# History & Structure of the Cardiac Safety Research Consrtium (CSRC)

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**Duke University Medical Center**

***Director, eECG Core Laboratory***

***Co-Director, CSRC***

**Duke Clinical Research Institute**

# CSRC History & Structure:
## *Presentation Overview*

- Background & Mission of CSRC
- CSRC Organization
- CSRC Activities

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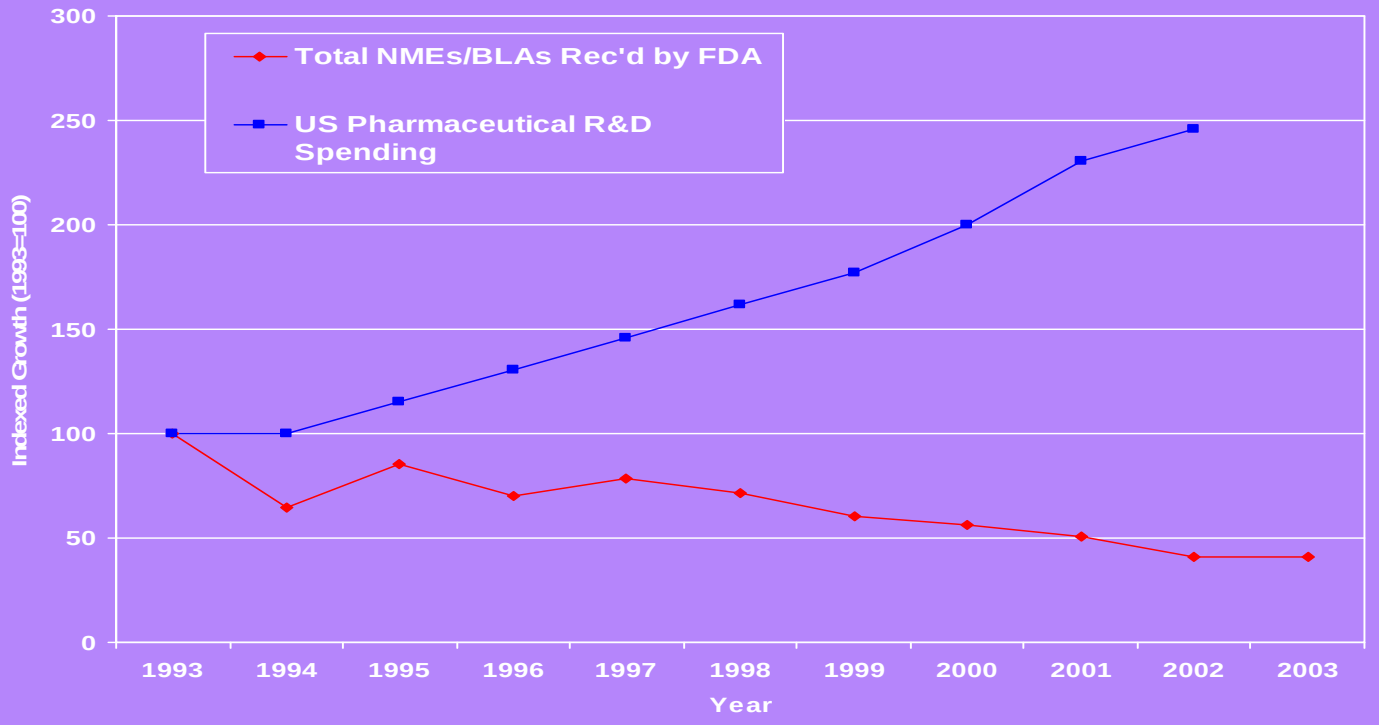
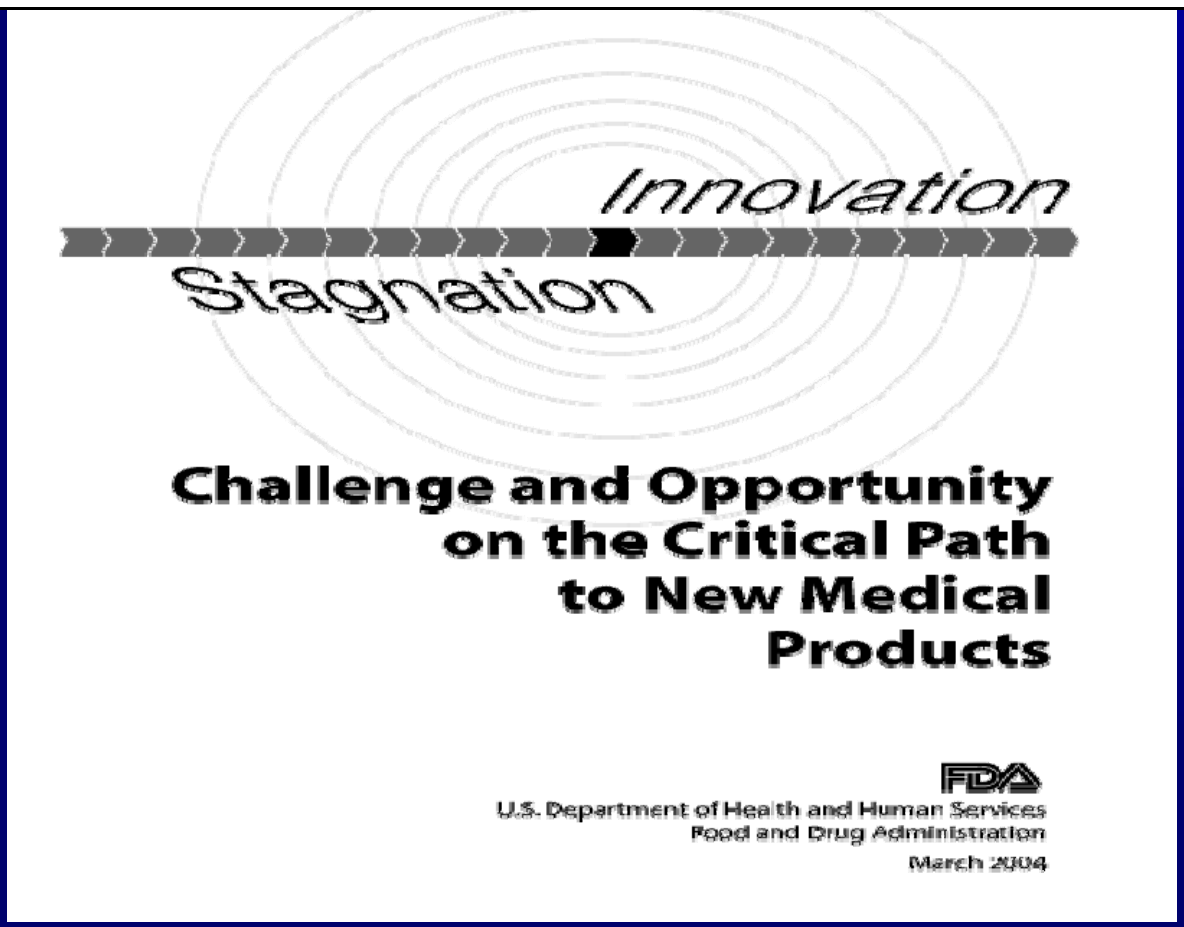
# Rising Costs, Slowing Innovation

