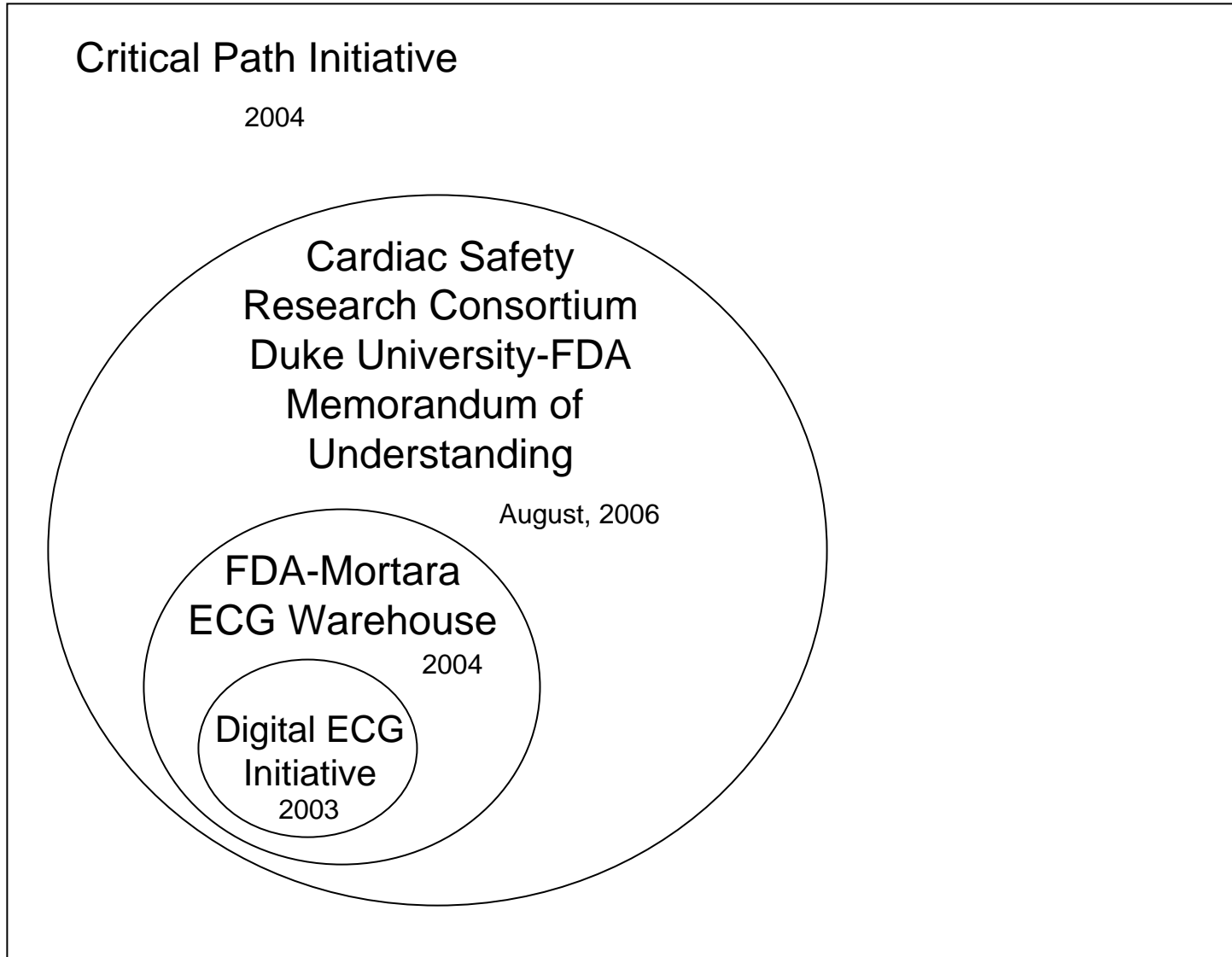


# CSRC AS A PUBLIC-PRIVATE PARTNERSHIP



# CSRC EVOLUTION

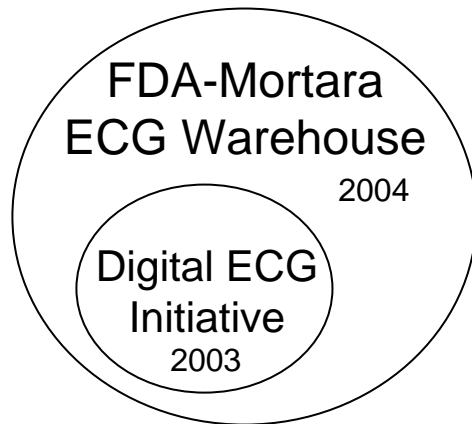


Industry/CRO submission  
of ECG measurements in  
support of drug safety

Digital ECG  
Initiative  
2003

Increasing FDA and Industry attention  
on the use of QT interval prolongation  
as a surrogate marker for the  
arrhythmogenic potential of new  
drugs

# CSRC EVOLUTION



CRATA agreement between FDA and Mortara Instrument for storage and management of digital ECG submissions

# CSRC EVOLUTION



## Critical Path Initiative 2004-

Developed by FDA to establish greater collaboration between regulators, academics, physicians, and scientists from industry. The spirit of the collaboration is intended to create opportunities by sharing existing knowledge and data that will facilitate the enhancing, refining, and ultimately improving of the process used to evaluate new medical products. A central tenet of the critical path is a focus on the evaluative science of the approval process, including both efficacy and safety measures.

