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Restructuring the National Cancer Clinical Trials and Translational Research Enterprise

Coordinating Center for Clinical Trials (CCCT)
CTAC Update

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

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Coordinating Center for Clinical Trials

- Clinical Trials Working Group (CTWG)
- Translational Research Working Group (TRWG)

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CTWG Restructuring Initiatives

- Enterprise-Wide/Integrated Management

  Restructure the extramural and intramural oversight of NCI clinical trials

- Prioritization/Scientific Quality
- Coordination
- Standardization
- Operational Efficiency

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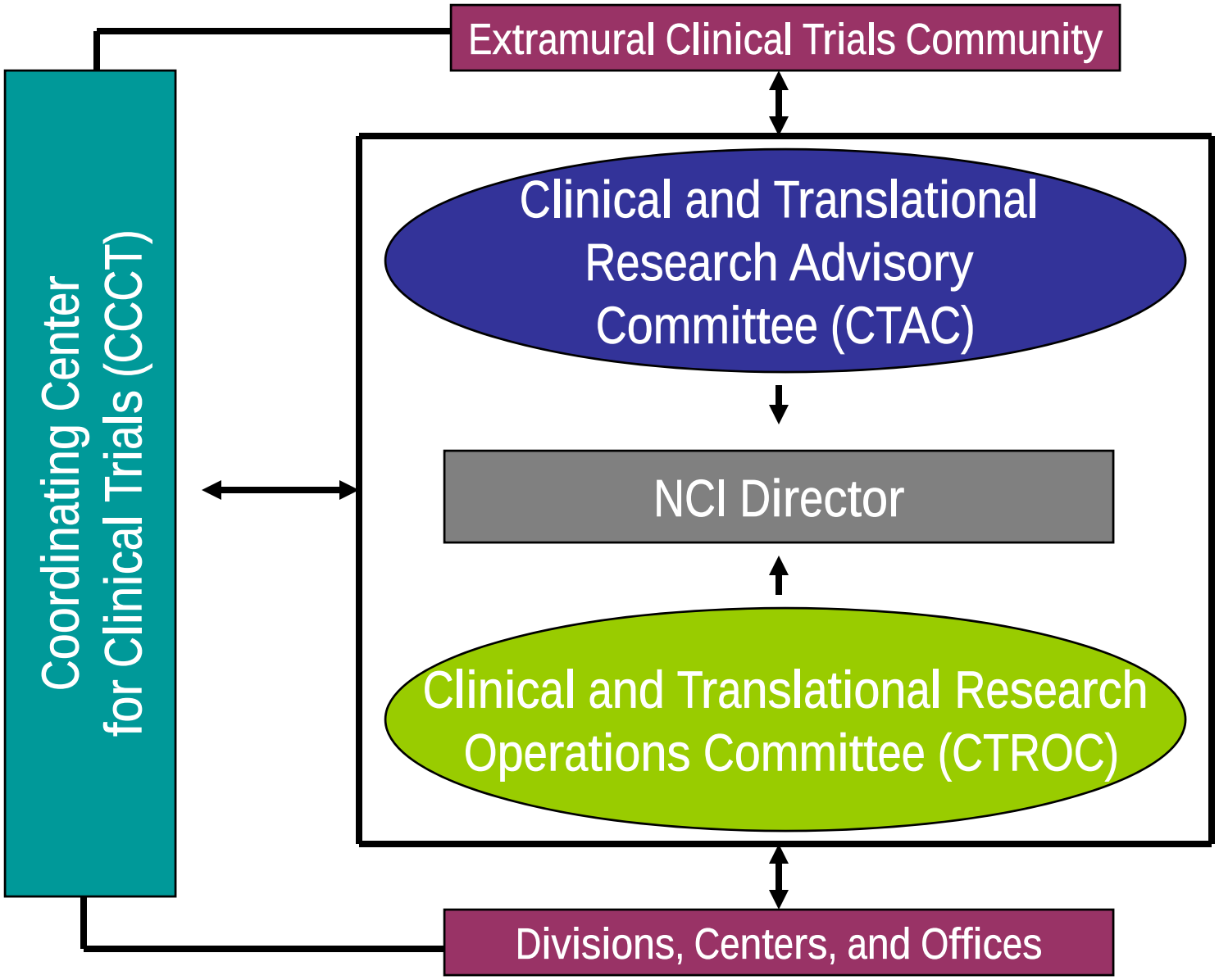
Integrated Management