## Trends in R&D Spending vs. New Drug & Biologic Applications



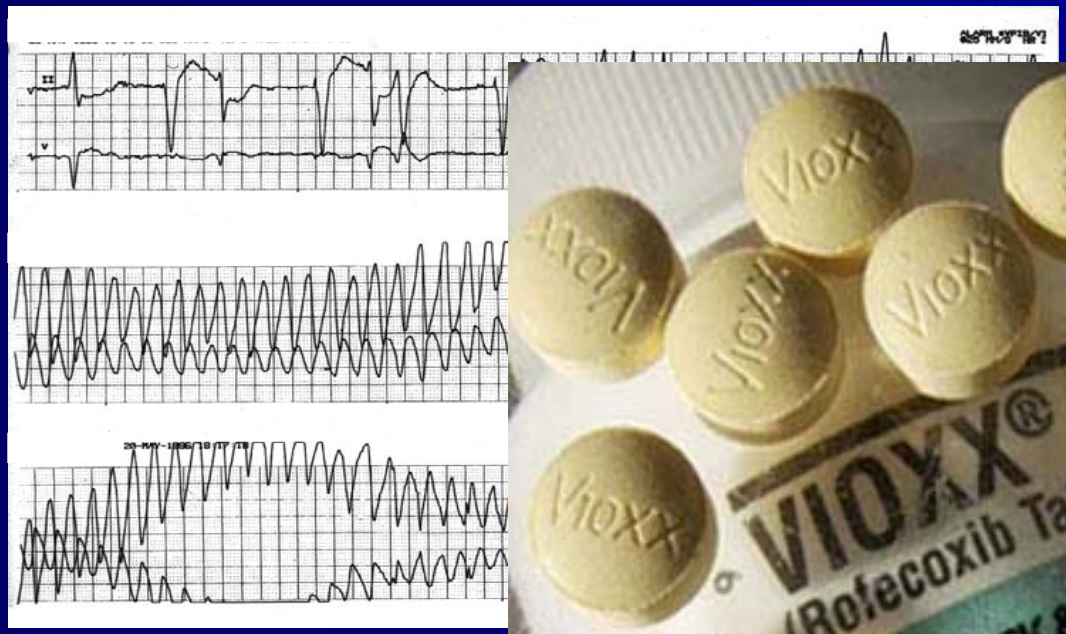
# Critical Path Initiatives: March 2004

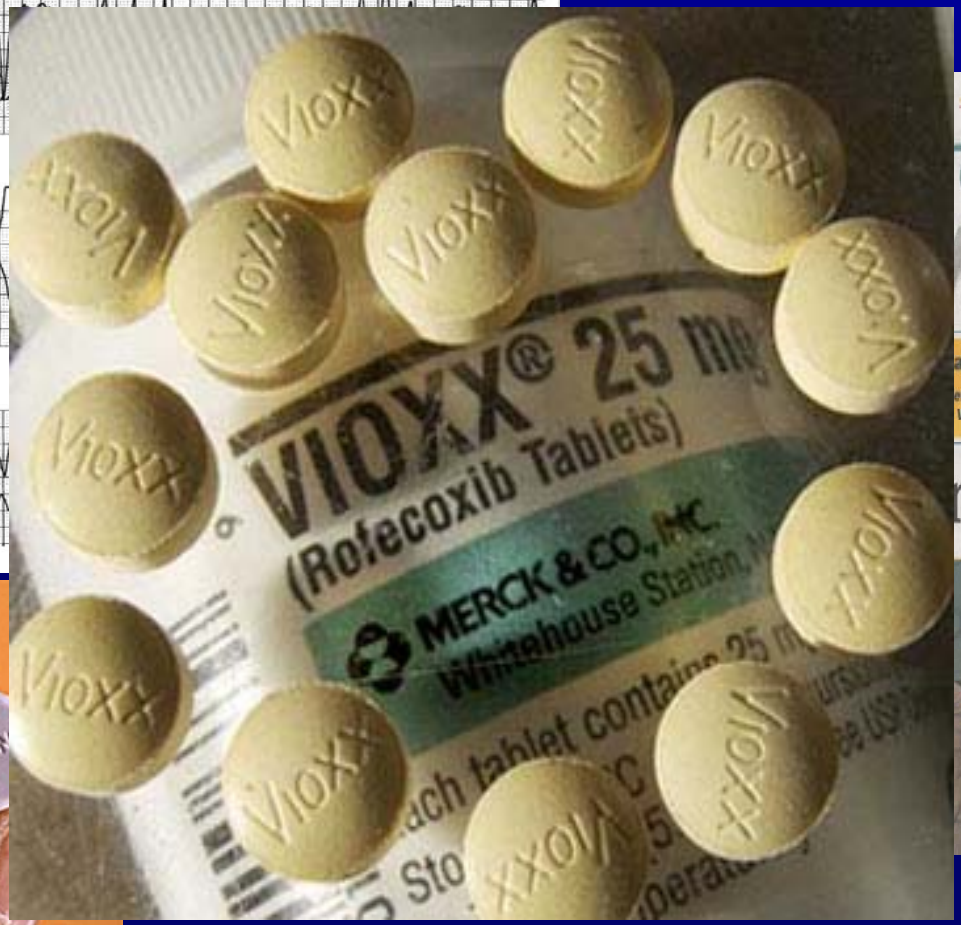