# CSRC EVOLUTION



## Critical Path Initiative

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

Bethesda North Marriott and Convention Center

- October, 2005
  - CSRC launched at Cardiac Safety Critical Path Initiative Think Tank meeting
- December, 2005
  - Executive Committee formed
- January, 2006
  - Structure initiated
- August, 2006
  - CSRC MOU signed

# CSRC EVOLUTION

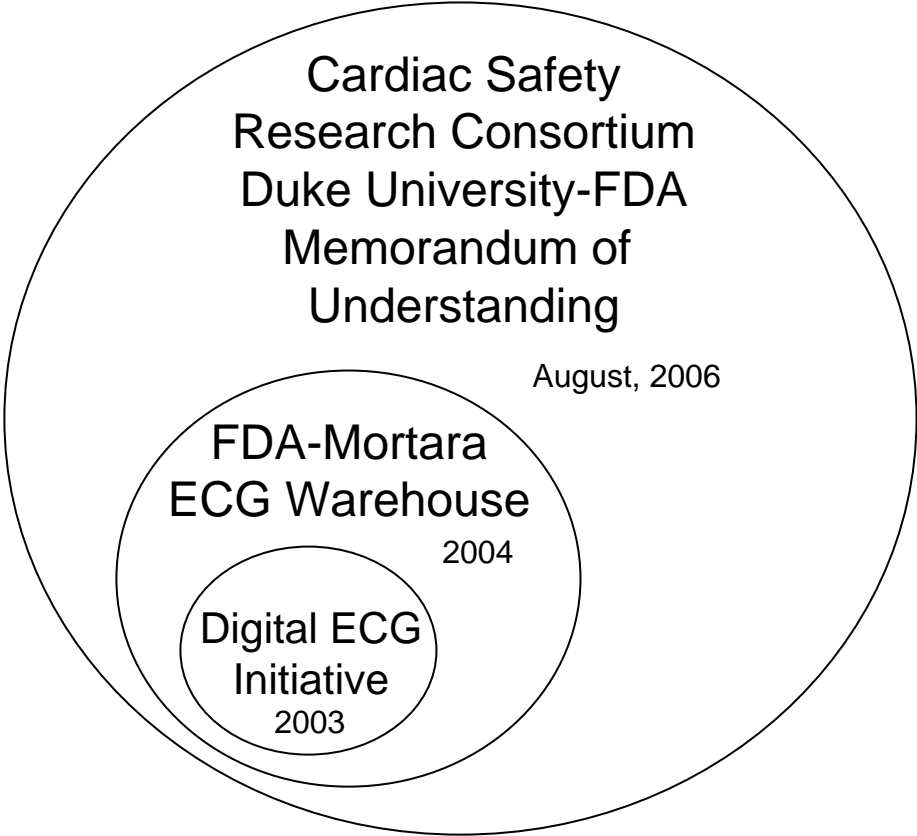
## Critical Path Initiative

### *FDA-Duke Memorandum of Understanding August, 2006*

- Leverage resources and expertise
- Work with partners
  - Public
  - Private
- Promote research
- Develop pre-competitive diagnostic and assessment tools
- Advance public health



# CSRC EVOLUTION



 U.S. Food and Drug Administration 

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**FDA News**

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

**Media Inquiries:**  
Press Office: 301-627-6242  
Consumer Inquiries:  
888-INFO-FDA

**FDA and Duke Clinical Research Institute Form Partnership to Collaborate on Cardiac Safety Virtual Warehouse<sup>®</sup> 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 serious side effects associated with both 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 Drug. "Through the development of digital ECG data standards in 2004, the development of the ECG warehouse in 2006, 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 efforts including PCSCs related to



A "Public-Private Partnership" involving Duke- FDA MOU, academia and industry

# CSRC EVOLUTION



Cardiac Safety  
Research Consortium  
*Mission*

To advance scientific knowledge of 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

