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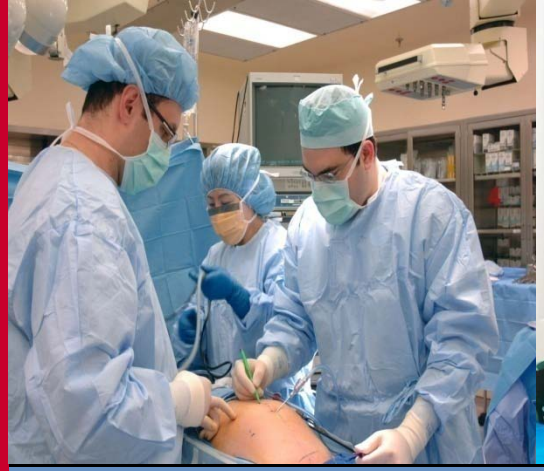

Changing the NCI's Clinical Trials System to Meet the Needs of the 21st Century: *Implementation of the Clinical Trials Working Group and the Institute of Medicine Recommendations*

James H. Doroshow, M.D.

Clinical Trials and Translational Research Advisory Committee

Bethesda, MD
September 21, 2010

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

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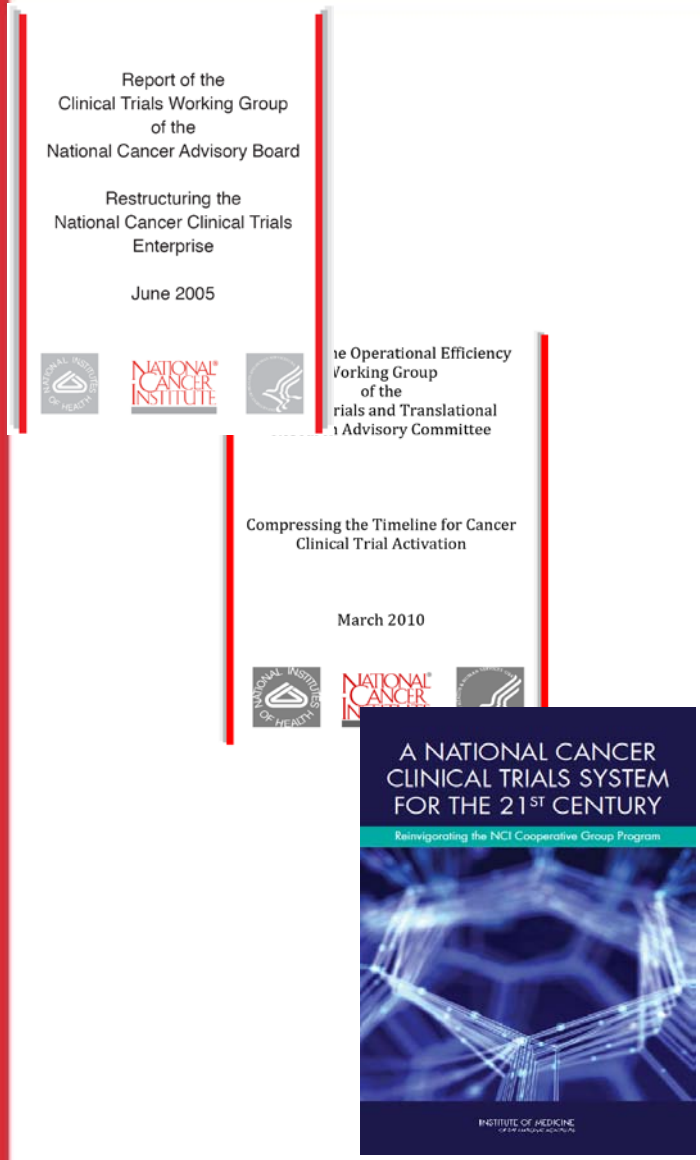
Changing the NCI's Clinical Trials System to Meet the Needs of the 21st Century



- *CTWG – June 2005*
- *OEWG – March 2010*
- *IOM – April 2010*

- *A comprehensive approach is needed to achieve a collaborative, public, national system that addresses the challenges and opportunities provided by our rapidly evolving understanding of cancer biology*

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IOM Goals Build on CTWG and OEWG

IOM Goals: What do we need to change?

