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Restructuring the National Cancer Clinical Trials Enterprise

Clinical Trials Working Group

NCAB Implementation Update

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

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Common Themes of the Restructuring Plan

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

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Enterprise-Wide: Integrated Management

CTWG Recommendation:

- Establish an external clinical trials oversight committee to advise NCI Director
- Develop a coordinated organizational structure within NCI to manage the clinical trials enterprise

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Clinical Trials Advisory Committee (CTAC)

- Federal advisory committee chartered in March 2006
  http://deainfo.nci.nih.gov/advisory/ctac/ctac.htm
- Membership:
  - ✓ Ten members current Boards (NCAB, BSA, BSC, DCLG)
  - ✓ Fourteen new members from extramural clinical trials community
- First meeting: January 10, 2007
- Functions:
  - ✓ Provide extramural oversight for CTWG implementation initiatives institute-wide, including clinical trial informatics
  - ✓ Strategic advice regarding entire NCI clinical trials portfolio
  - ✓ Advise on use of correlative science and quality of life funds
  - ✓ Develop recommendations for additional refinements to NCI-supported clinical trials system based on ongoing analyses: operational efficiency, financial analysis of phase III trial costs, and central IRB function
  - ✓ Advise on outcome of formal evaluations

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Clinical Trials Advisory Committee (CTAC)

- Informatics working group
  - Provide interface with NCICB and oversight of CTWG clinical trials IT initiatives
- Public/Private partnership working group
  - Initiatives to enhance NCI-sponsored clinical trials through prospective interactions with the private sector
- Coordination working group
  - Bring together Cancer Center Directors, Cooperative Group Chairs, and SPORE PIs to harmonize program guidelines and facilitate clinical trials interactions

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Clinical Trials Operations Committee (CTOC)

- Internal NCI committee established in December, 2005 to provide strategic oversight for NCI clinical trials programs and infrastructures
- Chair, Dr. John Niederhuber
- Membership from all NCI Divisions, Offices, and Centers involved in NCI-supported clinical trials including DCTD, DCP, OCTR, DCCPS, CCR, DCEG, NCICB, DEA and CCCT

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CTOC Activities Update

- Reviewed all RFAs and PAs involving clinical trials in past year
- Provided input to NCICB on the CTWG informatics implementation plan
- Evaluating feasibility of modifying clinical trials data reporting requirements for grant funded trials (e.g. R01, Program Project grants, etc.)
- Approved minority accrual supplements
- Portfolio reviews
  - Programmatic
  - Disease specific

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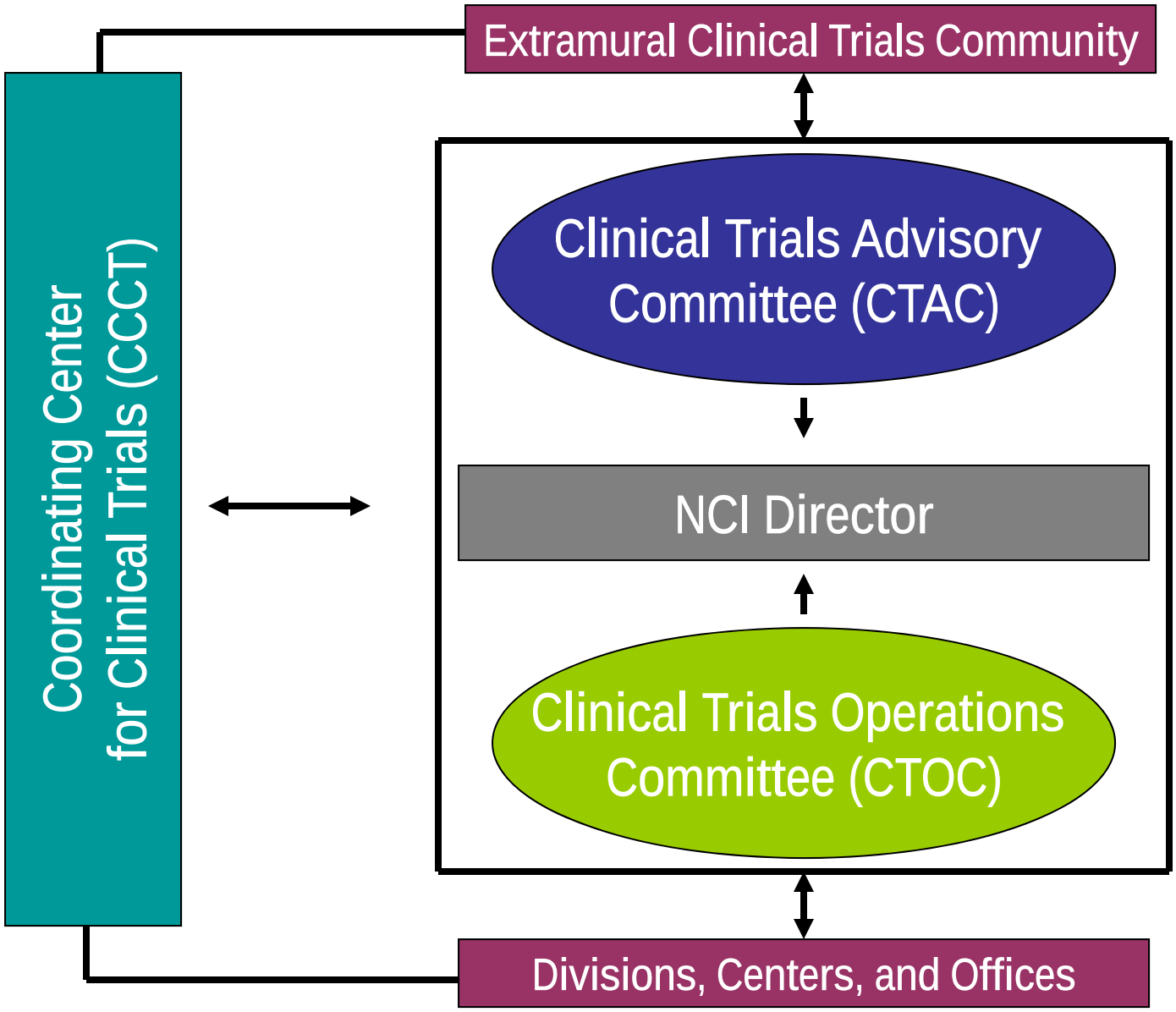
Integrated Management



