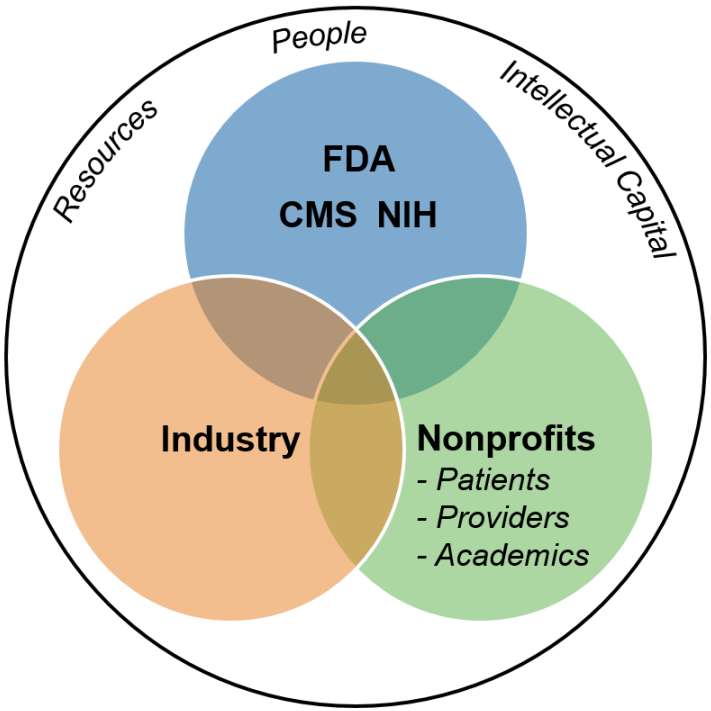
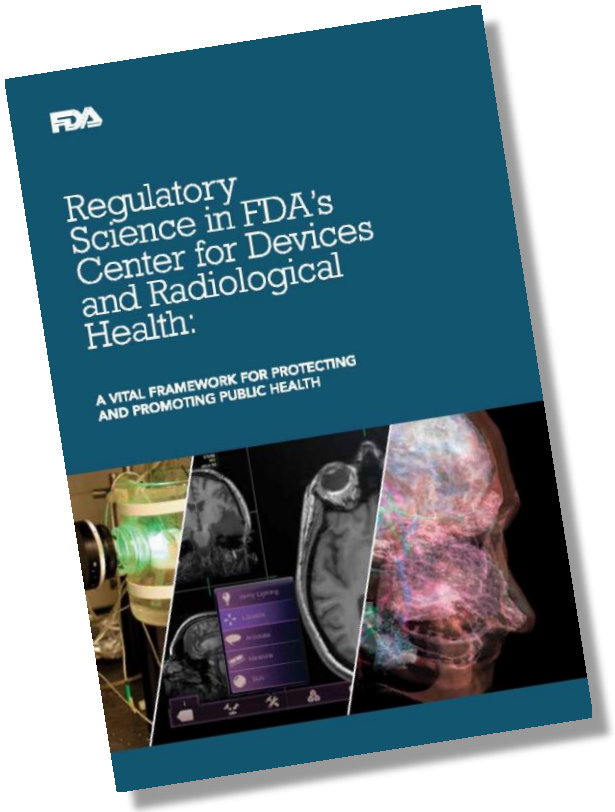
Public-Private Partnership
collaborating on Regulatory Science
to make patient access to new medical device technologies
faster, safer and more cost-effective



MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM
ALIGN | ACHIEVE | ACCELERATE

Dawn Bardot, PhD
Senior Program Manager

What is Regulatory Science?



