAFETY & EFFECTIVENESS	TESTING REQUIREMENTS
Marginal Minor	Administrative Clearance (**510k**)	Very Low Low	Consensus Standards & Special Controls
Moderate Major	PreMarket Approval (**PMA**)	High Very High	**PLUS** Supervised Clinical Trials & Special Audits

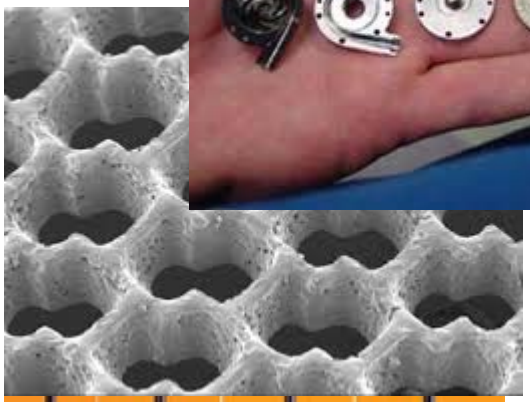
http://www.samaras-assoc.com/regulatory.htm



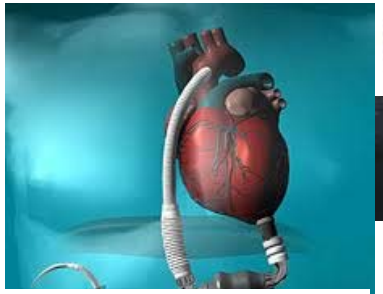

Suture Ring
Leaflets
Hinges








PHILIPS




E
Edwards


INDEX
Precision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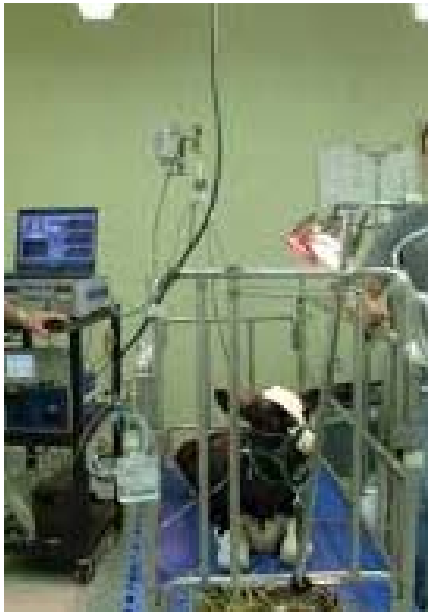
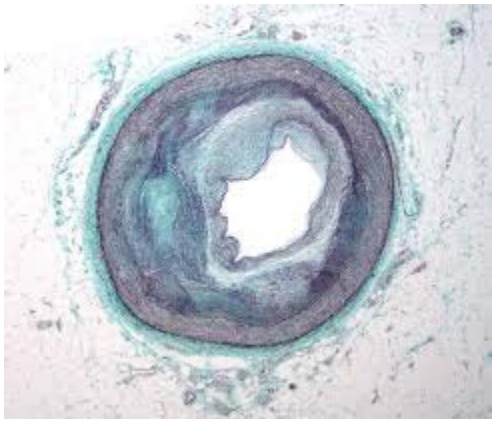
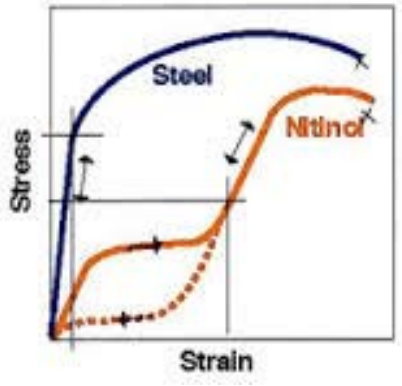
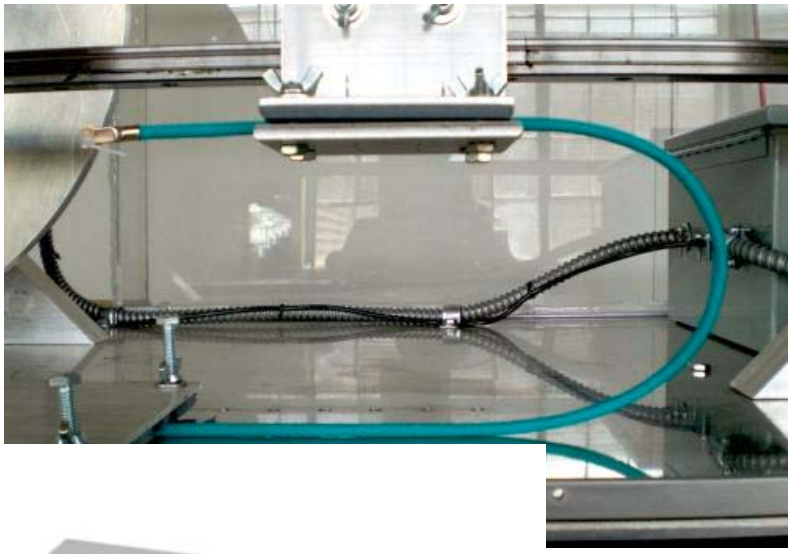
MULTIDISCIPLINARY