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Common Themes of the Restructuring Plan

- 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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Progress: Prioritization/Scientific Quality

- IDSC has been established with 5 task forces
  - ✓Formally integrated into establishment of CTEP drug development planning
- Disease-specific Steering Committees
  - ✓GI and GYN up and running
  - ✓H&N operational: Face-to-Face 12/06
  - ✓Symptom-Management/HRQOL launched: Face-to-Face 5/07
  - ✓SOPs developed
- SPORE members, community oncologists and advocates have been elected to all SC's
- Task Force defined prioritization criteria for correlative science studies

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Prioritization/Scientific Quality: 2007 Goals

- Expand role of IDSC for early phase trial prioritization utilizing evolving Task Forces
  - ✓ Identify priority issues in phase II trial design
  - ✓ Develop standards for biomarkers in early phase clinical trials
  - ✓ Review the clinical development plans for angiogenesis and signal transduction inhibitors
- Complete implementation of H&N and Symptom Management SC's; SOTS meeting in GI and GYN
- Establish process to ensure that correlative science and quality of life studies conducted in association with clinical trials conform to standard protocols and standardized lab practices: Biomarker Standardization Workshop Spring '07

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Common Themes of the Restructuring Plan

- 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

- Establish a comprehensive database containing regularly-updated information on all NCI-funded clinical trials

- Realign NCI funding, academic recognition, and other incentives to promote collaborative team science and clinical trial cooperation

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Promote Collaborative Team Science

- Award Guideline Modification
  - Cooperative Group program guidelines are in the process of modification to reflect collaboration with SPOREs and Cancer Centers positively
  - Plan to modify SPORE and Cancer Center program guidelines to consider collaboration with Cooperative Groups positively
- Funding Practice Modification
  - Evaluating feasibility of accruing patients to SPORE and Cancer Center clinical trials through NCI's Cancer Trials Support Unit (CTSU)
- New Forms of Recognition for Cancer Clinical Investigators
  - Cancer Clinical Investigator Team Leadership Award to recognize mid-level clinical investigators for exceptional participation in NCI-funded collaborative clinical trials

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Common Themes of the Restructuring Plan

- Enterprise-Wide/Integrated Management
- Prioritization/Scientific Quality
- Coordination
- Standardization: Standardize informatics infrastructure and clinical research tools
- Operational Efficiency

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Standardization Initiatives

1) Informatics infrastructure interoperable with caBIG™

2) Standard Case Report Forms incorporating Common Data Elements

3) Credentialing system for investigators and sites that is recognized and accepted by NCI, industry sponsors, clinical investigators and clinical trial sites

4) Establish commonly accepted clauses for clinical trial contracts

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Progress: Standardization

- CaBig Clinical Trials Steering Committee created: Clinical trialists, statisticians, IT experts—First meeting March '07
  - Establish strategic priorities and oversight for all CTWG informatics initiatives
  - Ensure coordination of CTWG informatics activities across NCI-supported clinical trials activities
- Inventory of NCI electronic CRFs is underway
- Preliminary meeting with industry held to discuss standard clauses for clinical trials contracts

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Common Themes of the Restructuring Plan

- 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 Initiatives

1) Restructure the funding model for phase III efficacy trials to incentivize more rapid rates of patient accrual

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

3) Expand current outreach programs to increase the recruitment of minority populations to cancer clinical trials

4) Develop approaches for enhancing adoption of centralized Institutional Review Board processes