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CTWG Restructuring Initiatives

- Enterprise-Wide/Integrated Management
- Prioritization/Scientific Quality

  Involve all stakeholders in design and prioritization of clinical trials that address the most important questions, using the tools of modern cancer biology
- Coordination
- Standardization
- Operational Efficiency

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Prioritization: Scientific Steering Committees

- Investigational Drug Steering Committee (IDSC) for early phase trial prioritization
- Disease-Specific Scientific Steering Committees (SSC's) for phase 3 trials and selected phase 2 studies
- Symptom Management and Health-Related Quality of Life Steering Committee (SxQOL) for symptom management trials and patient reported outcomes expertise
- Patient Advocate Steering Committee (PASC)

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Disease-Specific Steering Committees: Responsibilities

- Prioritize phase 3 and selected phase 2 concepts for therapeutic clinical trials
- Refine & collaborate on phase 3 and selected phase 2 concepts utilizing Task Forces when appropriate
- Convene Clinical Trials Planning meetings to identify critical issues/questions for study in the disease
- Information exchange on phase 2 and other studies
- Periodically review accrual and unforeseen implementation issues

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Disease-Specific Steering Committees

- Gastrointestinal Cancer
- Gynecologic Cancer
- Head and Neck Cancer
- Genitourinary Cancer
- Breast Cancer
- Thoracic Malignancy
- Timeline calls for completion of SSC transition by 2010 (Hematologic Malignancy in planning stage)

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Biomarkers, Imaging and QOL Studies Funding Program (BIQSFP)

- Program initiated in 2008 to support Cooperative Groups and CCOP Research bases so that critical biomarker, imaging and quality of life studies integral to national phase III clinical trials could be pursued in a timely manner
- Developed assay standardization criteria for use in prioritization of requests for these funds
- Developed evaluation criteria for prioritization of essential symptom management and quality of life studies

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BIQSFP Changes for 2009

- Anticipated funding – $10M
- Cooperative Group and CCOP Research Base studies with integral and integrated biomarker, imaging, or QOL studies associated with new concepts:
  - Phase 3 Prevention
  - Phase 3 Treatment
  - Symptom Management
- New additional requirement for description of the performance standards for proposed essential assays

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Timeline

- Open submission cycle throughout the year (http://ccct.nci.nih.gov)
- Scientific Steering Committees will review concepts with BIQSFP correlative components
- CTROC* will recommend & prioritize BIQSFP proposals at regular meetings throughout the year
- CTAC will make final recommendations to NCI Director

*NCI Clinical and Translational Research Operations Committee

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CTWG Restructuring Initiatives

- Enterprise-Wide/Integrated Management
- Prioritization/Scientific Quality
- Coordination

  Coordinate clinical trials research through data sharing and providing incentives for collaboration
- Standardization
- Operational Efficiency

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Coordination Initiatives: Progress

- Developing a comprehensive database of NCI-supported clinical trials
- Harmonize guidelines and develop incentives for collaboration across NCI clinical trials mechanisms including Cancer Centers, SPORE, and Cooperative Groups
- Developing mechanism to support multi-site translational clinical trials in rare diseases and areas not currently a major focus for Coop Groups
  - Pilot studies from H&N SSC and H&N SPORES initial focus utilizing the NCI's CTSU

Clinical Trials Reporting Program
www.cancer.gov/ncictrp

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

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Questions about cancer?

- 1-800-4-CANCER
- LiveHelp® online chat

NCI Highlights

Treatment of Metastatic Breast Cancer
Long-Term Smoking Cessation Cuts Risk

NCI is establishing a new Clinical Trials Reporting Program (NCI CTRP), based on a June 2005 recommendation submitted by the Clinical Trials Working Group (CTWG), which was approved by the National Cancer Advisory Board.