**http://www.fda.gov/oc/initiatives/criticalpath/**



# Cardiac Safety:

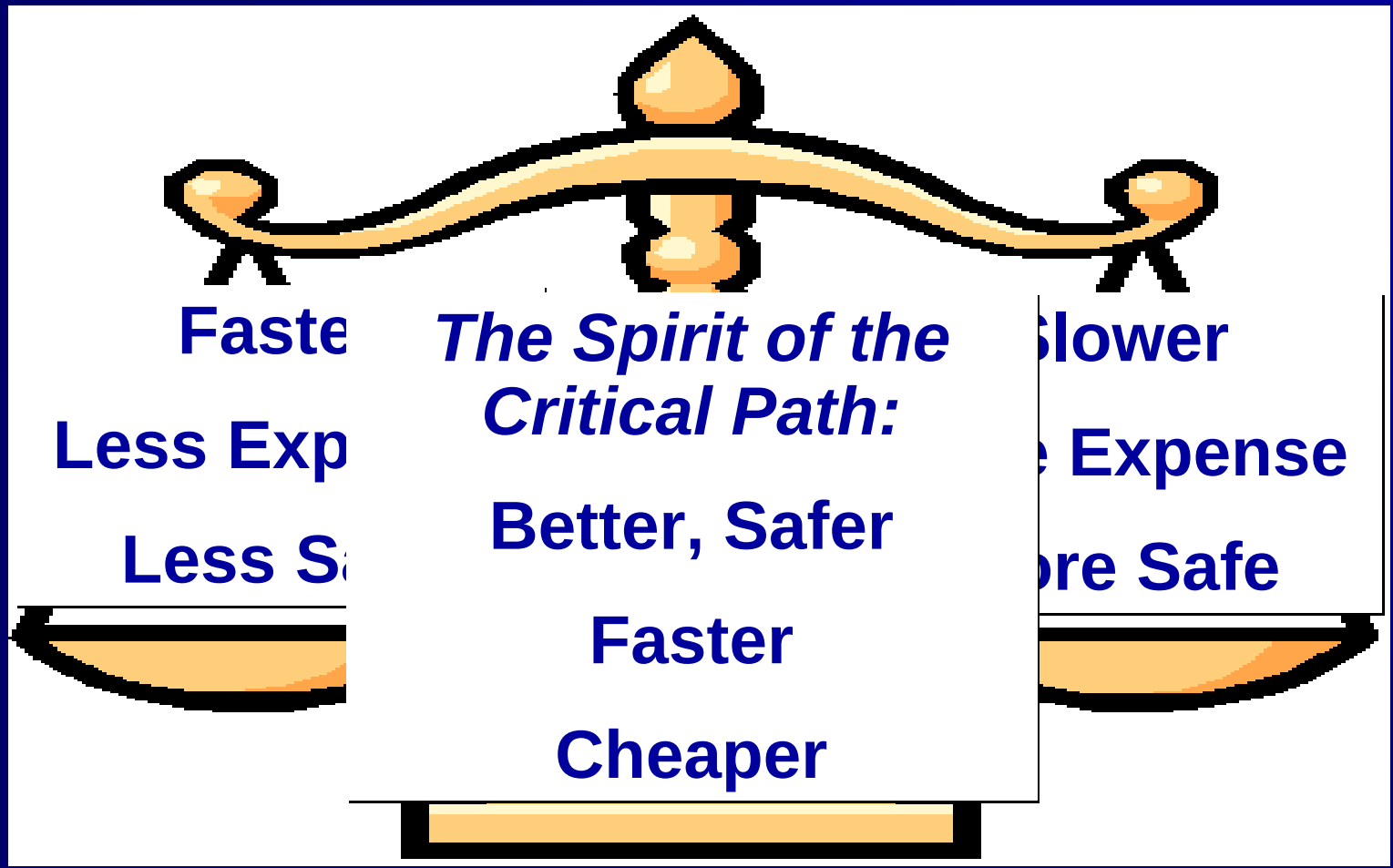
## *Evaluating rare but catastrophic events.*