- Improve the speed and efficiency of the development and conduct of trials
- Incorporate innovative science and trial design into our studies
- Improve prioritization, support, and completion of trials
- Incentivize the participation of patients and physicians in clinical investigations

What have we changed to date?

Where do we go from here?

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IOM Goal 1: Improving Speed and Efficiency

What have we changed to date?

- Developed operational efficiency standards for trial launch to achieve new target timelines for clinical trial activation
- Developed Standard Terms of Agreement for Research Trials (START) clauses for company and academic collaborations
- Enhanced & Speeded Up Central IRB functions (Jaci Goldberg)

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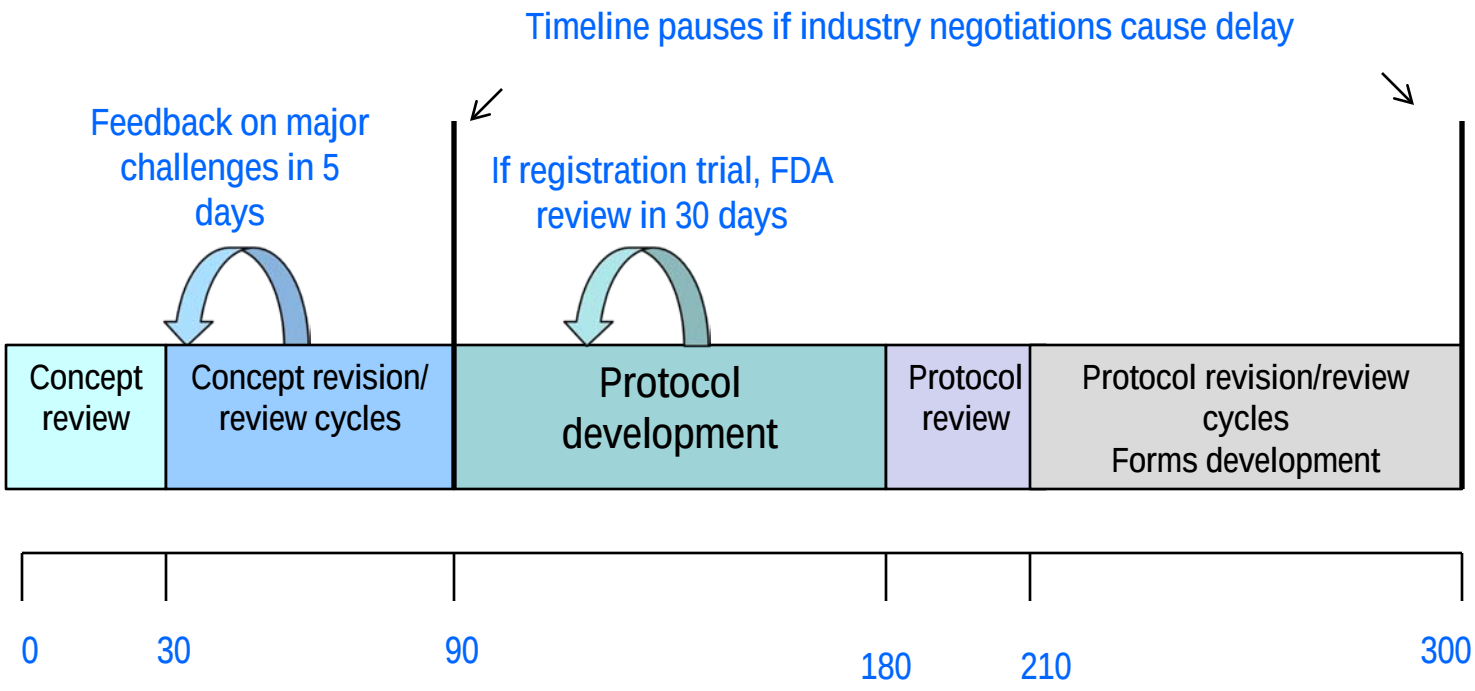
OEWG Target Timeline for Group Phase III Trials – 300 days



