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# CTWG and TRWG Implementation Update

*Presented to the BSA*

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

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# Today's Agenda

- Update on the implementation of CTWG initiatives
  - Integrated Management – Dr. Prindiville
  - Prioritization/Scientific Quality – Dr. Prindiville
  - Informatics – Dr. Buetow
  - Operational Efficiency – Dr. Doroshow
  - Baseline Evaluation – Dr. Doroshow
- Update on the implementation of the TRWG initiatives – Dr. Matrisian

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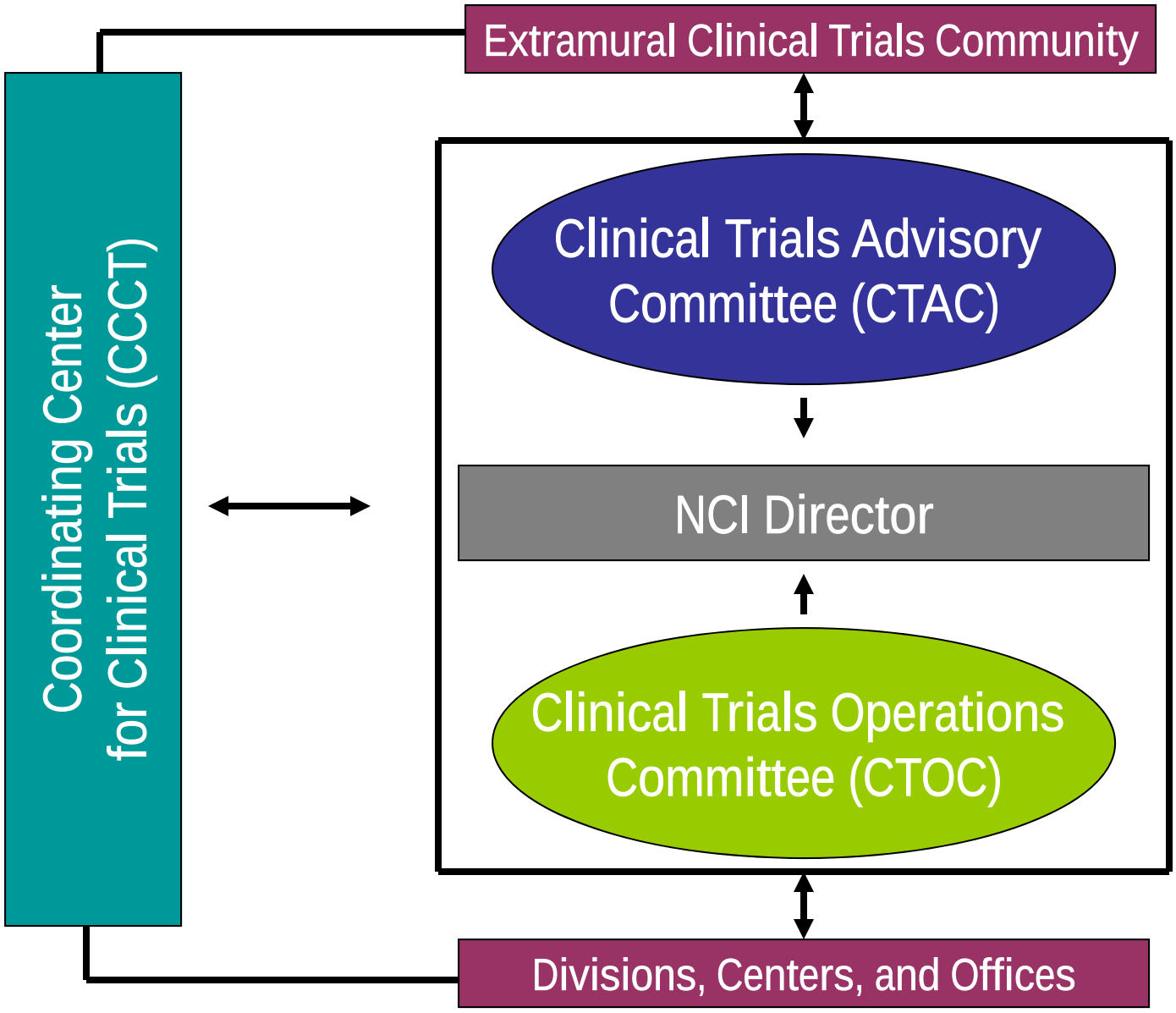
# Integrated Management