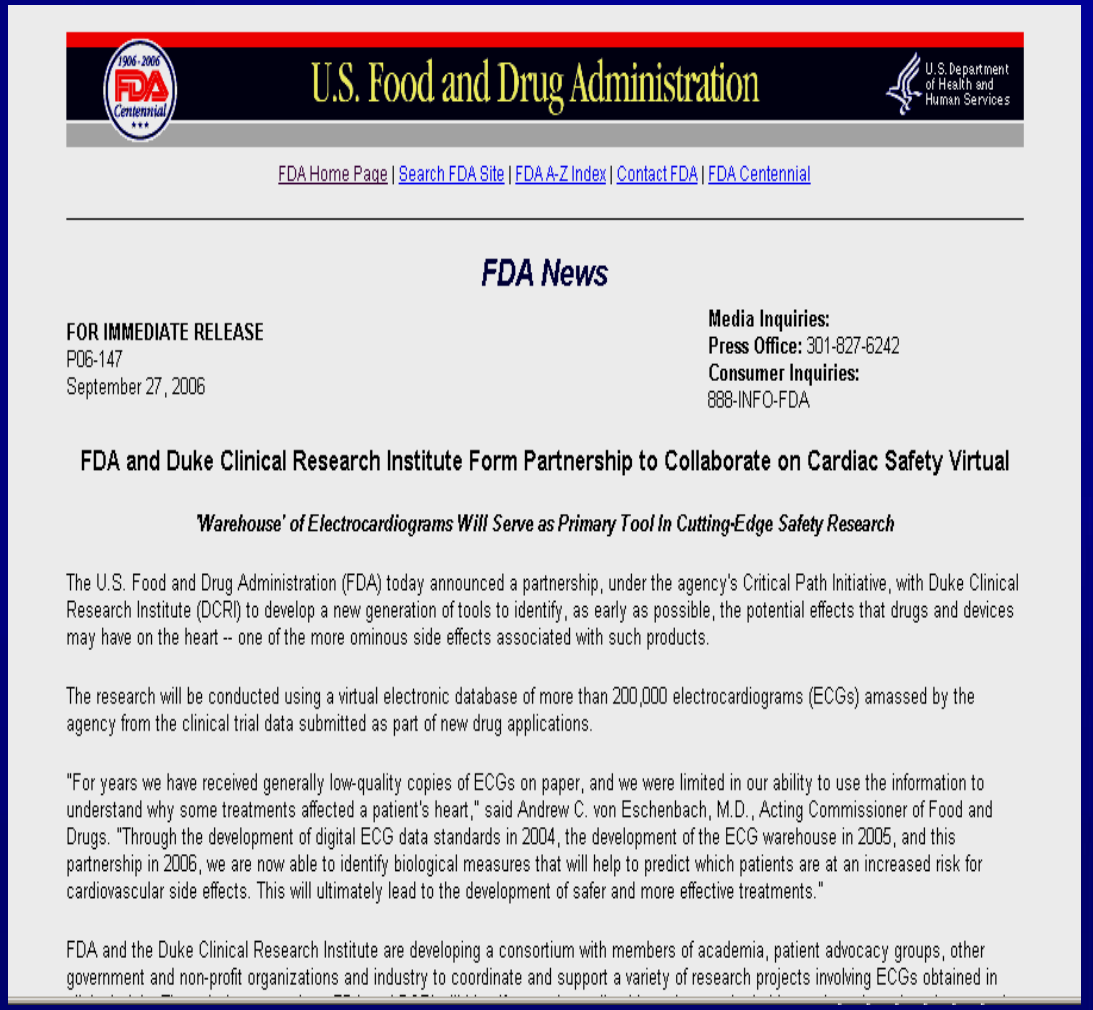


# The Paradox Illusion:
## *Advancing Medicine vs. Protecting Public Safety*



# 2006 FDA – Duke Memorandum Of Understanding (MOU)

- Leverage resources / expertise
- Public/Private Partnership (PPP)
- Advance pre-competitive assessment tools
- Advance public health
- www.cardiac-safety.org



U.S. Food and Drug Administration

U.S. Department of Health and Human Services

FDA Home Page | Search FDA Site | FDA A-Z Index | Contact FDA | FDA Centennial

**FDA News**

**FOR IMMEDIATE RELEASE**
P06-147
September 27, 2006

**Media Inquiries:**
**Press Office:** 301-827-6242
**Consumer Inquiries:**
888-INFO-FDA

**FDA and Duke Clinical Research Institute Form Partnership to Collaborate on Cardiac Safety Virtual**

*'Warehouse' of Electrocardiograms Will Serve as Primary Tool In Cutting-Edge Safety Research*

The U.S. Food and Drug Administration (FDA) today announced a partnership, under the agency's Critical Path Initiative, with Duke Clinical Research Institute (DCRI) to develop a new generation of tools to identify, as early as possible, the potential effects that drugs and devices may have on the heart -- one of the more ominous side effects associated with such products.