Timeline excludes contracting, drug supply, FDA review

Protocol terminated if not activated in two years

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Phase III Concepts:Timeline Data as of August 20, 2010

18 Concepts Proposing Phase III Trials Received Since April 1, 2010

- 3 concepts approved
- 6 concepts in review or in time-out (company &/or drug commitment)
- 5 concepts disapproved or withdrawn
- 4 concepts submitted to CTEP awaiting Steering Cmte. review

Approved Concepts (3):Target timeline for Concept approval –90 days if Group phase II > 100 pts or Group phase III

- Average number of days for concept approval by Steering Cmte. (without time-outs) = 41 days (n=2)
- Average number of days for ph II concept approval w/o SC (without time-outs) = 40 days (n=1)
- Average time-out length: NA (no time-outs among approved concepts)
- 0 concepts have exceeded the 90 day target

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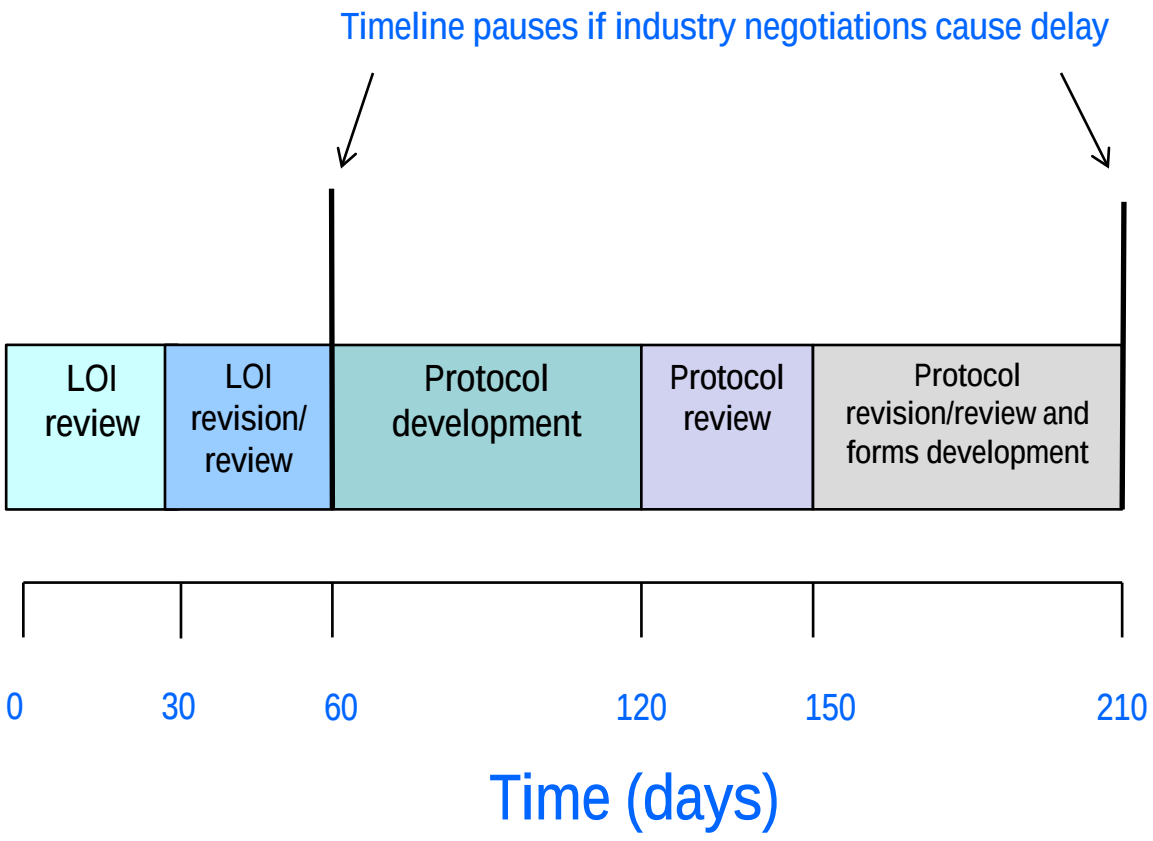
OEWG Target Timeline for Group Phase II Trials – 210 days