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# Clinical Trials Advisory Committee

- Provides extramural oversight for implementation of CTWG initiatives Institute-wide, including clinical trials informatics
- Chaired by NCI Director
- 24 members appointed by NCI Director represent the broad clinical trials community
- Disciplines represented include medical, surgical, gynecologic, urologic, radiation and pediatric oncology; pharma and biotech; nursing; behavioral sciences; epidemiology; biostatistics; basic sciences; and patient advocates
- 5th meeting, June 25, 2008; http://deainfo.nci.nih.gov

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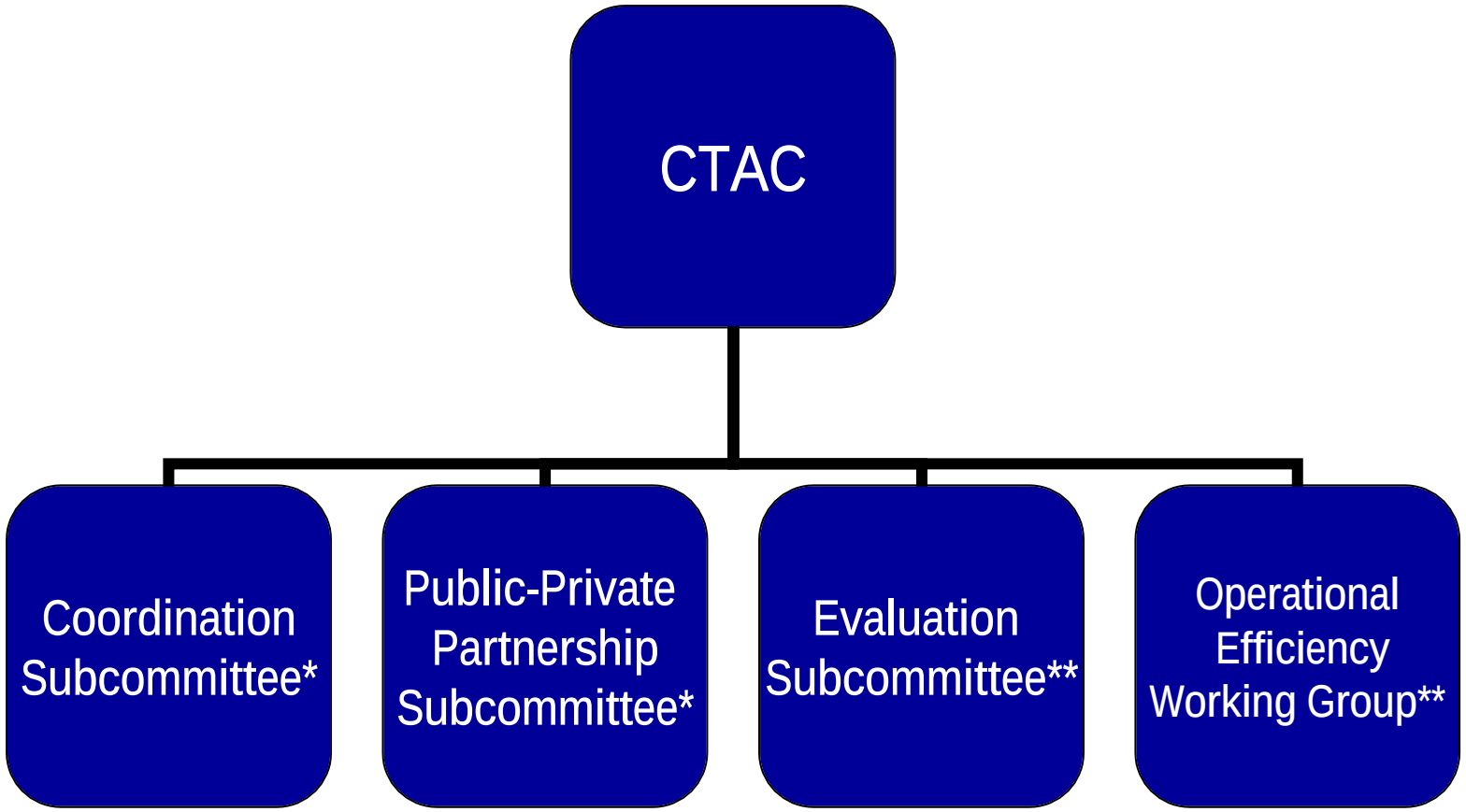
# Clinical Trials Advisory Committee (CTAC)