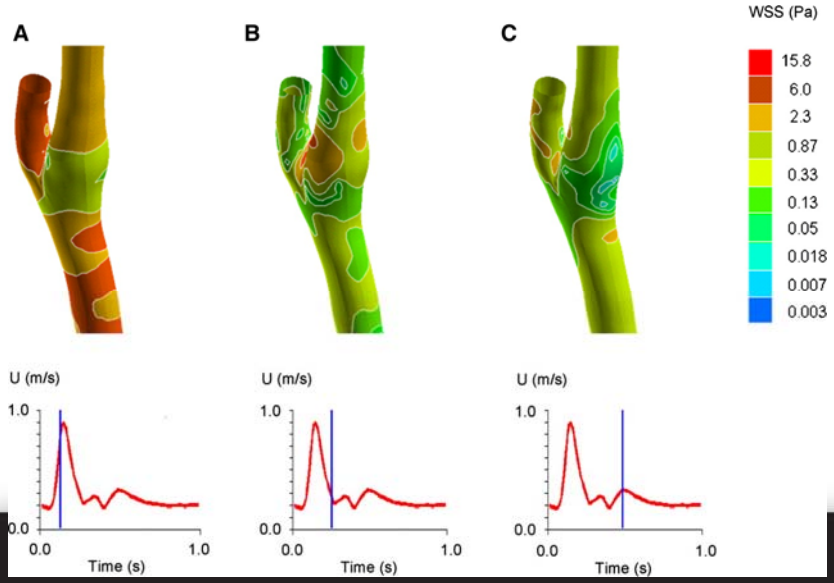
- Bench Testing
  - Fatigue testing
  - Accelerated wear testing
  - Dynamic failure mode
  - Stress/Strain curves
  - Failure Modes and Effects Analysis
  - Pressure/Flow
  - Flex testing
  - …..and more!
- Human Factors
- Computational Modeling
  - Finite element analysis
  - Shear stress
  - Fluid dynamics
- Animal Model
  - Biocompatibility/Genotoxicity
  - Implant/delivery testing
  - Histology
  - Pathology
- Trial Design
  - Clinical Endpoints
  - Sample size
  - Power
  - Significance
  - Human Factors
- Patient protection
  - Informed consent
  - Ethics of trial participation