Even though NCI grantees are currently subject to trial reporting requirements, an upgraded set of mandatory reporting requirements will apply starting January 2009. In the long-term, the new reporting measures will help provide critical data to assist NCI in better coordinating research efforts to optimize our nation's investment in cancer research.

NCI clinical trials reporting will include up-to-date information about the status of all NCI-funded and/or sponsored clinical research, regardless of drug development phase, type of intervention or treatment, study design, or program through which funding is provided.

For More Information

NCI's Clinical Trials Reporting Program
Frequently Asked Questions
Background

Timeline

January 1 - June 30, 2009
All open trials to be registered

October 31, 2009
First submission deadline for accruals and updates

2008 2009 2010 2011

Clinical Trials Database

Trial submitter registers with system

↓

Trial is registered
(and protocol document uploaded)

↓

NCI abstracts protocol from document to support CDS abbreviated reporting

↓

Submission of Accrual Data

↓

Comprehensive data accessible

CTRP Deployment: Production

- **Operational Pilot: July-December, 2008**
- **Production CTRP Registration began January 5, 2009**
- **First five sites:**
  - Dana-Farber
  - Northwestern
  - Mayo
  - St. Jude
  - Wake Forest
- **New interventional trials only**
  - activated (*i.e.*, IRB approval to register patients) as of 1/1/2009
- **No direct CTRP registration of CTEP / DCP trials; NCI is internally transferring these trials**

Staged Deployment, Learn as We Go

- **Interventional trials only for 2009**
- **First Quarter of 2009:**
  - Five pilot sites only, new trials only, no amendments
- **Second Quarter of 2009:**
  - Solicited “early adopter” Cancer Centers begin entering new trials, allow amendments, allow existing trials
- **Third Quarter of 2009 *(provisional)*:**
  - All Cancer Centers begin entering new trials
- **Fourth Quarter of 2009 *(provisional)*:**
  - Add Non-Cancer Center grantees begin entering new trials, begin collection of accrual data
- **First Quarter of 2010 *(provisional)*:**
  - Begin pilot reporting of outcomes, adverse events
  - Potentially add observational, ancillary / correlative studies

Timeline

	January 2009	April 2009	July 2009	September 2009	January 2010	April 2010
Pilot Cancer Centers	New trials	New and existing trials, amendments				
					Outcomes / AEs Pilot	
"Early Adopter" Cancer Centers		New trials, amendments	New and existing trials, amendments			
All Remaining Cancer Centers			New trials, amendments	New and existing trials, amendments		
Non-Cancer Center Grantees				New trials, amendments	New and existing trials, amendments	
All Grantees				Accruals		
					Observational / Ancillary / Correlative?	

Communications

- CTAC
- Cancer Center Administrators' Forum (March 15, 2009)
- caBIG® Clinical Trials Workspace meeting (March 18, 2009)
- caBIG® Clinical Trials Steering Committee meeting (April 4, 2009)
- Internal NCI Program Directors' updates (periodic)
- NCI Bulletin

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CTWG Restructuring Initiatives

- Enterprise-Wide/Integrated Management
- Prioritization/Scientific Quality
- Coordination
- Standardization

  Standardize informatics infrastructure and clinical research tools
- Operational Efficiency

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Standardization Initiatives: Progress

- Remote data capture system for Coop Group trials: Distribute to all NCI-supported Clinical Trials Sites
- Electronic Case Report Form Initiative
- Standard Clinical Trials Agreement Clauses