*Ad hoc subcommittee
**Proposed

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# Coordination Subcommittee

- Function
  - Provide advice to the Director, NCI on how to foster collaboration among the various components of the NCI-supported clinical trials infrastructure in order to develop a fully integrated clinical trials system
- Chair:  James Abbruzzese
- Projects
  - Harmonizing program guidelines among Cancer Centers, SPOREs, and Cooperative Groups to enhance clinical trials collaboration
  - CTAC Planning Working Group to discuss optimal integration of the TRWG initiatives implementation into CTAC activities

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# Ad Hoc Public Private Partnership Subcommittee

- Function
  - To provide advice to the Director, NCI on how to enhance NCI-sponsored clinical trials through collaborative interactions with the private sector
- Chair:  David Parkinson
- Initial focus
  - Extramural oversight for the collaborative project between NCI and the Life Sciences Consortium, CEO Roundtable to standardize clinical trials agreement terms

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# Standardization of Clinical Trial Agreement Terms

- Involvement of academic medical centers, Cooperative Groups, industry, and legal advisors has been solicited
- Multidisciplinary team compiling list of agreement terms to be standardized such as intellectual property and licensing, publishing rights, confidentiality, ownership of data, risk and indemnification
- Analyze agreements to identify differences in key terms and develop options for standardization/harmonization
- Develop modules of potential standardized clauses
- Develop a structured approach for achieving buy-in and consensus on the standardized modules by key stakeholders

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# Operational Efficiency Working Group

- Dr. David Dilts has conducted a process analysis of the institutional barriers to the timely activation of phase III clinical trials
- Findings have been presented to CTAC, Cooperative Groups and Cancer Center Directors
- Working Group is under formation to address the results, recommendations and develop strategies to overcome the barriers

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# Common Themes of the Restructuring Plan

- 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 design and prioritization

- Disease-Specific Scientific Steering Committees (SC's) for phase III trials

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# Investigational Drug Steering Committee

- Provide strategic input into the clinical development plans for new agents for which CTEP holds the IND
- Co-Chairs:  Mark Ratain, MD and Charles Erlichman MD
- Membership from PI's of all NCI's early phase U01 and N01 contracts as well as representatives from Cooperative Groups and other content experts

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# IDSC: Task Force Activities

- Signal Transduction Task Force reviewed potential cMet inhibitors and identified niche for CTEP studies
- Biomarker Task Force developing benchmarks for correlative markers in early phase therapeutics
- Angiogenesis Task Force addressing side effects of VEGF inhibitors
- Clinical Trial Design Task Force preparing manuscript from meeting on Phase II trial design

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# Prioritization Accomplishments: Early Phase Trials

- Transparency in NCI drug development process
- Strategic review of NCI's early phase clinical trials by type of agent
- Enhanced scientific input for novel therapeutics
- Recommended Career Development LOI program to engage young clinical investigators as PIs in NCI early phase clinical trials
- Transition from IDSC to Phase III Steering Committees facilitated by designated liaisons

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# Disease-Specific Steering Committees: Responsibilities