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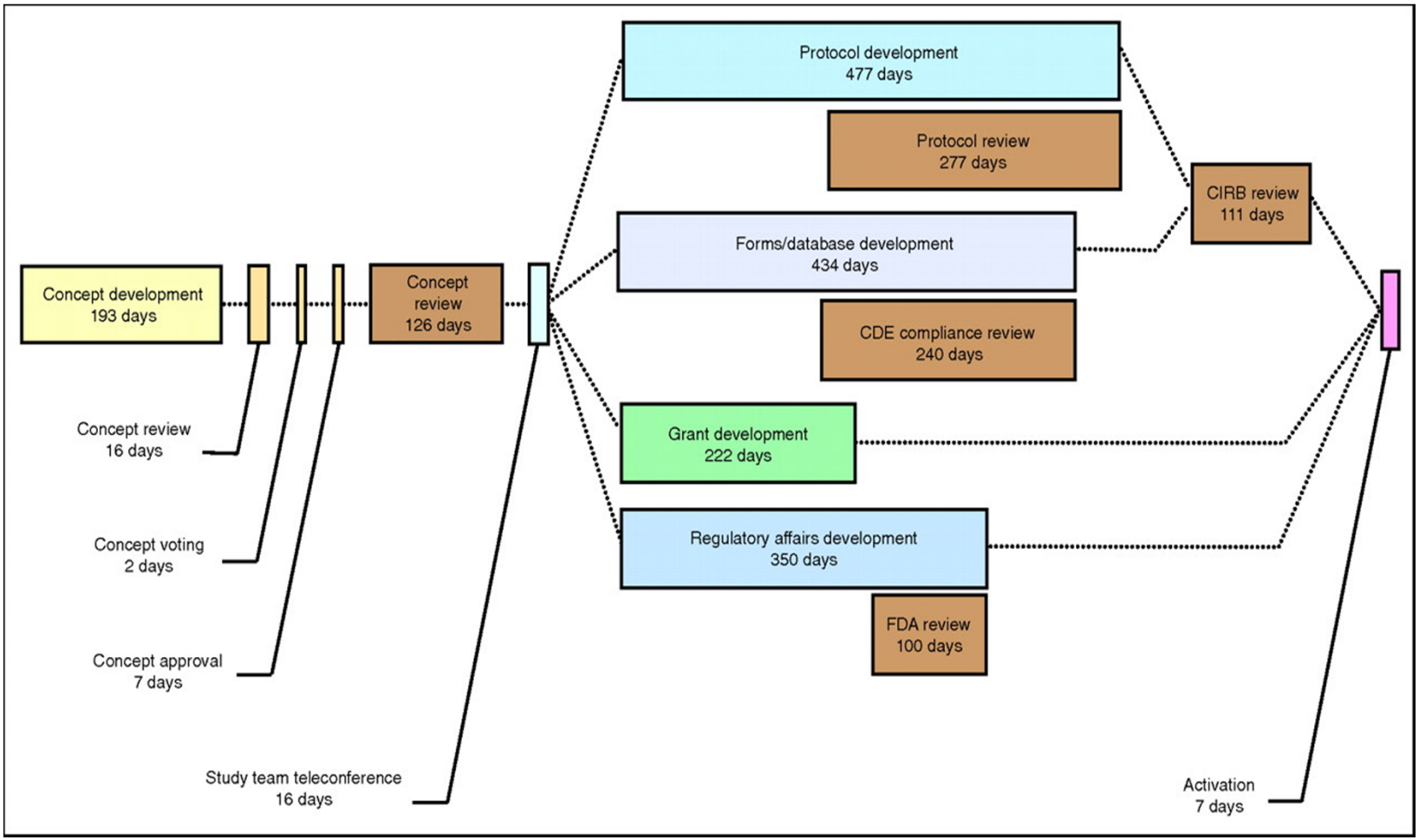
Financial Analysis

A financial analysis of phase III trial costs has been initiated:

- Identify areas of inadequate funding, where increased financial compensation could significantly improve clinical trial conduct
- Identify areas of overlap, duplication or redundancy which, if eliminated, could result in cost-savings
- Identify best practices for budget allocations and financial management that could potentially be standardized across Cooperative Groups
- Assess the cost savings that might result from closing sites that accrue very low numbers of patients

Process Flow Map for Phase III Studies



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

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Enhance Minority Accrual

- Trans-NCI Partnership formed to propose mechanisms and solicit concepts
- Programs receiving FY06 supplemental funding included:
  - Cancer Disparities Research Partnerships to expand available trials beyond radiation oncology to surgical and medical oncology trials
  - MBCCOP and Patient Navigator Research Program to evaluate the impact of Patient Navigators on minority accrual in cancer prevention and control trials capitalizing on the experience of both programs
- Timeline calls for expansion in FY07

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Enhance Adoption of Central IRB

- A analysis of the barriers to the acceptance of the NCI Central Institutional IRB (CIRB) has been initiated
- An analysis of the potential cost savings that would result from the use of the CIRB has been funded

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Evaluation and Outcome Measures

- Structured evaluation system
  - Designed by experienced evaluation specialists
  - Blend of quantitative and qualitative measures
  - External clinical trials expert panel has reviewed the proposed measures
- Baseline evaluation to be performed in FY07
- Periodic evaluations to assess impact of restructuring