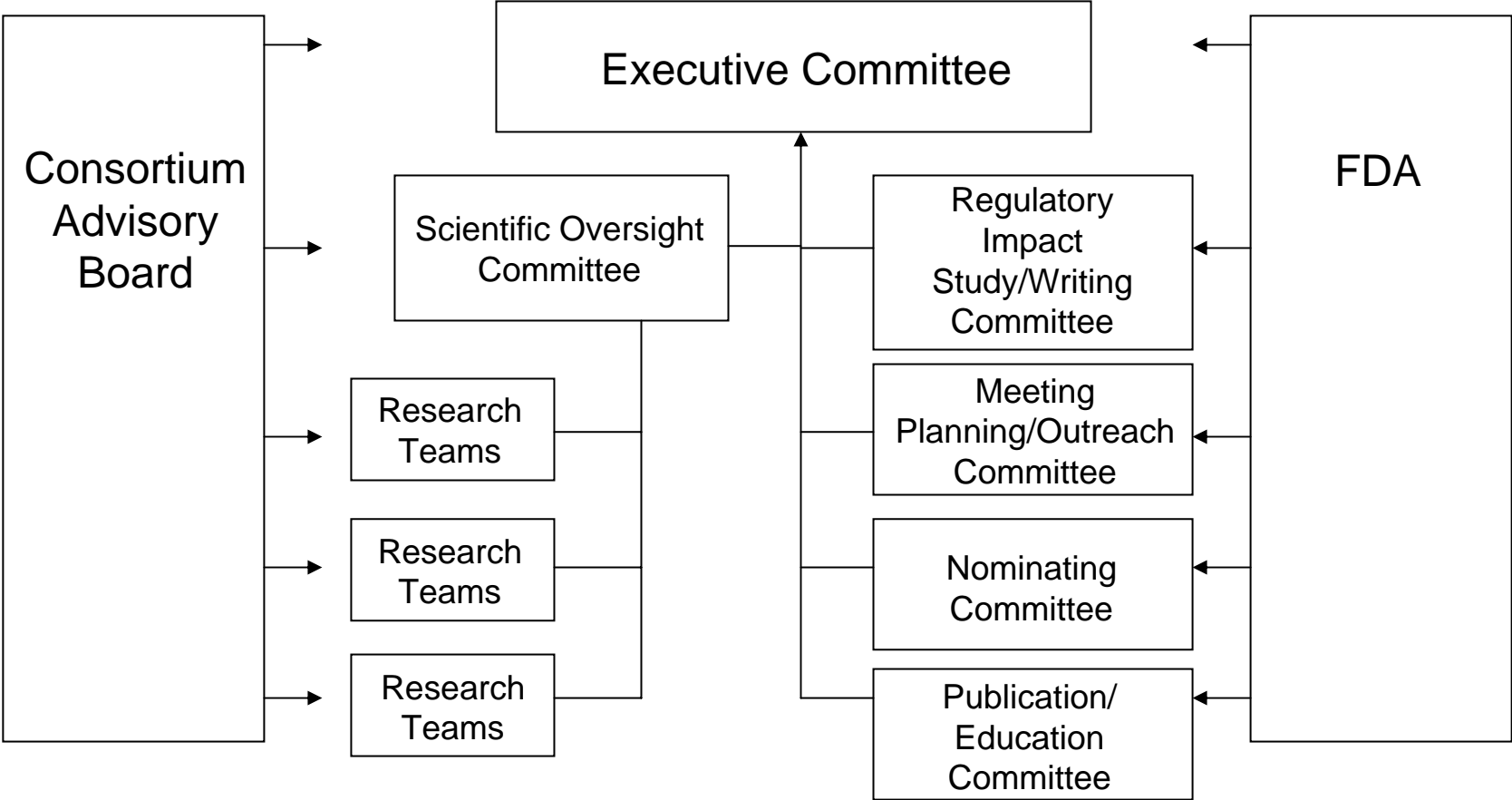
A "Public-Private Partnership" involving Duke- FDA MOU, academia and industry

# CSRC EVOLUTION

## *Key objectives:*

- To facilitate focused pragmatic research that will inform regulatory processes
- To create common nomenclature, standards, and draft regulatory guidance documents for cardiac safety evaluation
- To develop knowledge and improve the evaluative sciences in relation to cardiac safety and product development with a specific attention to the use and qualification of biomarkers for the assessment of cardiac safety
- To establish infrastructure and operational processes to support all objectives

# CSRC GOVERNANCE



# CSRC GOVERNANCE, JANUARY, 2008



## Executive Committee

### Chairs:

Mitch Krucoff (Duke)

Dan Bloomfield (Merck)

Marilyn Agin (Consultant)

Chris Cabell (Quintiles)

John Finkle (GSK)

Paul Kligfield (Cornell)

Justin Mortara (Mortara)

Philip Sager (AZ)

Ben Eloff (CDRH)

Wendy Sanhai (Comm Office)

Norman Stockbridge (CDER)