- Prioritize phase II and III concepts for therapeutic clinical trials
- Convene State-of-the-Science meetings to identify critical questions to prioritize strategies for NCI supported clinical trials
- Develop phase II and III concepts for new clinical trials utilizing Task Forces
- Periodically review accrual and unforeseen implementation issues

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# Initial Disease-Specific Steering Committees

- Gastrointestinal Cancer (Co-Chairs: Joel Tepper, MD and Daniel Haller, MD)
- Gynecologic Cancer (Co-Chairs: William Hoskins, MD and Gillian Thomas, MD)
- Head and Neck Cancer (Co-Chairs: Arlene Forastiere, MD, David Schuller, MD, and Andrew Trotti, MD)
- Symptom Management and Health-Related Quality of Life (Co-Chairs: Deborah Bruner, RN, PhD and Michael Fisch, MD, MPH)

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# Disease-Specific Steering Committee: Membership

- Co-Chairs
- Cooperative Group Disease Committee Chairs
- SPORE Representatives
- R01/P01 Translational scientists
- Biostatistician
- Community Oncologists
- Patient Advocates
- NCI CTEP Staff
- Investigational Drug Steering Committee Liaison
- Symptom Management & Health-Related QOL Steering Committee Liaison

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# GI Steering Committee: Activities

- Reviewed 8 concepts (6 phase III); 4 approved or approved pending revisions
  - Disease sites (pancreas, colorectal, esophagus)
  - Therapeutic modalities included chemotherapy, monoclonal antibodies, radiation, and surgery
  - Review occurring in a timely fashion
- Six task forces: Colon, Esophagogastric, Pancreas, Rectal-Anal, Hepatobiliary, and Neuroendocrine
- Pancreas Cancer State of the Science meeting convened in 2007

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# GYN Steering Committee: Activities

- Fifteen concepts reviewed to date; nine approved or approved pending revisions
- Committee reviewing both phase III and randomized phase II concepts
- Three Task Forces have been actively involved in concept evaluation: Cervical, Uterine, and Ovarian
- Cervical Cancer State of the Science convened in 2007

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# Head and Neck Steering Committee

- Head and Neck Intergroup transitioned to a Steering Committee in December, 2006
- Four Task Forces identified:
  - Metastatic/Recurrent Disease
  - Rare Tumors
  - Previously Untreated, Locally Advanced
  - Tumor Biology and Imaging
- Committee will review both phase II and III studies

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# Symptom Management/Health-Related QOL (SxQOL) Steering Committee Activities

- Developed plan to evaluate and prioritize symptom management clinical trial concepts to be conducted through the CCOP mechanism.
- Identified liaisons to disease-specific committees to provide input to studies with secondary quality of life endpoints in cooperative group treatment studies.
- Developed prioritization criteria for QOL and symptom management studies that are eligible for the Biomarker, Imaging, and Quality of Life Supplemental Funding Program.

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# Disease-Specific Steering Committee Timelines

- CTWG timeline called for completion of the implementation of Steering Committee structures by the end of 2010
- Plan to launch Genitourinary and Lung & Mesothelioma Steering Committees in 2008
- Patient Advocate Steering Committee forming in collaboration with Office of Advocacy Relations
- Remainder of committees in FY09 and FY10

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# CTWG Prioritization /Scientific Initiative #4

- Establish a funding mechanism and prioritization process to ensure the most important correlative science and quality of life studies can be initiated in a timely manner in association with clinical trials.

- Primary purpose is to fund studies conducted in association with phase 3 trials when the cost of such studies is too large to be covered by the Cooperative Group mechanisms in a timely manner.

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# CTWG Prioritization /Scientific Initiative #4

- Task Force of the Program for the Assessment of Clinical Cancer Tests (PACCT) developed criteria for prioritization and evaluation of correlative science studies (essential marker and imaging studies) which were approved by CTAC in July 2007.

- Symptom Management and Health-Related QOL (SxQOL) SC developed criteria for prioritization and evaluation of essential QOL studies which were approved by CTAC in November 2007.