Steel
Nitinol
Stress
Strain

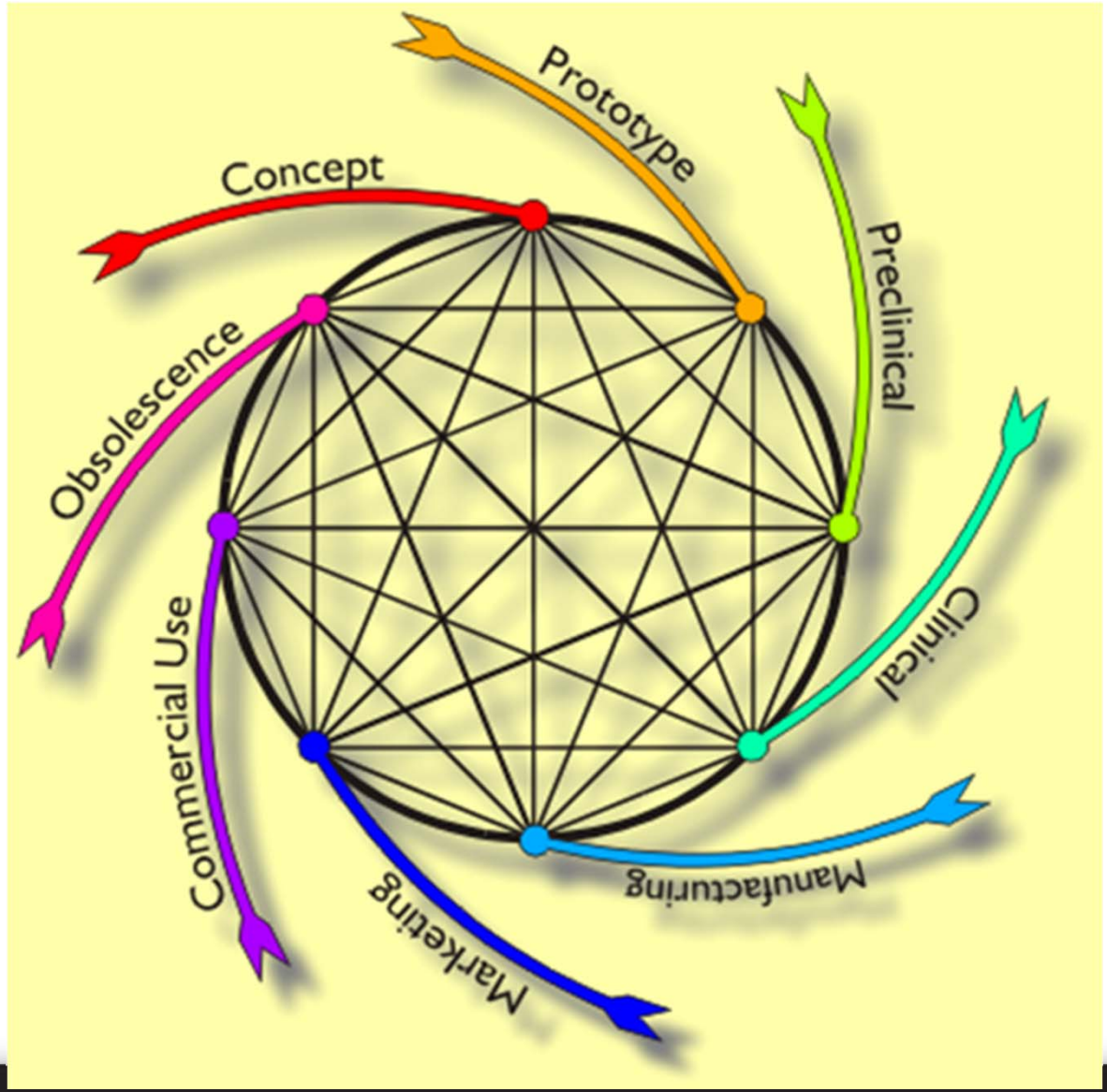



A
B
C
WSS (Pa)
15.8
6.0
2.3
0.87
0.33
0.13
0.05
0.018
0.007
0.003
U (m/s)
1.0
0.0
0.0
1.0
Time (s)

LOTS OF DATA, LOTS OF PEOPLE

- Review Team
  - Lead Reviewer
  - Scientific reviewers (engineers, scientists – multidisciplinary)
  - Medical Officers (physicians, veterinarians)
  - Statisticians (biostatisticians from OSB)
  - Consultants from CDER, CBER (combination products)
  - Nurses
  - Epidemiologists
  - Manufacturing
- Experienced versus Inexperienced
- Regulator versus Innovator