Library of Standard Case Report Form Modules

Demography CRF Module

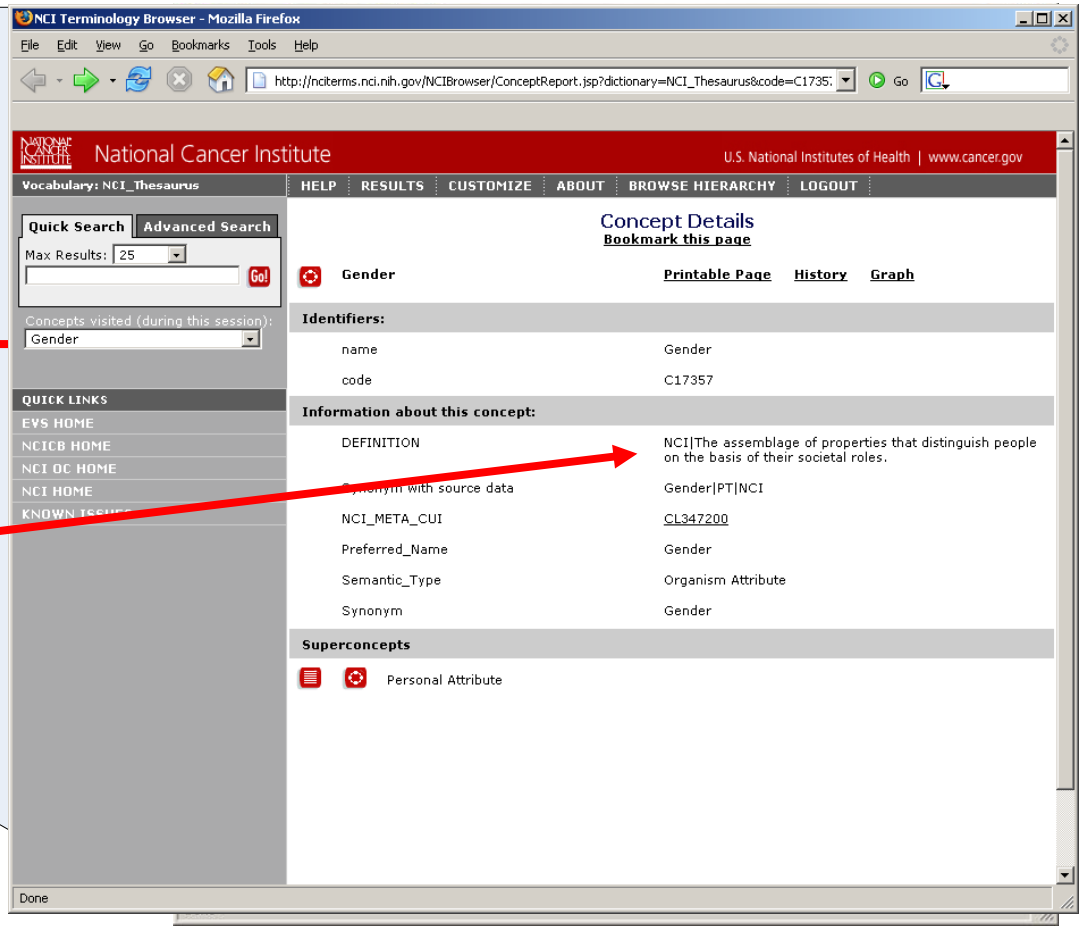
Patient Name: _____

Patient Gender (Check one):

- ☐ Male
- ☐ Female
- ☐ Unknown
- ☐ Not Determined

Patient Race (Check all that apply):

- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or other Pacific Islander
- ☐ White
- ☐ Unknown
- ☐ Not Reported



CRF Module Workflow

1. Module created by Working Group
2. Module approved for wider review within NCI (CTROC)
3. Module circulated for wide review outside NCI:
   - Cancer Policy Today, other ASCO vehicles
   - caBIG Clinical Trials Workspace and Steering Committee
4. Comments received / analyzed
   - None required modification of data elements
5. CTROC approves module as an NCI standard
6. Pilot each module with Early Adopter group

Harmonization with Industry

- **Clinical Data Interchange Standards Consortium (CDISC) initiative called Clinical Data Acquisition Standards Harmonization (CDASH) has a common goal: harmonizing and standardizing data collection for clinical research**
  - CDASH focus: elements that are common to all clinical studies
  - caBIG® focus: oncology studies
- **caBIG® modules will include all CDASH "mandatory" questions, plus additional oncology content**
- **Review of content of first forms with CDASH standard: 84% match on first pass**
  - All areas of disparity have since been reconciled