The research will be conducted using a virtual electronic database of more than 200,000 electrocardiograms (ECGs) amassed by the agency from the clinical trial data submitted as part of new drug applications.

"For years we have received generally low-quality copies of ECGs on paper, and we were limited in our ability to use the information to understand why some treatments affected a patient's heart," said Andrew C. von Eschenbach, M.D., Acting Commissioner of Food and Drugs. "Through the development of digital ECG data standards in 2004, the development of the ECG warehouse in 2005, and this partnership in 2006, we are now able to identify biological measures that will help to predict which patients are at an increased risk for cardiovascular side effects. This will ultimately lead to the development of safer and more effective treatments."

FDA and the Duke Clinical Research Institute are developing a consortium with members of academia, patient advocacy groups, other government and non-profit organizations and industry to coordinate and support a variety of research projects involving ECGs obtained in

# CSRC Mission

**To advance scientific knowledge on cardiac safety for new and existing medical products by building a collaborative environment based upon the principles of the FDA's *Critical Path Initiative* as well as other public health priorities.**

# CSRC Objectives

- To facilitate focused pragmatic research that will inform regulatory processes
- To create common nomenclature, standards, and draft medical product development strategy documents related to cardiac safety evaluation
- To develop knowledge and improve the evaluative sciences in relation to cardiac safety and product development
- To establish infrastructure and operational processes to support all objectives

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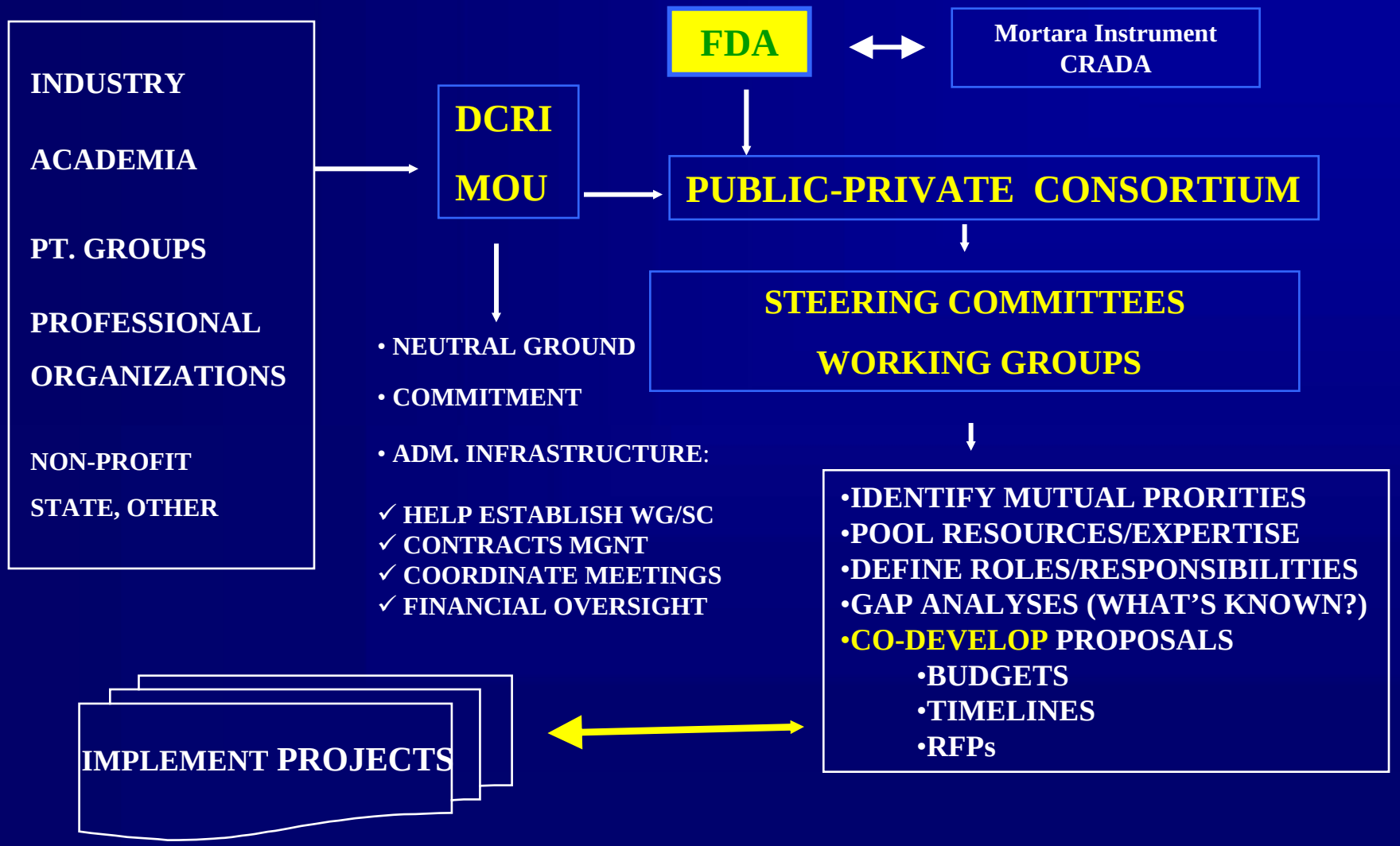
# PPP COLLABORATION MODEL



