History & Structure of the Cardiac Safety Research Consortium (CSRC)

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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

- Total NMEs/BLAs Rec'd by FDA
- US Pharmaceutical R&D Spending


Indexed Growth (1993=100)
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

Faster
Less Expense
Less Safe

Slower
More Expense
More Safe

The Spirit of the Critical Path:
Better, Safer
Faster
Cheaper

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Leverage resources / expertise

Public/Private Partnership (PPP)

Advance pre-competitive assessment tools

Advance public health

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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.

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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

- INDUSTRY
- ACADEMIA
- PT. GROUPS
- PROFESSIONAL ORGANIZATIONS
- NON-PROFIT STATE, OTHER

FDA

DCRI MOU

PUBLIC-PRIVATE CONSORTIUM

STEERING COMMITTEES
WORKING GROUPS

- NEUTRAL GROUND
- COMMITMENT
- ADM. INFRASTRUCTURE:
  - HELP ESTABLISH WG/SC
  - CONTRACTS MGNT
  - COORDINATE MEETINGS
  - FINANCIAL OVERSIGHT

- IDENTIFY MUTUAL PRIORITIES
- POOL RESOURCES/EXPERTISE
- DEFINE ROLES/RESPONSIBILITIES
- GAP ANALYSES (WHAT’S KNOWN?)
- CO-DEVELOP PROPOSALS
  - BUDGETS
  - TIMELINES
  - RFPs

Mortara Instrument CRADA

IMPLEMENT PROJECTS

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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
  - Theresa Wright—Eli Lilly
  - Cindy Green—Duke

- **FDA Liaisons:**
  - Norm Stockbridge—CDER
  - Wendy Sanhai—OC
  - Ben Eloff—OC
  - William McFarland--CDRH

- **Operations:**
  - Valarie Morrow—Duke

Duke Clinical Research Institute

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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

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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 accommodate 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

- Project Proposal
- Concept Clearance
- Project Plan Development

- Project Approval
- Secure Funding
- Secure Partner Commitments

- Project
- Results
- Publication

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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

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CSRC: Educational/Informational “Thinktanks”

- Collect expertise
- Spontaneous dialogue
- Share ideas
- Identify needs
- Cultivate interest
- Develop novel directions
- Produce white papers
Assessing proarrhythmic potential of drugs when optimal studies are infeasible

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, David J. Whellan, MD, MHS, Brian R. Berridge, DVM, PhD, John K. Finkle, MD, Syril D. Pettit, MEM, Norman Stockbridge, MD, PhD, Jean-Pierre Valentin, PhD, Hugo M. Vargas, PhD, and Mitchell W. Krucoff, MD, 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
Beyond thinktanks: Incubator environments to mobilize unique public health interest collaborations related to cardiac 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*

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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
SAFE INTHE PATIENT POPULATION.
Trans-Radial Education, Assessment & Training

The TREAT Registry

Obligatory Device-Drug Interaction:

Impact of device technique on drug safety (bleeding) profiles

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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

Sponsor -Released TQTs (3000-10000 ECGs each)
  - N=10
  - Delivered TQTs
    - N=5
  - Vetted TQTs
    - N=3

“Learning” Series
  - N=2

“Testing” Series
  - N=1

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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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