Status: Round One Modules

- Round One: Demography Module
  - Reviewed and approved
  - Form template with instructions are in the NCI Cancer Data Standards Repository (caDSR)
  - Already harmonized with CDASH
  - Ready for deployment and adoption
  - In “early adoption” pilot now
  - Began early adoption: January 2009
    - University of Nebraska, Georgetown/Lombardi, Duke University, Childrens’ Oncology Group, NCI Center for Cancer Research, NCI Division of Cancer Prevention
  - Will conclude early adoption: April 2009

Status: Round Two Modules

- **Round Two Modules developed:**
  - Adverse Events
  - Medical History
  - Physical Exam
  - Participant Identification
  - Registration
  - Enrollment
  - Protocol Deviations
- **Initial CTROC and community review completed**
- **Comments reconciled by workgroup**
- **Harmonized with CDASH**
- **Undergoing final reconciliation and preparation of form template with instructions**
- **Final CTROC review: March 12, 2009**

Future

- **Phased development of additional modules**
- **Community adoption essential for success**
- **Plan for ongoing maintenance includes annual review of the total library of CRFs necessary changes**
- **Modifications will be requested and changes will be vetted by community and NCI**

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Standard Terms for Clinical Trials Agreements

- Negotiation of clinical trials agreements is a key barrier to timely initiation of trials
- Collaborative project with Life Sciences Consortium of the CEO Roundtable, Cancer Centers, and Cooperative Groups
- Analyzed agreements between academic medical centers and industry to identify differences in key terms
- Final negotiated agreements showed greater than 67% convergence on the vast majority of concepts analyzed
- Developed common language as starting point for negotiations with input from legal and business participants

http://cancercenters.cancer.gov

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Communication Plans

- START clauses: Standard Terms of Agreement for Research Trials
- Dissemination of clauses to Sponsored Research Offices at Cancer Centers
- Collaborating with Life Sciences Consortium on communications with industry
- Communications materials include:
  - Website: http://cancercenters.cancer.gov
  - Brochure
  - CD/USB drives with clauses and supporting documents loaded
  - FAQs
  - E-card for electronic communications

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Standard Terms of Agreement for Research Trial (START) Clauses

Streamlining Clinical Trial Contract Negotiations

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Participants in Development of START Clauses

CEO Roundtable on Cancer Life Sciences Consortium

- AstraZeneca
- Eli Lilly & Company
- GlaxoSmithKline
- Johnson & Johnson
- Novartis
- OSI Pharmaceuticals
- Pfizer, Inc.
- Quintiles Transnational
- Sanofi-Aventis
- Schering-Plough
- Wyeth Pharmaceuticals

NCI-Designated Cancer Centers

- City of Hope
- Dana-Farber/Harvard
- Fox Chase
- Johns Hopkins
- Mayo Clinic
- MD Anderson
- Moffitt
- Roswell Park
- UNC Lineberger
- University of Arizona
- University of California, San Francisco
- University of Chicago
- University of Colorado
- University of Pittsburgh

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CTWG Restructuring Initiatives

- Enterprise-Wide/Integrated Management
- Prioritization/Scientific Quality
- Coordination
- Standardization
- Operational Efficiency:

  Use resources most efficiently through improved cost-effectiveness and accrual rates, and more rapid trial initiation