The science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products

- *Benefits patients by speeding the rate of important technologies reaching market*
- *Reduces time and resources needed for device development, assessment, and review. For example:*
  - *Can lead to quicker, more efficient device approvals*
  - *Can decrease the size and duration of pre-market clinical trials*

Faster, Safer, More Cost-effective

FDA Strategic Plan, August 2011
Advancing Regulatory Science at FDA

MDIC Membership Roster

1. Abbott Vascular
2. Abiomed, Inc
3. ACRP
4. AdvaMed
5. Advanced Bionics
6. AIMBE
7. ANSYS
8. B. Braun Medical
9. BD
10. Boston Scientific
11. Cardiovascular Research Foundation, Skirball Center
12. CD-adapco
13. CMS
14. Cook Group, Inc
15. Creganna-Tactx Medical
16. CVRx
17. Cyberonics
18. Edwards Lifesciences Foundation
19. Exponent, Inc.
20. FasterCures
21. FDA
22. Focused Ultrasound Foundation
23. Global Center for Medical Innovation
24. HeartFlow, Inc
25. Holaira
26. ICON plc
27. Immucor, Inc
28. Integra Lifesciences
29. IT'IS-USA
30. Johnson & Johnson
31. LifeScience Alley
32. MDMA
33. Medtronic
34. NIH
35. NORD
36. NVCA
37. NAMSA
38. NxThera, Inc
39. PCORI
40. The Pew Charitable Trusts
41. SIMULIA
42. Southern Research Institute
43. St. Jude Medical
44. Stryker Corp.
45. Sysmex Americas, Inc
46. Terumo BCT
47. Vital Images, Inc
48. W.L. Gore & Associates

Updated 6/2/15

Project Initiatives

Clinical Trial Innovation & Reform

Goal: Improve the function of the clinical trial process while increasing efficiency and utility through a Total Product Lifecycle (TPLC) framework

MDIC:
Board Champion| Rick Kuntz, MD
Senior VP & Chief Scientific, Clinical & Regulatory Officer| Medtronic
Program Manager | Stephanie Christopher | MDIC

FDA:
Primary Investigator | Bram Zuckerman, MD | Supervisory Medical Officer | Office of Device Evaluation (ODE)
Primary Investigator | Kathryn O'Callaghan | Health Scientist| Office of the Center Director | Center for Devices and Radiologic Health (CDRH)

Patient Centered Benefit-Risk Assessment

Goal: Develop a framework for incorporating patient preferences into B/R assessment

MDIC:
Board Champion | Ross Jaffe, MD
Director | Versant Ventures, and
Managing Director | National Venture Capital Association
Program Manager | Stephanie Christopher | MDIC

FDA:
Primary Investigator | Randall Brockman, MD | Chief Medical Officer | Office of Device Evaluation (ODE)
Primary Investigator | Robert Becker, MD | Medical Officer | Office of In Vitro Diagnostics & Radiological Health (OVD)

Computer Modeling & Simulation

Goal: Increase confidence in safety and efficacy, reduce clinical trial size and accelerate device review through regulatory grade computer models & simulations

MDIC:
Board Champion| Randy Schiestl
VP, Global Operations & Technology | Boston Scientific
Senior Program Manager | Dawn Bardot, PhD | MDIC

FDA:
Primary Investigator | Kyle J. Myers, PhD | Director, Division of Imaging, Diagnostics and Software Reliability Applied Mathematics | Office of Science & Engineering Laboratories (OSEL)

Clinical Trial Innovation & Reform

Early Feasibility Studies (EFS)

MDIC

MEDICAL DEVICE INNOVATION CONSORTIUM

ALIGN | ACHIEVE | ACCELERATE

Definition

Early Feasibility Study

- Small number of study subjects
- Device may be early in development, typically before the device design has been finalized
- May involve a new intended use for a device that has already been in clinical use
- May be done before, after, concurrently, or in conjunction with non-US studies

Slides provided by Dorothy Abel, FDA

2014-2015 CDRH Strategic Priority

EFS Specific

Goal - Increase the number of early feasibility/first-in-human IDE studies submitted to FDA and conducted in the U.S.

Target - By June 30, 2015, increase the number of early feasibility/first-in-human IDE studies submitted to each premarket Division compared to FY 2013 performance.