Timeline excludes contracting, drug supply, FDA

Protocol terminated if not activated in 18 months

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Group Phase II LOIs:Timeline Data as of August 20, 2010

21 Group LOIs received since April 1, 2010

- 5 Group LOIs approved; 2 protocols submitted
- 4 Group LOIs in review or in time-out
- 12 Group LOIs disapproved, withdrawn, or declined by Pharma

Approved LOIs (5):Target timeline for Group LOI approval – 60 days

- Average number of days for Group LOI approval – 42 days
- Average time-out length – 15 days (among the approved Group LOIs)
- 1 Group LOI has exceeded the 60-day target

Protocols (2): Target timeline for Protocol Submission – 90 days

- Average time from Group LOI approval to Protocol submission – 61 days

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UO1/NO1 Phase I/II LOIs:Timeline Data as of August 20, 2010

20 U01/N01 LOI's received since April 1, 2010

- 8 U01/N01 LOI's approved; 1 U01/N01 Protocol submitted
- 7 U01/N01 LOI's in review or in time-out (drug commitment or grant approval)
- 5 U01/N01 LOI's disapproved or withdrawn

Approved U01/N01 LOI's (8): Target timeline for LOI Approval – 60 days

- Average number of days for LOI approval (without time-outs) – 36 days
- Average time-out length – 32 days *(all for drug commitment)*
- No LOI's have exceeded the 60 day target

6 other (P50, R01, R21, DoD) LOIs submitted

- 4 in review
- 2 withdrawn/disapproved

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Intramural Phase I/II LOIs:Timeline Data as of August 20, 2010

6 intramural LOI's received since April 1, 2010

- 2 intramural LOI's approved; 2 protocols submitted
- 2 intramural LOI's in review
- 2 intramural LOI's disapproved

Approved intramural LOI's (2): Target timeline for LOI Approval – 60 days

- Average number of days for LOI approval (without time-outs) – 38 days
- Average time-out length – 2 days (drug commitment)
- No intramural LOI's have exceeded the 60 day target

Protocols Submitted (2): Target timeline for Protocol Submission – 60 days

- Average time from LOI Approval to Protocol submission – 59 days

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NCI Initiatives to Achieve OEWG Goals

- Kick-off meeting late March with Groups, Consortia, and Phase I/II UO1s and NO1s to establish common understanding and collaborative procedures
- Hire Project Managers to oversee OEWG processes
- Standardized CTEP consensus reviews and provide comments in Track Change® Mode

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NCI Initiatives to Achieve OEWG Goals (cont.)

- Modified/developed internal SOPs to streamline processes and improve communication
- Identified at-risk trials (First quarter of CY11)
- Established teleconference calls to discuss/resolve outstanding issues
- Developed secure, role-based, web-portal to share tracking reports with intramural and extramural investigators and support staff
- Two OEWG working groups meet monthly via conference calls to discuss OEWG processes:
  - OEWG Cooperative Groups Working Group
  - OEWG Early-Phase Clinical Trials Working Group