# CSRC GOVERNANCE, JANUARY, 2008

Scientific Oversight Committee
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Chairs:

Philip Sager (AZ)

Paul Kligfield (Cornell)

Borje Darpo (Consultant)

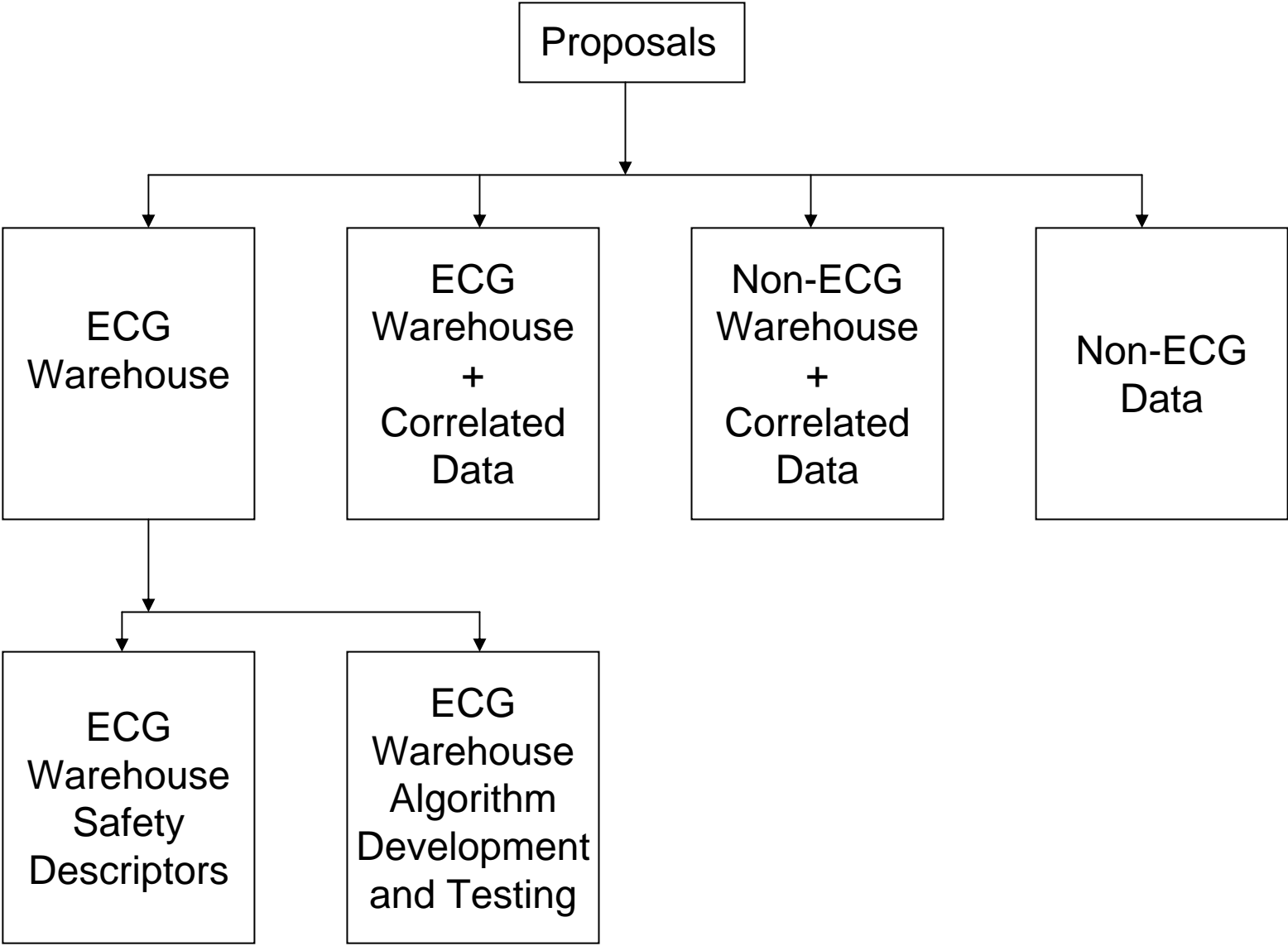
Peter Kowey (Jefferson)

Wojciech Zareba (Rochester)

Ben Eloff (CDRH)

Norman Stockbridge (CDER)

# CSRC SOC



# CSRC SOC



# CSRC SOC PROPOSALS AND DISPOSITION/PROGRESS

## Proposal

## SOC Disposition and Progress

POC: QT analysis of ECG Warehouse  
Marilyn Agin

*Approved* Pending database  
release

QT interval in patients with diabetes  
Olga Gumieniak (GSK)

*Approved* Pending clarification  
and project team

Genetic basis of drug-induced QT prolongation  
Martin Armstrong (AZ)