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# Essential Biomarker & Imaging Correlative Science Prioritization Summary

- Prioritization of essential marker and imaging studies
  - *Integral* studies – required for trial
    - Test to establish patient eligibility
    - Test for patient stratification
    - Test to assign patient to treatment arm, including early response endpoints for assignment of treatment during a trial
  - *Integrated* studies - identify or validate for use in future trials
- Companion document - Requirements for assays standards approved by CTAC

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# Examples of *Integral* Tests

- Test to establish patient eligibility
  - In vitro assessment of HER2 for adjuvant trials of trastuzumab
- Test for patient stratification
  - Measurement of 18qLOH and MSI for assignment of risk in stage 2 colon cancer
- Test to assign patient to treatment arm, including early response endpoints for assignment of treatment during a trial
  - OncotypeDX™ to assign to study arm, such as in TAILORx trial
  - FDG-PET scan after initial course of therapy to assess response and determine whether to continue treatment

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# Implementation of the Program – FY08

- Funding via Administrative Supplements
  - Cooperative Group Program
  - CCOP Program - Research Bases
- Announcement by programs (CTEP and DCP) made in December 2007
- Anticipate funding up to $5M in FY08

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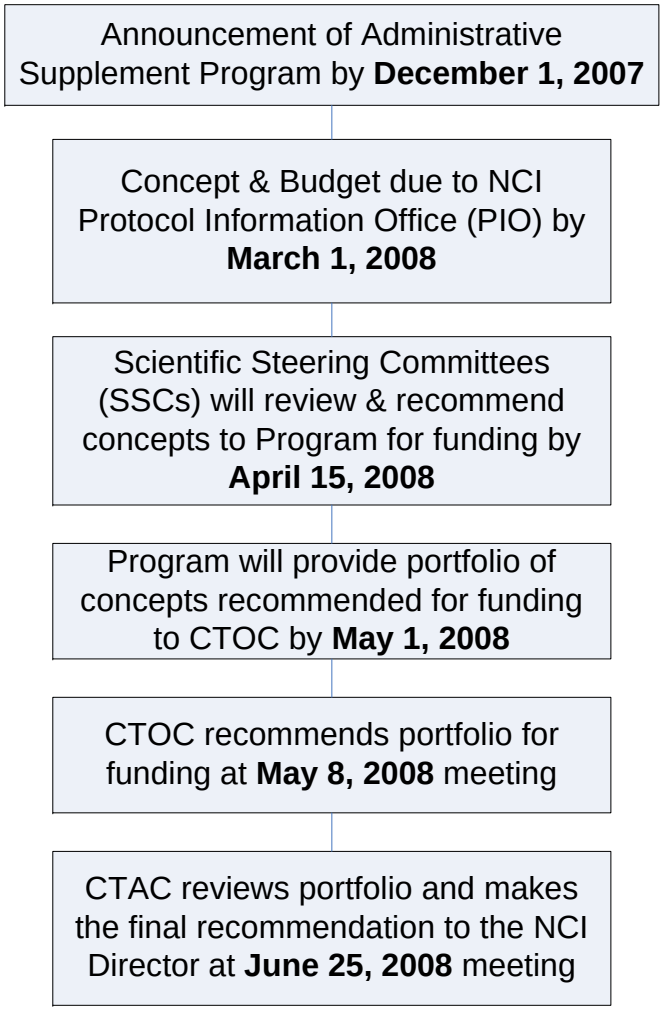
# Review & Prioritization – FY08

- Scientific Steering Committees
  - Review proposed studies in association with the review of the parent trial concept
  - Existing CTEP review process will be used when no Scientific Steering Committee exists
- Program (CTEP & DCP)
  - Develops funding plan based on studies recommended for funding by the Scientific Steering Committees
- Clinical Trials Operations Committee (CTOC)
  - Recommends funding plan across disciplines (biomarker, imaging, and quality of life) for consideration by CTAC
- Clinical Trials Advisory Committee (CTAC)
  - Reviews portfolio and makes final funding recommendation

# FY08 Prioritization and Funding Process for Essential Marker & Imaging Studies*




*Dates approximate