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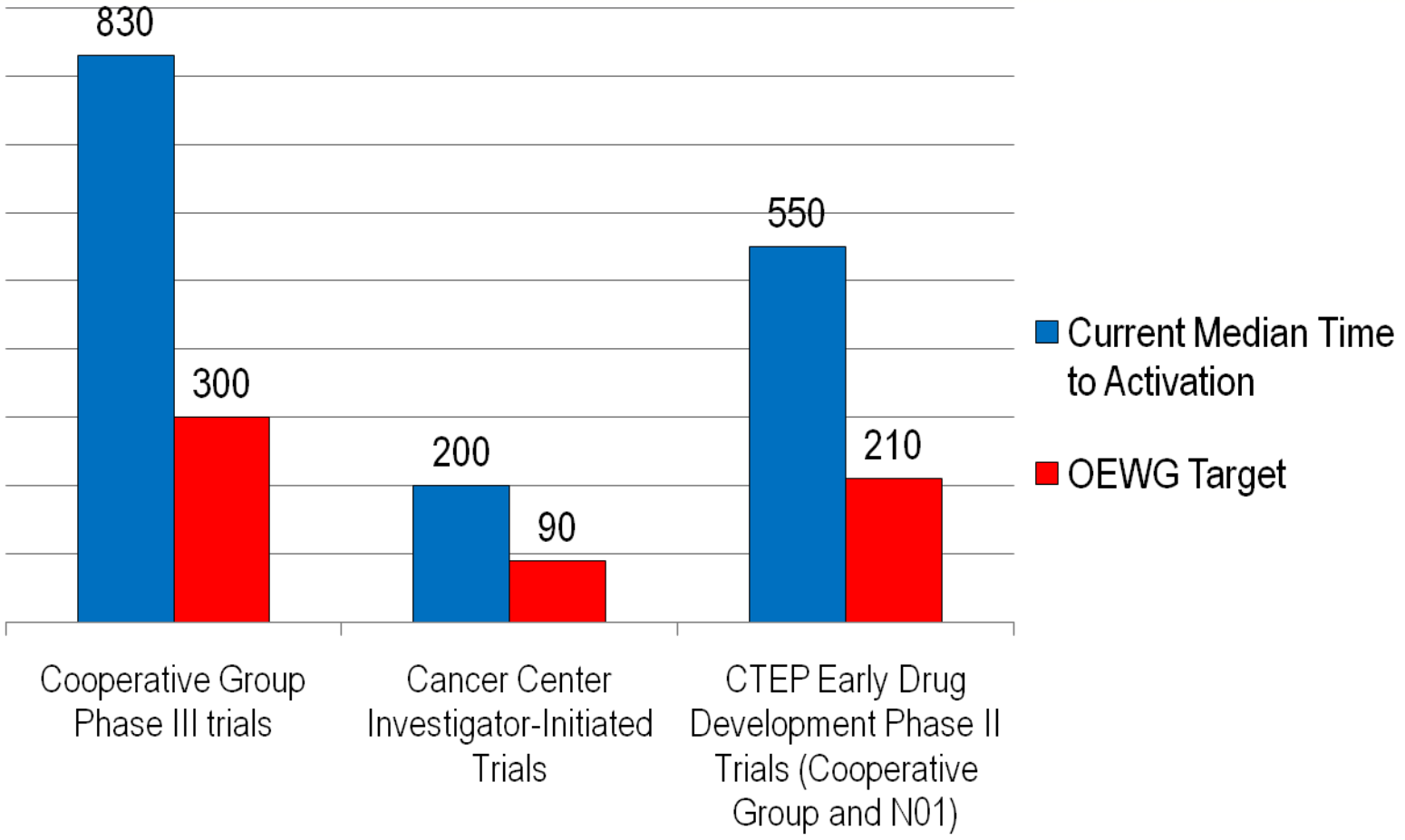
Changing the NCI's Clinical Trials System Improving Efficiency



First 6 months of implementation (targets and absolute drop dead dates): Hitting timeline targets; 60% improvement

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NCI Timeline Reports

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U.S. National Institutes of Health | www.cancer.gov

Timeline Reports

The application is primarily for NCI CTEP internal and external collaborators to access data reports generated from the CTEP Enterprise System.

Version 1.0:

The first version of the application will allow users to generate Protocol Development Timeline (PDT) reports to track the amount of time it takes to develop a protocol from Concept or LOI receipt to Protocol Activation. The PDT reports will be available in 4 different formats for comparison and analysis. The users of the application should have an ACTIVE CTEP-IAM account.

LOGIN TO TIMELINE REPORTS

Username:

Password:

Login

Account Management

Forgot Password | Reset Password

Annual Registration | Request New Account

Quick Reference Guide

Quick Reference Guide

Tutorial

Version Information

1.0.0

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IOM Goal 2: Incorporating Innovative Science

What have we changed to date?