*Approved* Development of  
project team

Long term arrhythmias in healthy volunteers  
Sherene Min (GSK)

Referred for further development  
as Points to Consider Document

ECG algorithm evaluation database sets  
(CSRC)

*Approved* Pending database  
use policy

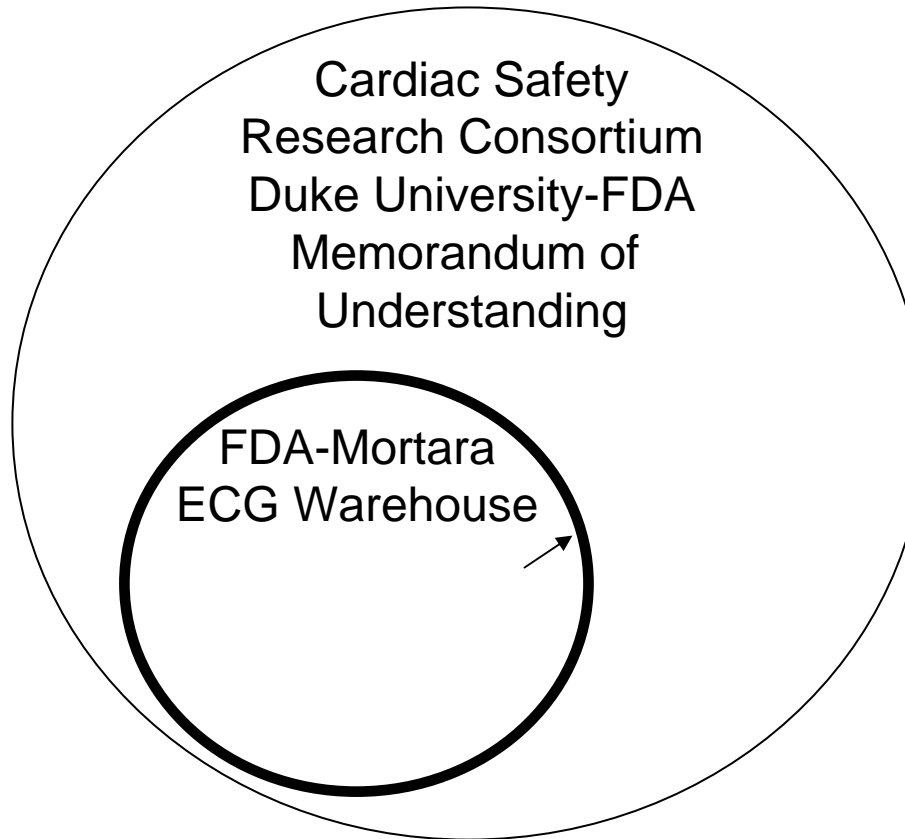
T wave analysis methodology  
Neil Sedransk (NISS)

Clarifications requested

Telemetric and Holter ECG Warehouse  
Jean-Philippe Couderc (Rochester)

Enthusiasm, discussion needed  
regarding data location, use,  
MOU issues, IP development