Slides provided by Dorothy Abel, FDA

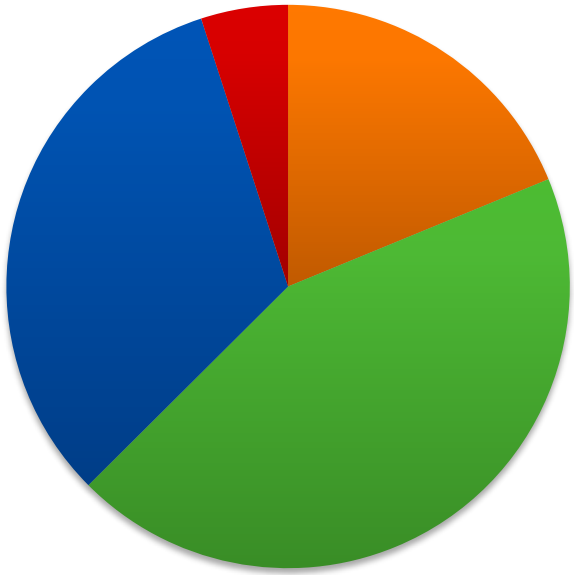
Components of the EFS Guidance

- Targeting approval for an Early Feasibility Study IDE Application
- Report of Prior Investigations
- Investigational Plan
- Iterations during early feasibility studies
- Design Controls
- Extensive appendices with examples

Results from MDIC EFS Survey

The FDA early feasibility guidance document introduces new approaches to facilitate timely device and clinical protocol modifications during EFS including 5-day notice expanded application, contingent approval option and interactive review.

Based on your experience with medical device development, what is your feeling about EFS in the US now that the new guidance has been issued?



- **a. I would be interested in pursuing EFS first in the US based on the increased clarity in the guidance document.**
- **b. I would like to "test the waters" in the US and try Early Feasibility Studies but will pursue parallel pathways in the US and OUS to minimize risk.**
- **c. I would like to see others document success with the program prior to committing, as the risk for failure may delay my device approval for a larger IDE.**
- **d. I would not initiate EFS in the US because other challenges persist beyond the regulatory aspect.**

Results from MDIC EFS Survey

Do you feel that your (regulatory) team is well aware and informed about the regulatory changes implemented for EFS (i.e., what qualifies a EFS, whom to contact at FDA, interactive review process, etc…).

- **a. Yes, we are very well versed and are very familiar with the new process.**
- **b. We have some knowledge but will certainly benefit from more information/education.**
- **c. No, we are not. We would like to know more.**

MDIC Blueprint for Early Feasibility Study Success

Draft in progress

- A tool to help sponsors and investigators approach and plan a US-based Early Feasibility study
- Blueprint topics include:
  - Planning phase
  - Execution phase:
    - Protocol Design and Investigational Plan
    - Regulatory: Your interactions with FDA
    - Protection of Human Subjects: Your Interactions with Institutional Review Boards (IRB)
    - Legal/IP considerations
    - Other logistical consideration (Insurance, reimbursement, site selection)
    - Support and Funding Opportunities through NIH
    - Patient Early Access to Novel Technologies
  - Appendices (including a link to the FDA guidance)

Resources

- FDA EFS Guidance
  - http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm279103.pdf
- FDA EFS overview slides with FDA contacts
  - http://www.fda.gov/downloads/Training/CDRHLearn/UCM371840.pdf
- FDA Q-Sub Guidance: requests for FDA feedback
  - http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf

Patient Centered Benefit-Risk

MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM
ALIGN | ACHIEVE | ACCELERATE

MDIC PCBR Framework Report

Available for download

- "*A Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology*"
  - Overarching report of MDIC Patient Centered Benefit-Risk Project
  - Resource for CDRH, MDIC members, and industry on when and how to collect patient preference information for incorporation into the regulatory process
  - Incorporates Catalog of Methods as appendix

Resources

- FDA Patient Preference Draft Guidance
  - http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM446680.pdf?source=govdelivery&utm_medium=email&utm_source=govdelivery
- FDA Benefit Risk Guidance
  - http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm296379.pdf
- MDIC A Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology
  - http://mdic.org/wp-content/uploads/2015/05/MDIC_PCBR_Framework_Web.pdf

Computer Modeling and Simulation

MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM
ALIGN | ACHIEVE | ACCELERATE