- Biomarker, Imaging, and Quality of Life Studies Funding Program (BIQSFP): a novel mechanism to facilitate the early development of integral components of phase 2 and 3 clinical trials
- Developed standards for biomarker assays used in clinical trials
- Consolidating Cooperative Group biospecimen banks into a national banking system that supports Cooperative Group and other NCI-supported clinical trials
- Developed the Clinical Assay Development Program and Patient Characterization Center: Operational 1/11
- Novel designs for phase 1/2 trials to better predict successful phase 3 trials (Adjei et al, Clin Cancer Res 2009)

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IOM Goal 3: Prioritizing and Supporting Trials

What have we changed to date?

- Scientific Steering Committees
- Developing a unified clinical trials informatics system
  - Comprehensive database (Clinical Trials Reporting Program)
  - Standardized case report form modules
  - Credentialing repository (launched 2010)
  - NCI will be the first Institute to provide a robust, standardized, off-the-shelf clinical trials management (software) system to all of its grantees that includes a standardized “look and feel” as well as protocol development and data collection modules
- Reimbursement for phase 2 trials increased

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Disease-Specific Steering Committees: Prioritizing Clinical Trials

Steering Committee	Year Established	Co-Chairs Disease-Specific Steering Committees (SCs)
GI	2006	Dan Haller, MD & Joel Tepper, MD
Gyn	2006	David Gershenson, MD, Gillian Thomas, MD, & Michael Birrer, MD
Head & Neck	2007	Arlene Forastiere, MD, David Schuller, MD, & Andy Trotti, MD
GU	2008	Eric Klein, MD, George Wilding, MD, & Anthony Zietman, MD
Breast	2008	Charles Geyer, MD & Nancy Davidson, MD
Thoracic	2008	David Harpole, MD, William Sause, MD, & Mark Socinski, MD
Leukemia	2009	Wendy Stock, MD & Jerry Radich, MD
Lymphoma	2009	Oliver Press, MD Julie Vose, MD
Myeloma	2009	Morie Gertz, MD, & Nikhil Munshi, MD
Brain	2010	Ian Pollack, MD & W.K. (Al) Yung, MD
Pediatrics		TBD - 2010

Approximately 98 Concepts evaluated since inception of SCs with an approval rate of 56% to 60%; see http://ccct.nci.nih.gov for other SSC & rosters

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IOM Goal 4: Patient and Physician Participation

What have we changed to date?

- Cancer Clinical Investigator Team Leadership Award
  - CTWG initiative to enhance recognition for mid-level clinical investigators at academic institutions who promote successful clinical research programs
  - Program launched in 2009 with 11 awardees receiving partial salary support for up to $50,000 per year for two years
  - 12 awardees in 2010

- Guidelines Harmonization Working Group (GHWG)
  - Chair: Jim Abbruzzese
  - Common clinical trials program guidelines to promote collaboration
  - Incentives

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2010 Clinical Investigator Team Leadership Awardees

- Dr. Rafat Abonour, Indiana University
- Dr. Jeffrey Bradley, Washington University
- Dr. Steven Cohen, Fox Chase Cancer Center
- Dr. Linda Duska, University of Virginia
- Dr. Naomi Haas, University of Pennsylvania
- Dr. Elisabeth Heath, Wayne State University
- Dr. Susan Kelly, University of Texas MDACC
- Dr. Smitha Krishnamurthi, Case Western Reserve University
- Dr. Suresh Ramalingam, Emory University
- Dr. David Rizzieri, Duke University
- Dr. Cheryl Saenz, University of California-San Diego
- Dr. Sheri Spunt, St. Jude Children's Research Hospital