# CSRC-SOC CHALLENGES

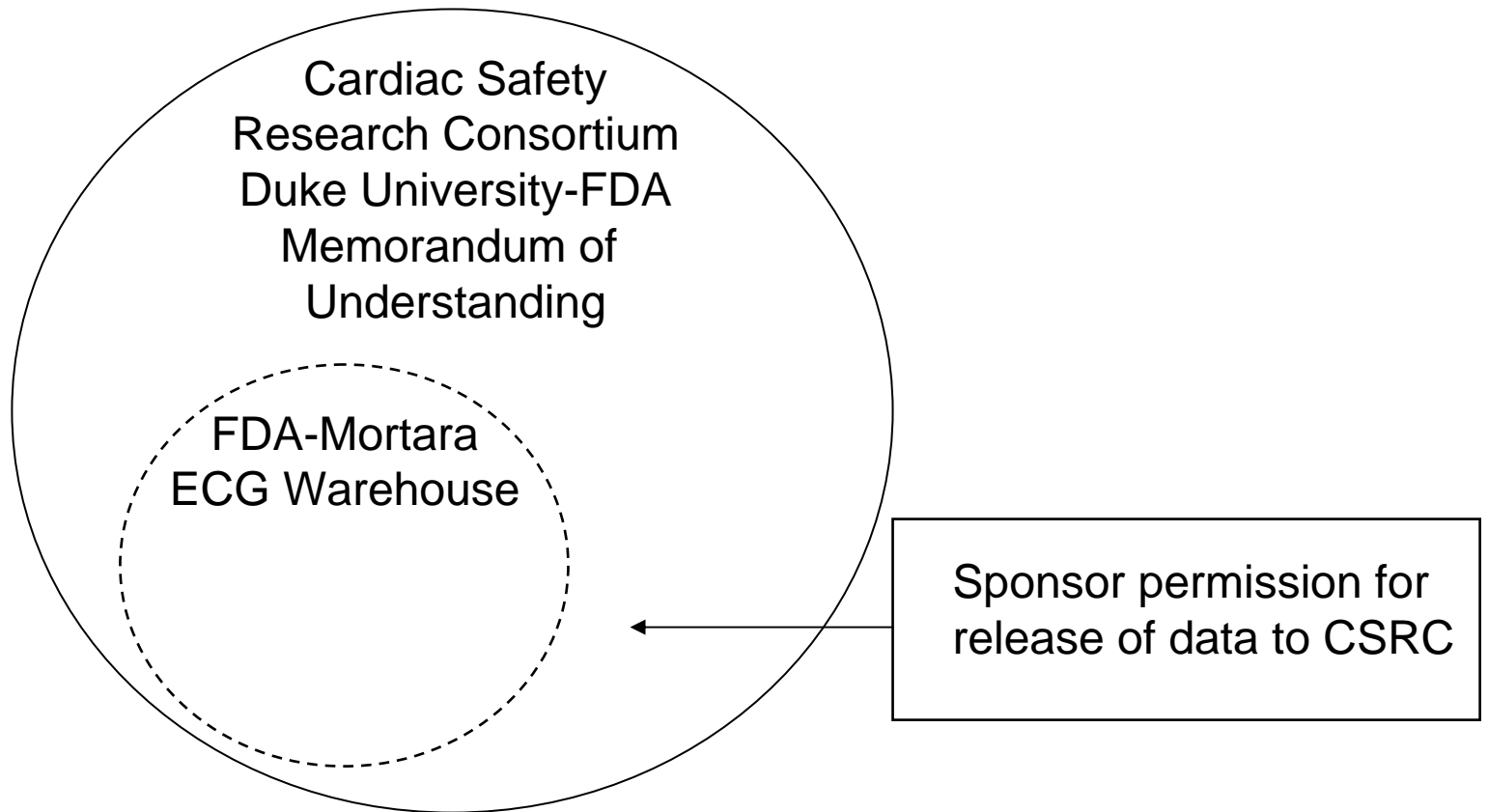


Project  
Management

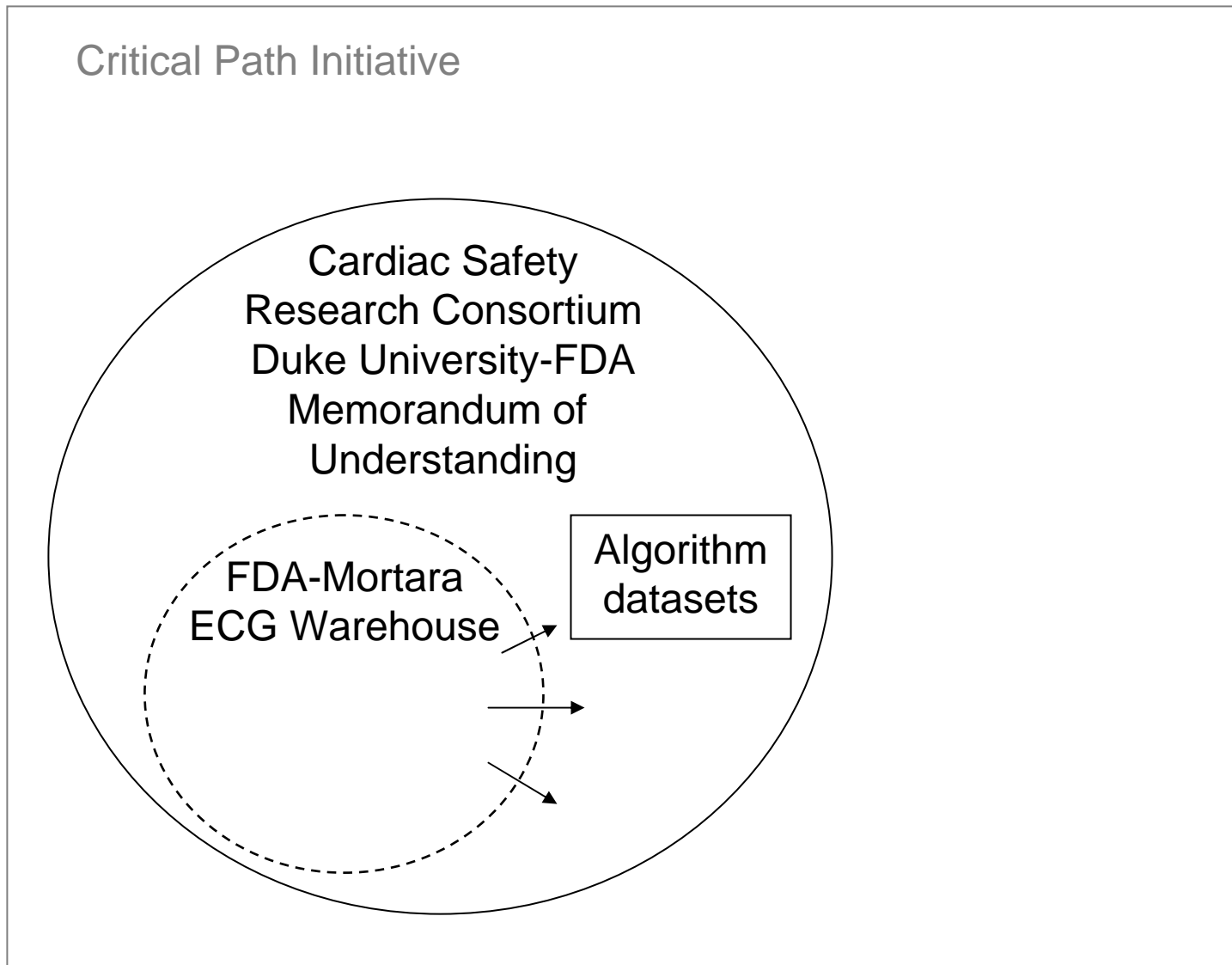
Intellectual  
Property