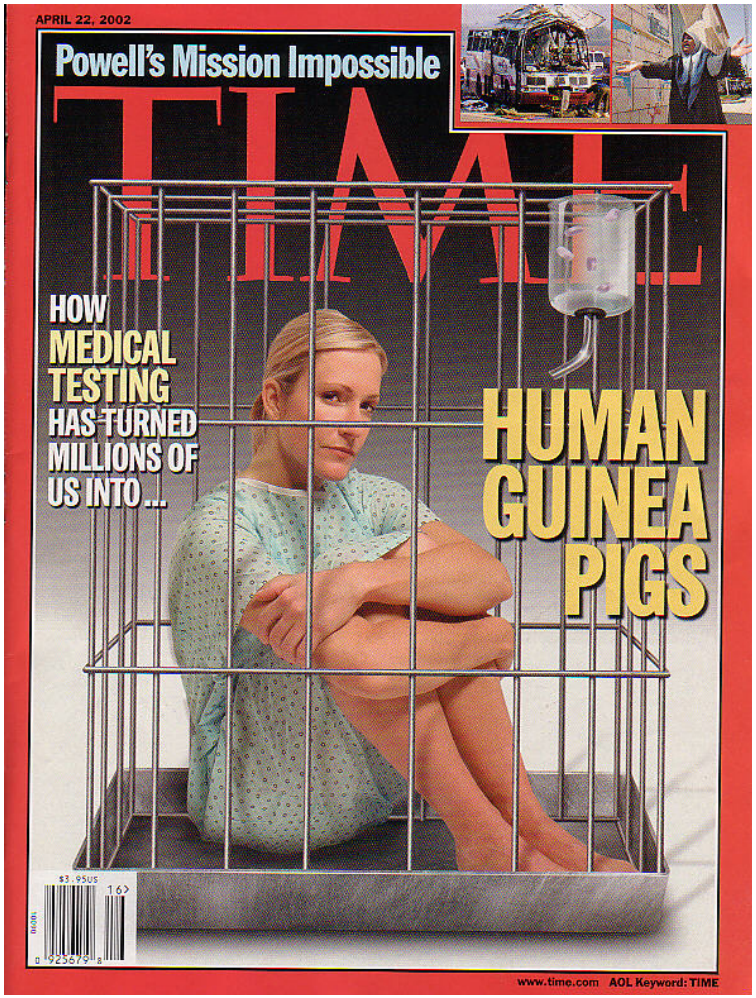
BENCH TO BEDSIDE – TOTAL PRODUCT LIFE CYCLE



CURRENT PARADIGM

- Pre-Clinical
  - Bench Testing
  - Animal
  - Computational
- Clinical Study
  - Feasibility
  - Pivotal

CAN YOU GET THERE FASTER?



SHIFTING THE PRE-CLINICAL PARADIGM

- Pre-clinical testing
  - Challenge: Accelerated wear test takes too long
  - Solution: Begin clinical study while certain pre-clinical tests are ongoing
- Computational Modeling (Personalized Medicine)
  - Challenge: Few patients in which to test device and make changes
  - Solution: Leverage computational modeling to design devices, assess in patients in early feasibility trial, and pursue any changes

SHIFTING THE CLINCAL AND POST-MARKET PARADIGM

- Clinical Study
  - Challenge: Unreasonable to conduct large patient study
  - Solution: Conduct clinical study and assess additional data in a post-market study
- Post-market
  - Challenge: Limited post-market data available because device is used off-label
  - Solution: Submit data from existing registry in support of label expansion


MEDICAL DEVICE ECOSYSTEM
Manufacturer
Clinician
FDA
Patient

THE FUTURE

- Changing paradigm for pre-clinical/clinical requirements prior to approval
- Consider transfer of some risk assessment from FDA/government to patients (need appropriate education plan
- Leverage post-market data into an approval package
- Encouragement for first in human, FIRST in US
- Globalization and greater acceptance of OUS data
- Improved alignment with other organizations (Centers for Medicare and Medicaid Services, professional societies, etc.)

SUMMARY - LEAST BURDENSOME PATH TO MARKET

- Talk to FDA – early and often
- Need to know versus want to know
- Plan a reasonable strategy – EARLY

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Thank you!

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