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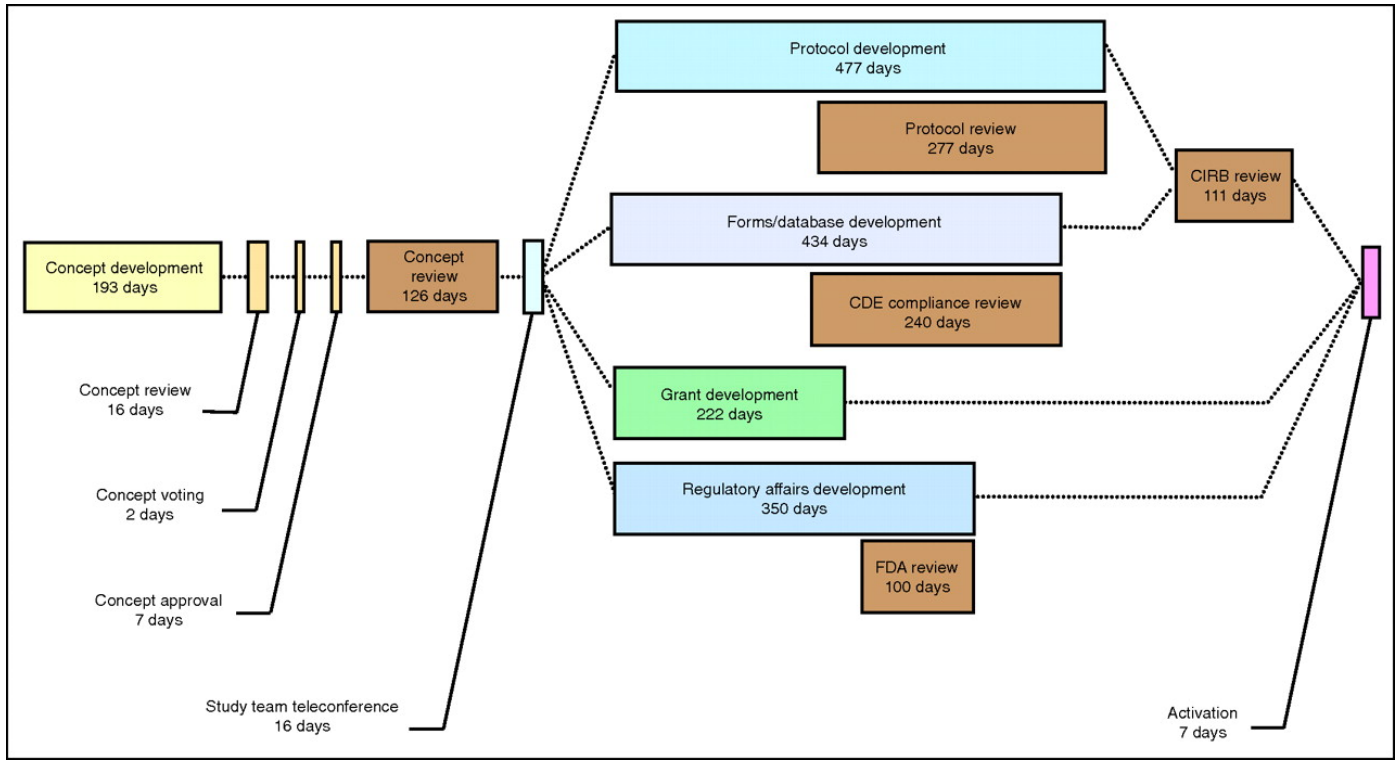
Operational Efficiency Initiative #2

Identify the institutional barriers that prolong the time from concept approval to accrual of the first patient, and develop solutions for overcoming these barriers



Dilts, D. M. et al. J Clin Oncol; 24:4553-4557 2006

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Operational Efficiency Working Group

The Clinical Trials Advisory Committee (CTAC) Charge:

Establish a CTAC Operational Efficiency Working Group (OEWG) to recommend strategies for reducing the time for activation of NCI-supported clinical trials.

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OEWG Highlights

- The OEWG - constituted
  - ~ 62 members
    Chair: Gabriel Hortobagyi, MD
    Co-Chair: James Doroshow, MD
- Orientation Teleconferences (5)– October ,2008
  - Scope (type of trials)
  - Components of trial activation
  - Obstacles to trial activation
- OEWG Face-to-Face Meeting – 12/19/08

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OEWG Membership

- 62 clinical trial stakeholder representatives
  - Cancer Centers – leadership and protocol/trial specialists
  - Cooperative Groups – leadership and protocol/trial specialists
  - Pharma/Biotech
  - FDA
  - CMS
  - Patient Advocates
  - Community Oncologists
  - Statisticians
  - Patient Advocates
  - NCI – DCTD, DCP, CCR, & OD

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OEWG Mission

- Phase I: Develop strategies and implementation tactics for reducing the time for *initiation* of Cooperative Group and Cancer Center trials
  - Reduce study activation time by at least 50%
  - Optimize NCI, sponsor, and investigator interactions to reduce delays
- Phase II: Develop strategies and implementation tactics for reducing the time for *completion* of Cooperative Group and Cancer Center trials
  - Increase the percentage of studies successful in reaching accrual target
  - Assure timely completion of studies