Neurostimulation Working Group

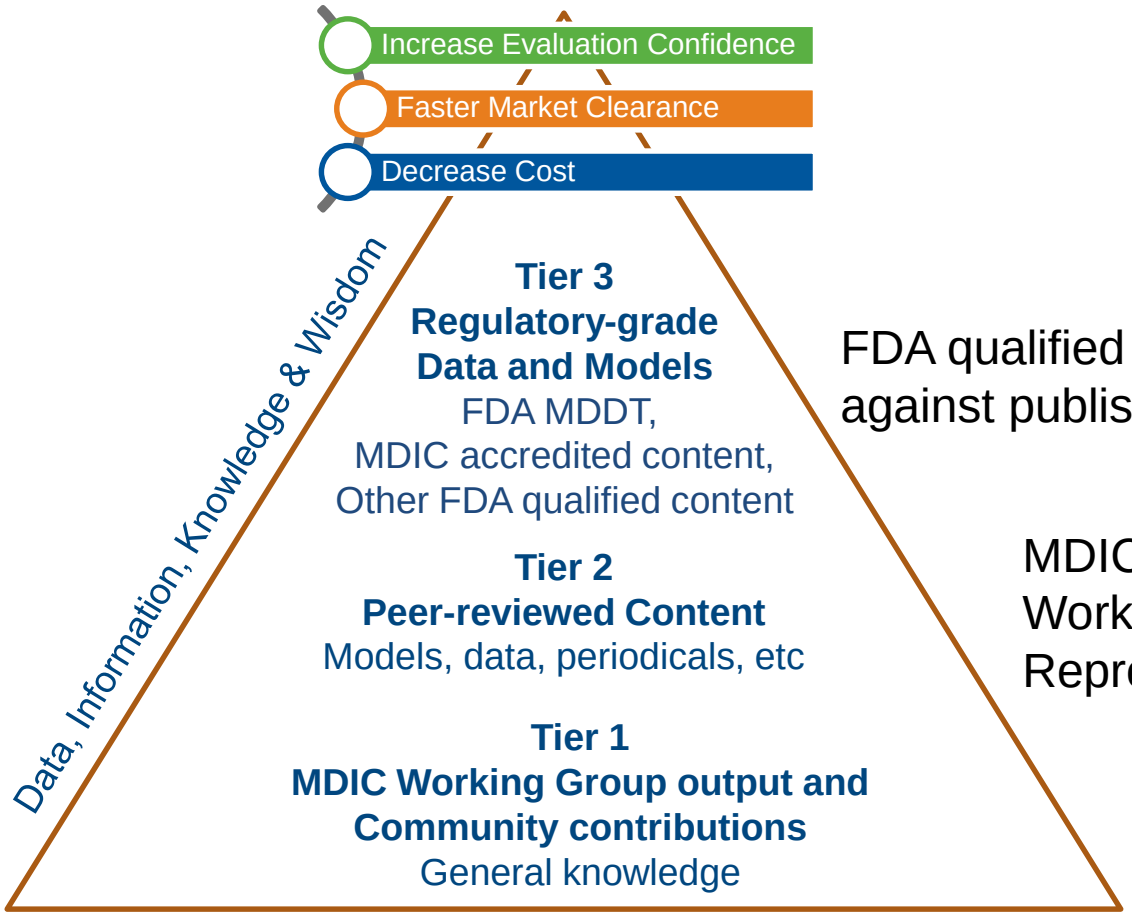
- **Mission:** an improved understanding of safety criteria for electrical stimulation of neural tissue. The goal of this work is to better understand the mechanism(s) of damage and provide directions for safety considerations; both with respect to electrode design and evaluation methods.

- **IP:** all work is precompetitive, not focused on devices from any particular manufacturer and work output will be placed in the public domain through publications

- **MDIC Collaborator-in-Residence**: Postdoctoral fellow working within OSEL laboratory at the FDA and supervised by CDRH/OSEL Dr. Pavel Takmakov.

Library Infrastructure for Data and Models

Phase 1 construction underway



FDA qualified or MDIC panel accredited against published standards

MDIC Journal with Editor and AEs, Working Group and Academic Representation, DOI Number

MDIC Working Groups and Community

Resources

- FDA Medical Device Development Tools Draft Guidance
  - http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM374432.pdf
- Follow MDIC
  - http://mdic.org/subscribe/