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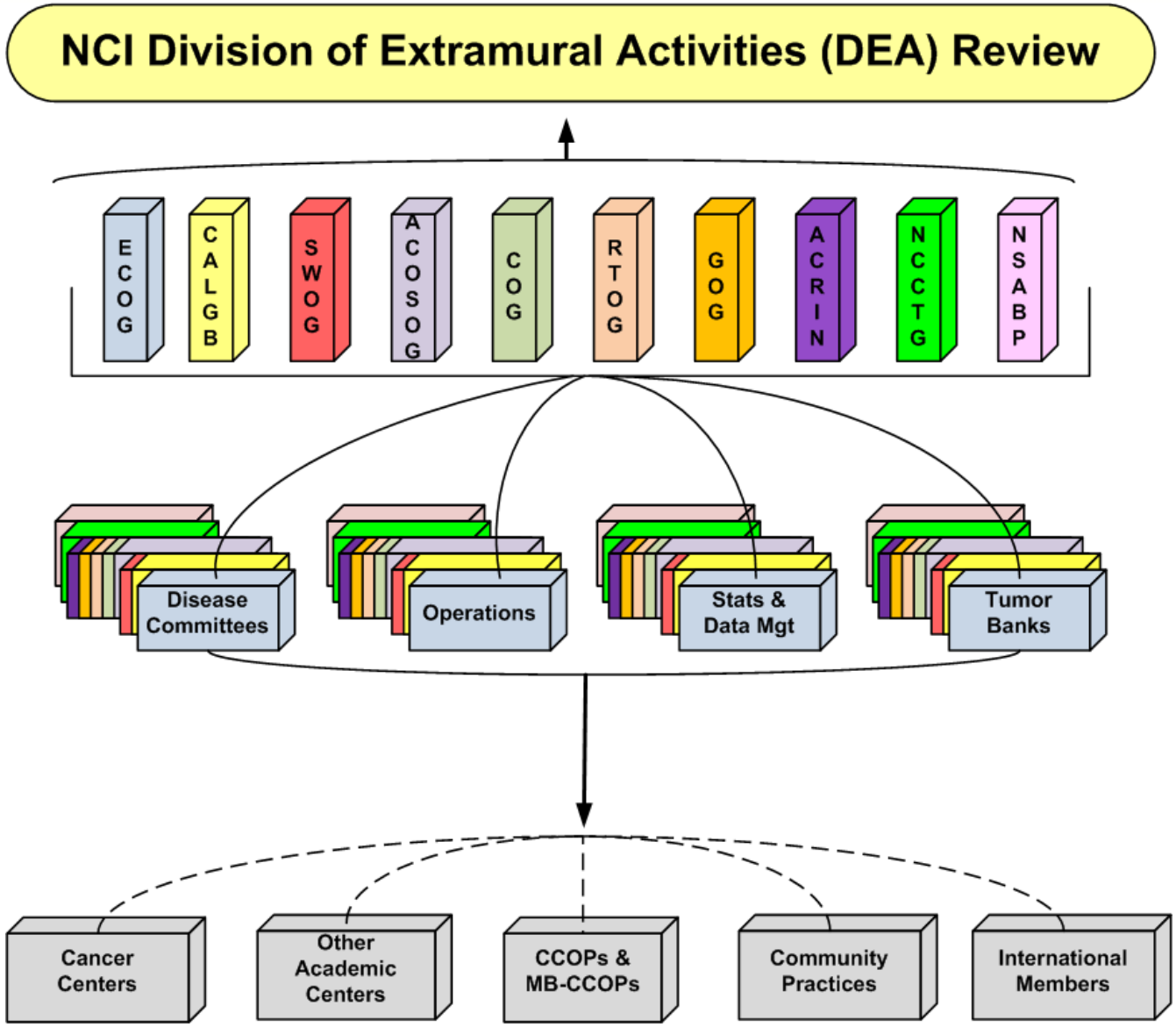
Organizational Structure 2005: Pre-CTWG