# CSRC Committee Structure

- **Executive Committee**
- **Membership Committee**

  ***(Dan Bloomfield, Theressa Wright)***
- **Scientific Oversight Committee**

  ***(Phil Sager, Ben Eloff)***
  - ***Research Teams:***

    **Project planning & execution (Team chairs)**
    **White papers (John Finkle, Cook Uhl)**

# CSRC Executive Committee

- ***Co-Directors:***
  - Mitch Krucoff – Duke
  - Dan Bloomfield – Merck
- ***Committee:***
  - Paul Kligfield – Cornell
  - John Finkle - GSK
  - Philip Sager – CardioDx
  - Justin Mortara – Mortara Instr
  - Theressa Wright—Eli Lilly
  - Cindy Green--Duke
- ***FDA Liasons:***
  - Norm Stockbridge—CDER
  - Wendy Sanhai—OC
  - Ben Eloff—OC
  - William McFarland--CDRH
- ***Operations:***
  - Valarie Morrow—Duke

# CSRC Membership: New DRAFT Proposal

- **Levels & Categories of Membership:**
  - Founding, Full, Associate
  - Corporation, NFP, Individual
- **Privileges of Membership:**
  - Organizational participation, leadership
  - Meeting discounts
  - “Team” discounts

# Proposal Review Criteria

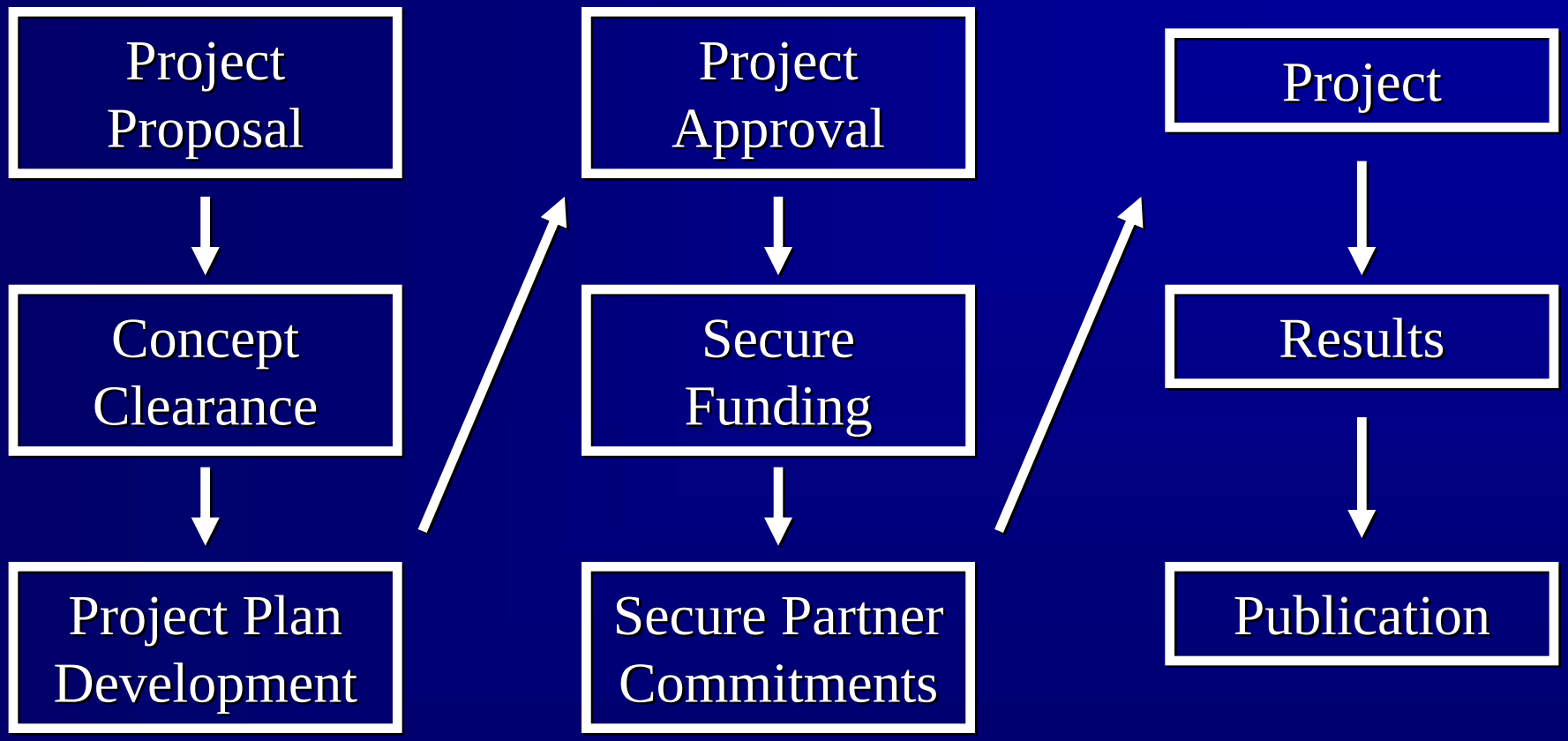
- Collaborative approach
- Scientific importance
- Clinical importance
- Unique
- Regulatory importance
- Feasibility
- Sharing of data
- Funding