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OEWG Trial Activation Situations

1. Cooperative Group Phase II and III Trials
2. Cooperative Group Investigational Drug Branch (IDB) Trials
3. Cancer Centers – Investigator-Initiated Trials
4. Cancer Centers – Cooperative Group Phase II and Phase III Trials
5. Cancer Centers – Investigational Drug Branch (IDB) Trials

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OEWG Progress

For Cancer Centers and Cooperative Groups there is:

- Agreement on the components of the trial activation process to be examined
- Agreement that timelines for opening all of the clinical trial types must be reduced by at least 50%
- Agreement on existing barriers to speedy trial activation
- Agreement that to substantively improve trial activation timelines will require major changes in every component of the system

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OEWG: Next Steps

- Analyze potential solutions identified at the OEWG December meeting and refine target timelines
- Develop draft recommendations to address barriers and reduce time to activation
- Next OEWG meeting in Spring 2009 to:
  - Prioritize recommendations
  - and identify implementation strategies
- Develop implementation plans for prioritized recommendations

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CTWG: New Financial Model Rationale

- Current system – large differential between NCI per-case costs and actual clinical trial costs is not sustainable over time for the Cooperative Groups nor CCOPs
- There may be some cost inefficiencies in the current system
- Sites that accrue only a few patients per year may result in a high per-case cost because of fixed costs

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New Funding Model Implementation Plan

- Collaboratively with the Cooperative Groups, develop a new phase III trial funding model incorporating information from the ongoing financial analysis
  - Align reimbursement with trial complexity
  - Incentivize & reward high accruing, cost-efficient sites
  - Reduce duplication of administrative functions
  - Establish minimum accrual standards
- Final recommendations for future funding strategies to be made in concert with OEWG deliberations and data from financial analysis

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Trial Complexity Model

- Trial Complexity Model developed in collaboration with the Cooperative Groups
  - Align reimbursement with trial complexity
  - Not impact the current $2000 base capitation rate
  - Develop a system to ascertain trial complexity
  - Simple, standardized model

- 14 studies deemed “complex” in 2008 and will receive an additional $1000 capitation over $2000 base

- Anticipate continued support (up to $7.5M) in 2009

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CTWG Minority and Underserved Populations Accrual Enhancement Initiative

- Rationale
  - Minority and underserved populations are underrepresented in Cooperative Group clinical trials
- Recommendation
  - Expand established NCI programs to increase the recruitment of minority and underserved populations to cancer clinical trials

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Progress

- Convened NCI stakeholders with established minority clinical trials programs
- Solicited proposals for administrative supplements to established programs from eligible grantees
  - MBCCOPs or CCOPs
  - Cancer Disparity Research Partnerships (CDRP)
  - Patient Navigator Research Program, CRCHD
  - Community Networks Program, CRCHD
- Proposals evaluated by internal and external reviewers
- 12 programs funded in 2008 for two-years with supplements of ~ $100,000 per year

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CTWG Minority/Underserved Supplements Review and Metrics:

- Definitive plan to enhance accrual
- Ability to enhance and support additional minority and underserved accrual
- Sustainability of activity over time
- Change in enrollment in DCP and CTEP funded trials from baseline

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Today's agenda

- Enhancing and providing incentives for collaborative clinical and translational research
  - Dr. Abbruzzese (Harmonziation Working Group Update)
  - Dr. Erlichman (Investigational Drug SC)
  - Dr. Tepper (GI Steering Committee)
  - Committee Discussion
- Enhancing Minority and Underserved Accrual to Clinical Trials
  - Dr. McCaskill-Stevens
  - Mr. Williams (Eliminating Disparities in Clinical Trials recommendations)
- Process to Accelerate Science (PATS) Working Group Update
  - Dr. Matrasian

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Coordinating Center for Clinical Trials

- Clinical Trials Working Group (CTWG)
- Translational Research Working Group (TRWG)