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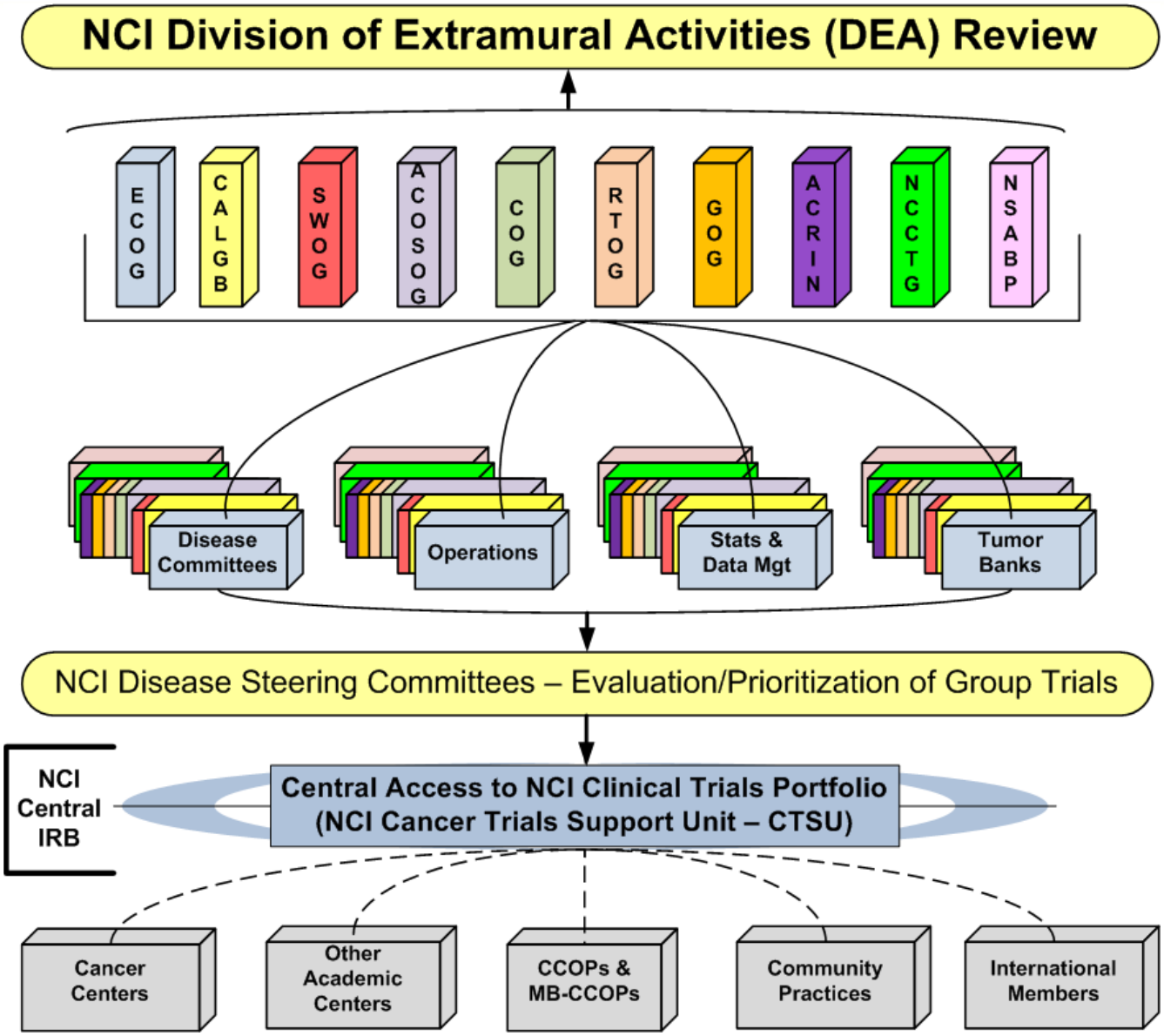
Organizational Structure of the System: 2010



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Changing the NCI's Clinical Trials System
What Else Do We Need To Do?

- Consolidation: How to restructure current system into a harmonized network; Size? Working parameters?

- How to incentivize cooperation and greater participation in the NCI's clinical trials system?

- How to optimally provide access to needed molecular tools to answer critical scientific questions?

- How best to facilitate interactions with FDA and CMS to bring the most effective treatments to patients rapidly?

- How best to extend benefits of clinical trials participation to underserved populations?