**The Cardiac Safety Research Consortium (CSRC)**
**Project Concept Submission Form**

The table will expand to accomodate text as added

| | | |
|---|---|---|
| 1. Title of Project Concept | | |
| 2. Submission Date | | |
| 3. Submitter name, title, email address, and phone number | | |
| 4. Name and address of submitting organization | | |
| 5. Name(s) of other partner organization(s), if Applicable | Name of Organization | Organizational Contact |
| 6. What scientific gap/public health need is addressed by this project? | | |
| 7. What technologies are addressed by this project (ECG, imaging, molecular, genetic, etc.)? | | |
| 8. Has the proposed concept received any formal review? If so by whom? | | |
| 9. What is the estimated budget for the project? Please include specific resource and research needs. | | |
| 10. Will this project be self funded? Please identify known and potential funding partners. Are firm commitments made? Are any funds being requested from the consortium? | | |

# CSRC SOC Project Review Process



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# CSRC SOC Research Team Focal Point Areas

- **ECG safety signals:**
  - QT
  - Non-QT
- **Cardiac markers**
- **Blood pressure**
- **Genetics**
- **Unique compounds**
- **Unique patients:**
  - Pediatrics
  - Diabetes

- **Special “incubator” areas:**
  - **DES-DAPT**
  - **Atrial fibrillation ablation**
  - **Rheologic drugs & bleeding**

# CSRC: Educational/Informational "Thinktanks"


Cardiac Safety and the Critical Pathway Initiative Think Tank - October 11, 2005

- Collect expertise
- Spontaneous dialogue
- Share ideas
- Identify needs
- Cultivate interest
- Develop novel directions
- Produce white papers

# Medical Product Development Strategy Consensus Documents

Progress in Cardiology

## Assessing proarrhythmic potential of drugs when optimal studies are infeasible

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Christi
Peter R.
Shari L.
*and Wy*
*Ottawa,*

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Cardiac Safety Research Consortium Conference

## Current challenges in the evaluation of cardiac safety during drug development: Translational medicine meets the Critical Path Initiative

Jonathan P. Piccini, MD, MHS,[a] David J. Whellan, MD, MHS,[b] Brian R. Berridge, DVM, PhD,[c] John K. Finkle, MD,[d] Syril D. Pettit, MEM,[e] Norman Stockbridge, MD, PhD,[f] Jean-Pierre Valentin, PhD,[g] Hugo M. Vargas, PhD,[h] and Mitchell W. Krucoff, MD[a], for the CSRC/HESI Writing Group *Durham and Research Triangle Park, NC;*

**2008 Annual Meeting:**

**CSRC & Health and Environmental Sciences Institute (HESI): Pre-clinical & Clinical Cardiac Safety Models**

# CSRC: Educational/Informational Programs


Cardiac Safety and the Critical Pathway Initiative Think Tank - October 11, 2005

Registration: 7:00–8:00 am | Program: 8:00 am–4:30 pm

- Collect expertise
- Share ideas
- Produce white papers

**Beyond thinktanks: Incubator environments to mobilize unique public health interest collaborations related to cardiac safety**

Pre-Session: Conference Host Welcome and Introduction
Session 1- Critical Path Initiative: Impact on Drug Safety

# CSRC Thinktank-Incubator Launch Programs: *Obligatory Drug-Device Safety Interactions*

- **DAPT-DES:**

***Dual Anti-Platelet Therapy and Drug Eluting Stents***

- **SAFARI:**

***Safety of Atrial Fibrillation Ablation RegIstry***

- **TREAT:**

***Trans-Radial Education, Assessment & Training***

# DAPT-DES Public Health RCT

## Harvard Clinical Research Institute Enrolls First Patients into DAPT Study to Advance Understanding of Dual Antiplatelet Therapy Following Drug-Eluting Stent Procedures

Oct 02, 2009 6:30 AM CDT

***Four-year, Public Health Study to be Conducted Through an Unprecedented Collaboration between Industry, FDA and Academia***

BOSTON-- (BUSINESS WIRE) -- The Harvard Clinical Research Institute (HCRI) announced today that the first patients have been enrolled in the DAPT Study, marking the official initiation of the four-year clinical trial to investigate the duration of dual antiplatelet therapy (DAPT, the combination of aspirin and a thienopyridine/antiplatelet medication to reduce the risk of blood clots) following drug-eluting stent implantations. The large-scale public health study is expected to bring clarity to the global medical community regarding the benefits of 12 versus 30 months of dual

# Safety of Atrial Fibrillation Ablation RegIstry (SAFARI)

FDC REPORTS "The Gray Sheet"

MEDICAL DEVICES, DIAGNOSTICS & INSTRUMENTATION

May 04, 2009
Volume 35 | Number 018 | page 9

**FDA, Cardiac Safety Research Consortium To Develop AF Ablation Registry**

01350180006

**Printed by Benjamin Eloff Firm: FDA Hfd 230 [May 04 2009]**

A consortium of academics, manufacturers and government agencies plans to launch a r
atrial fibrillation ablation registry, based on input from a variety of stakeholders at a meeti
27 and 28 at FDA's White Oak, Md., headquarters.

