

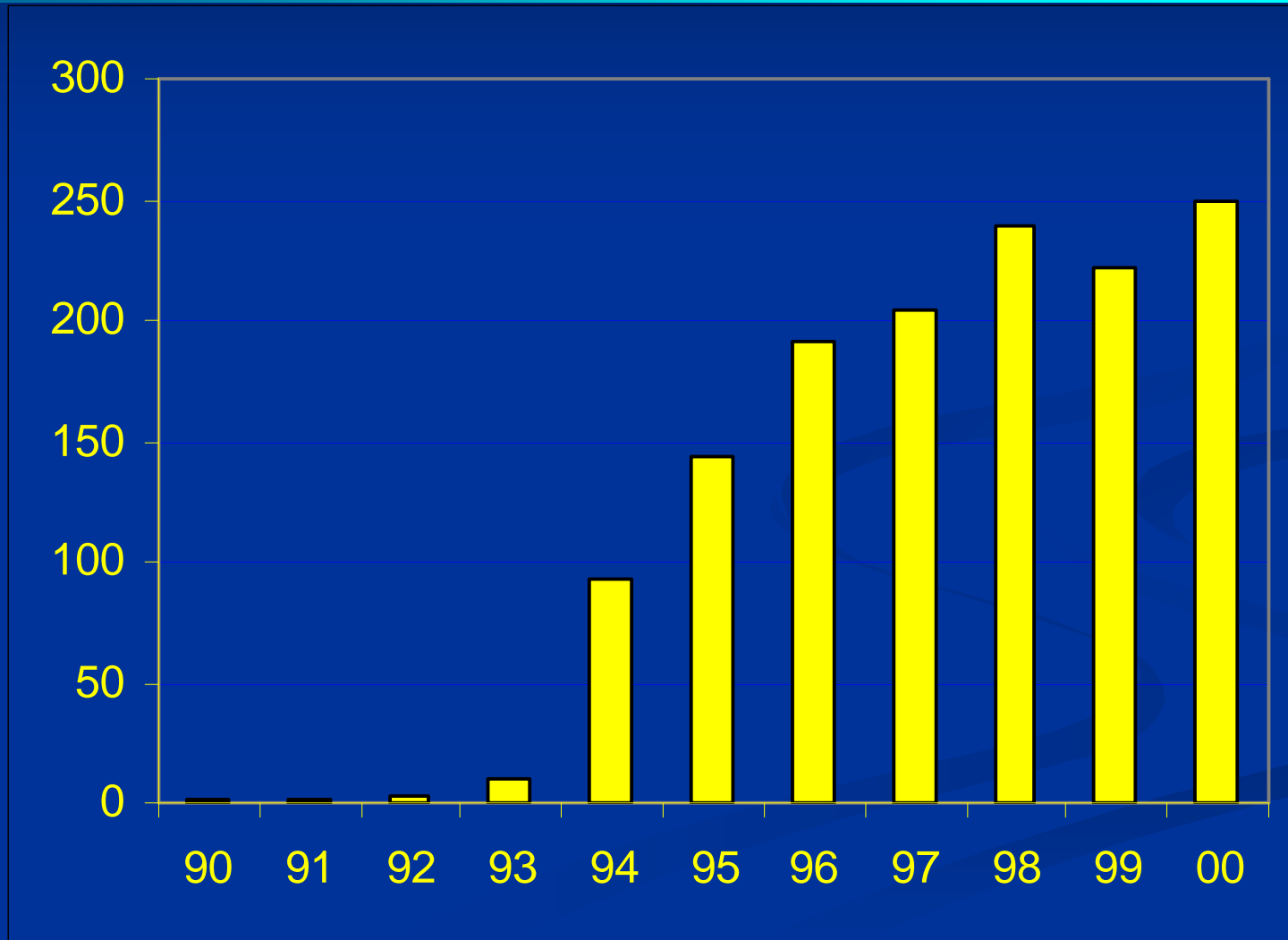
# **The ECG Warehouse**

**A community effort**

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**Division of Cardiovascular and Renal  
Products, FDA**

# Cases of TdP Reported in Post-Marketing 1990-2000



# Drugs Removed From Market for Arrhythmia Risk

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<b>n</b>	<b>Encainide (Enkaid<sup>®</sup>)</b>	<b>1991 (1986)</b>
<b>n</b>	<b>Terfenadine (Seldane<sup>®</sup>)</b>	<b>1998 (1985)</b>
<b>n</b>	<b>Astemizole (Hismanal<sup>®</sup>)</b>	<b>1999 (1988)</b>
<b>n</b>	<b>Grepafloxacin (Raxar<sup>®</sup>)</b>	<b>1999 (1997)</b>
<b>n</b>	<b>Cisapride (Propulsid<sup>®</sup>)</b>	<b>2000 (1993)</b>
<b>n</b>	<b>Levomethadyl (Orlaam<sup>®</sup>)</b>	<b>2003 (1993)</b>

**\* year of removal (year of approval)**

# Response - 1

## n Regulatory

- n Health Canada-FDA
- n ICH S7B, E14

## n CDER QT Interdisciplinary Review Team

- n Clinical data repository

## n Technological

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## n Technological

- n ECG data standards
  - n HL7
  - n Copious documentation
  - n Controlled vocabulary
  - n Public domain viewer

# Standard development

- n Nov 2001 FDA proclaims a need
- n Jan 2002 Working group forms
- n Oct 2002 Presentation to HL7
- n Nov 2002 FDA review; draft guidance
- n Dec 2002 HL7 ballot
- n Jan 2003 HL7 informative standard

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Interdisciplinary Review  
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- n ECG Warehouse  
CRADA