Ownership of ECG data  
within the ECG warehouse  
resides with the sponsors

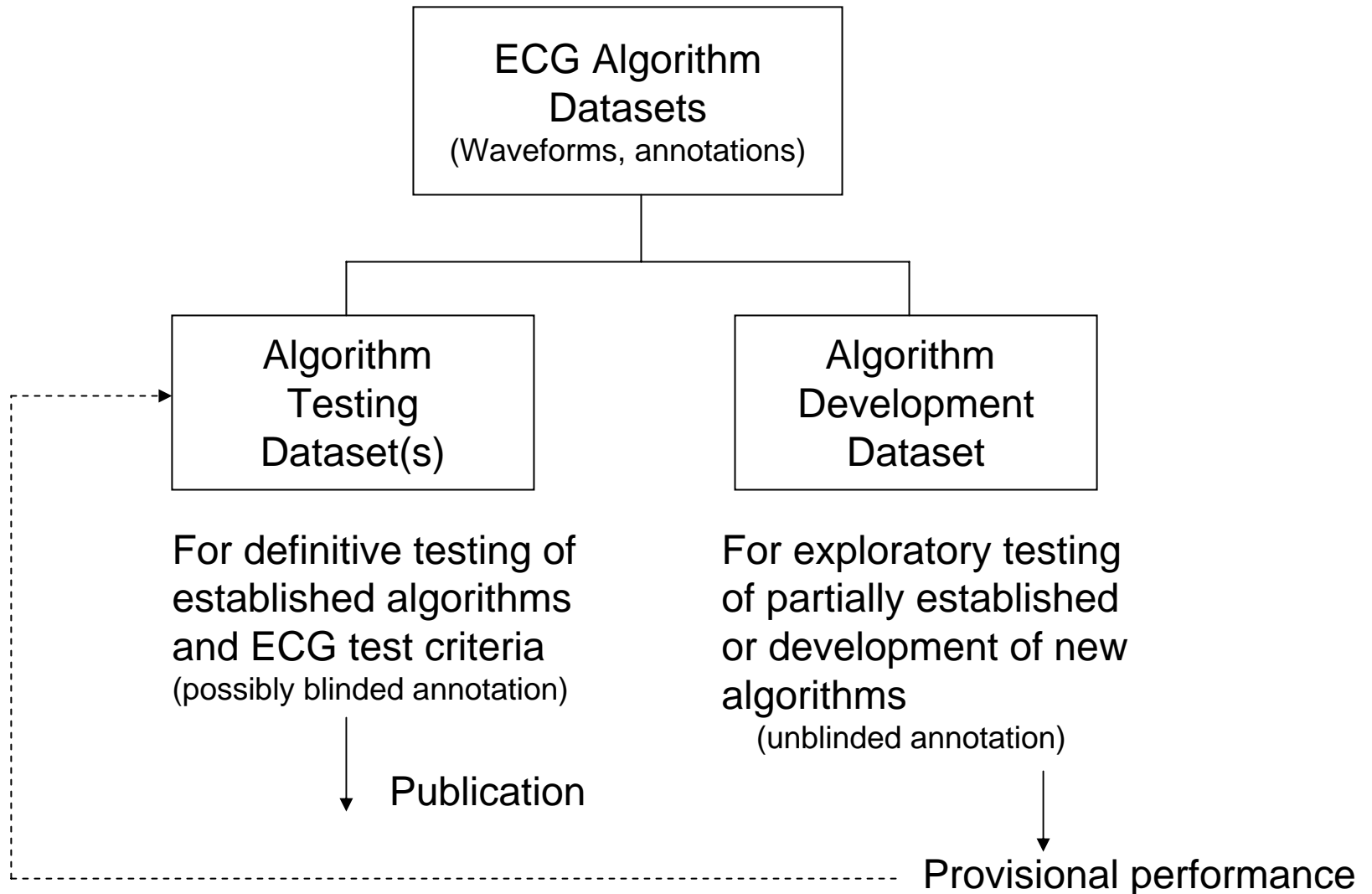
# CSRC EVOLUTION