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FDANEWS DEVICE DAILY BULLETIN

Vol. 6, No. 89 Thursday, May 7, 2009

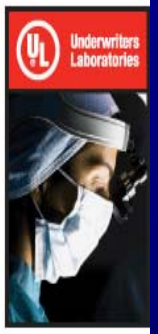
In this issue...

- FDA Plans National Registry to Monitor AF Ablation Safety
- Economy, Government to Slow Growth in Implant Markets
- Bayer Starts Program for Contraceptive Patch
- Device World Daily

**FDA Plans National Registry to Monitor AF Ablation Safety**

A national registry to monitor the safety of atrial fibrillation (AF) ablation procedures and outcomes is in the works and could support evaluations of new devices and reimbursement decisions, according to the FDA. The registry also could serve as a tool for devicemakers conducting postmarket surveillance. The FDA held a joint meeting with the NIH, AdvaMed, the Heart Rhythm Society, the American College of Cardiology, the Cardiac Safety Research Consortium and Duke Clinical Research Institute to examine how to best balance support for innovative devices for AF with an adequate assessment of safety.

Devices & Diagnostics Letter






Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

CARDIAC SAFETY www.cardiac-safety.org

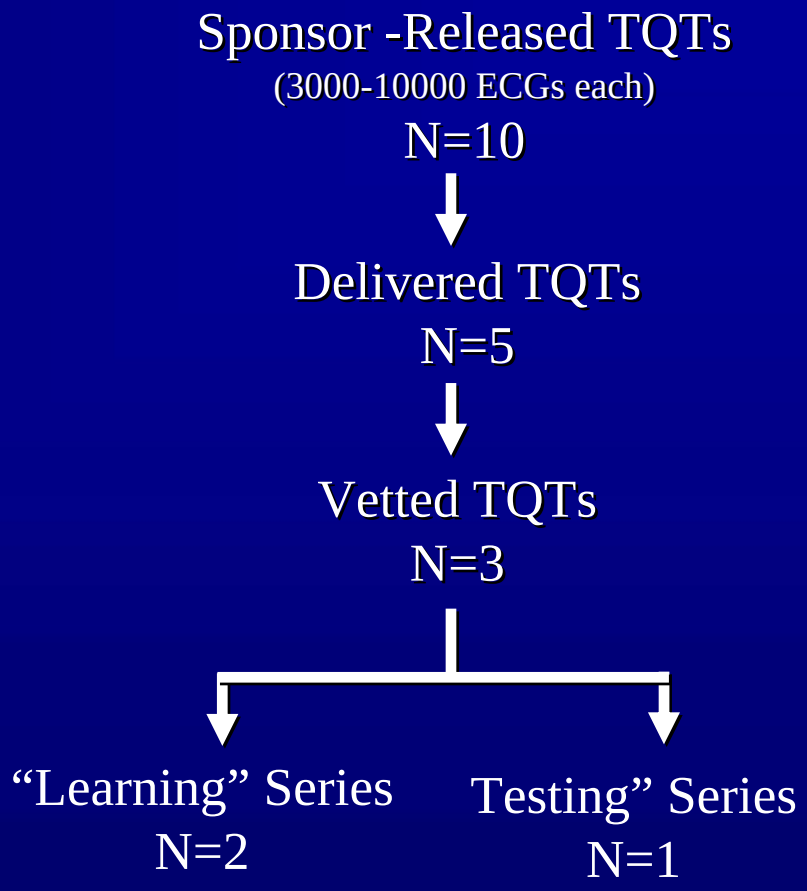
# Trans-Radial Education, Assessment &Training *The TREAT Registry*

***Obligatory Device-Drug Interaction:***

***Impact of device technique on drug safety (bleeding) profiles***

# CSRC QT Warehouse Algorithm Datasets

- "Free the waveforms" data release instrument
- Data contributions:
  - Eli Lilly
  - GlaxoSmithKline
  - Merck
- Construction & management
  - DCRI
  - FDA
  - Mortara Instrument
- SOC approved proposals



# CSRC History & Structure: Conclusion

- CSRC focus includes many pre-competitive aspects of cardiac safety evaluation of new therapeutics
- CSRC structure: PPP with emphasis on collaborative efforts, combining expertise
- CSRC history:
  - 3 years of infrastructure development
  - 2 years of productivity, and GROWING!!!!

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***Professor of Medicine / Cardiology***

**Duke University Medical Center**

***Director, eECG Core Laboratory***

***Co-Director, CSRC***

**Duke Clinical Research Institute**