# ECG Warehouse

- n 2003 CRADA
- n 2004 Warehouse and review tool
  - n Discontinued use of freestanding viewer
- n 2005 Direct upload of ECG data
  - n No longer sent to FDA

# Response - 2

## n Regulatory

- n Cardiac Safety Research Consortium

## n Technical

- n ECG Warehouse research portal

# Cardiac Safety Research Consortium

- n 2005: Digital ECG Warehouse on-line
- n October 2005: FDA-DCRI sponsor meeting to discuss research priorities
- n September 2006: FDA-DCRI Memorandum of Agreement
- n November 2006: Second research priorities meeting
- n January 2007: CSRC Governance structure

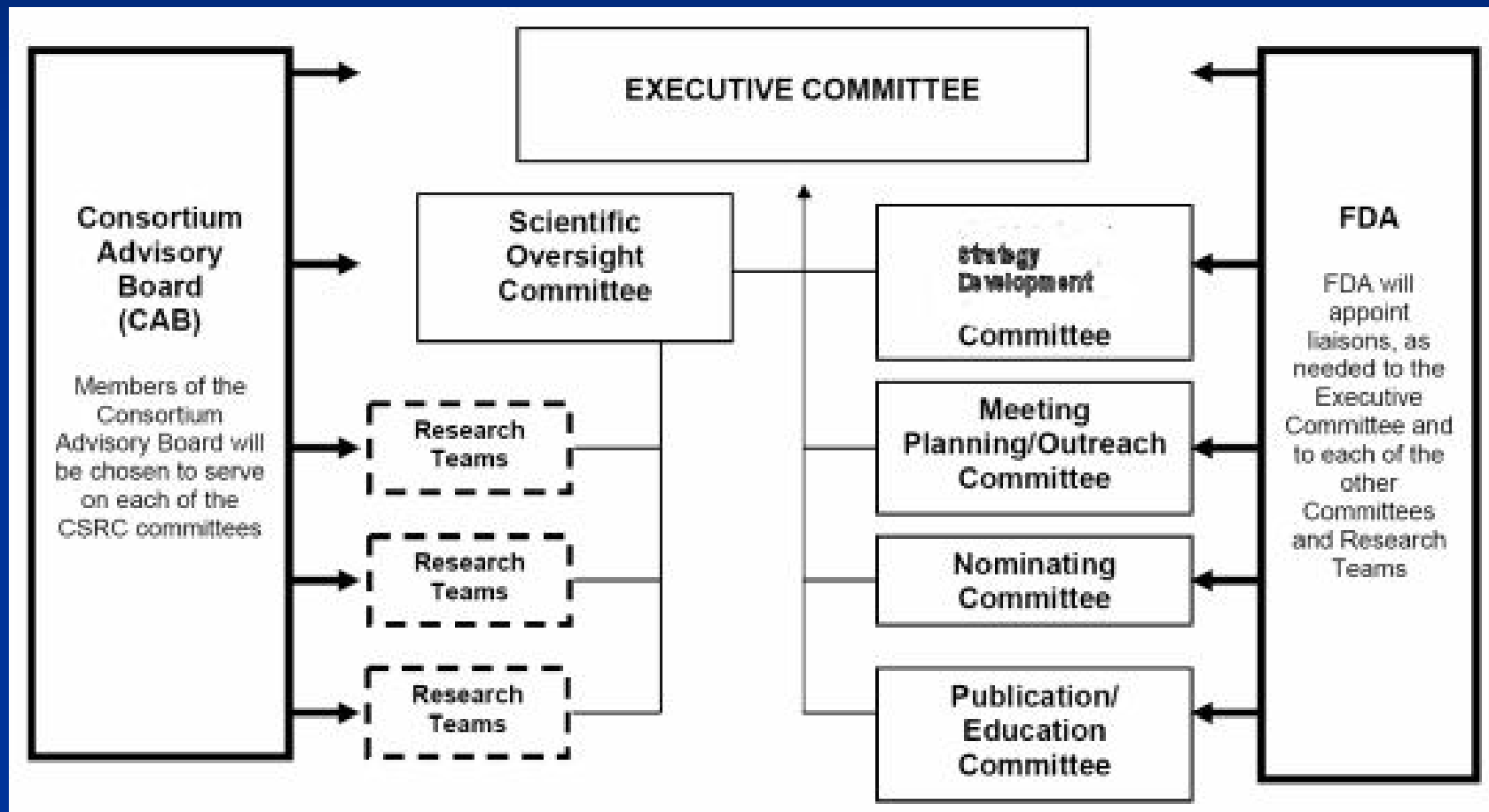
# CSRC Mission

“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.”

# Operating principles

- n Transparency
- n Inclusion of stakeholders
  - n FDA, Pharma, CRO, tech companies, academics
- n Leverage existing resources
  - n ECG data
  - n Other cardiovascular clinical datasets
  - n Data collection when necessary

# Organization



# Coordinated response?

1998

2000

2002

2004

2006

2008

Seldane  
Hismanal  
Propulsid



Canada-US Concept paper  
ICH S7B, E14  
QT Interdisciplinary Team  
CSRC



Digital ECG standard  
ECG Warehouse



# Divine Interventions

- n Colette Strnad (Health Canada)
- n Scott Getzin (Lilly)
- n Chris Cabell (DCRI)



# Summary

- n The final product is a pretty good system for collecting information about a biomarker and involving many interested parties in its exploration.
- n In some ways, the response to the proarrhythmic risk problem worked remarkably well, but only because a few key parties stepped up at just the right time.
- n The response was the result of evolution. It was not engineered. Our goal ought to be to engineer and manage such efforts.