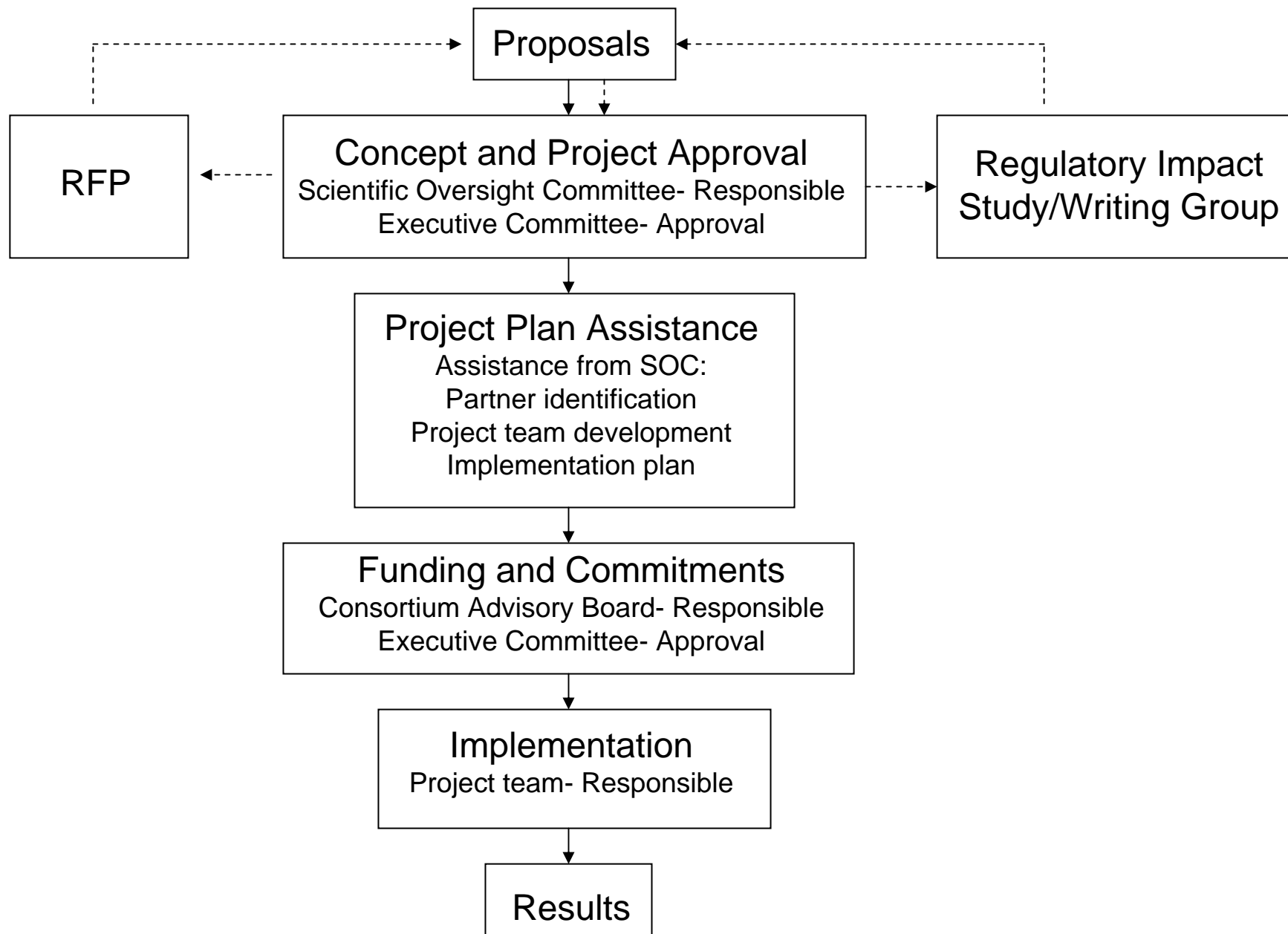
# CSRC ALGORITHM DATASET PROCESS



# CSRC ALGORITHM DATASET PROCESS



# CSRC SOC



# WHAT WILL BE THE FUTURE?

