

CTWG and TRWG Implementation Update

*Presented to the NCAB
February 6, 2008*

Sheila A. Prindiville, MD, MPH

Ken Buetow, PhD

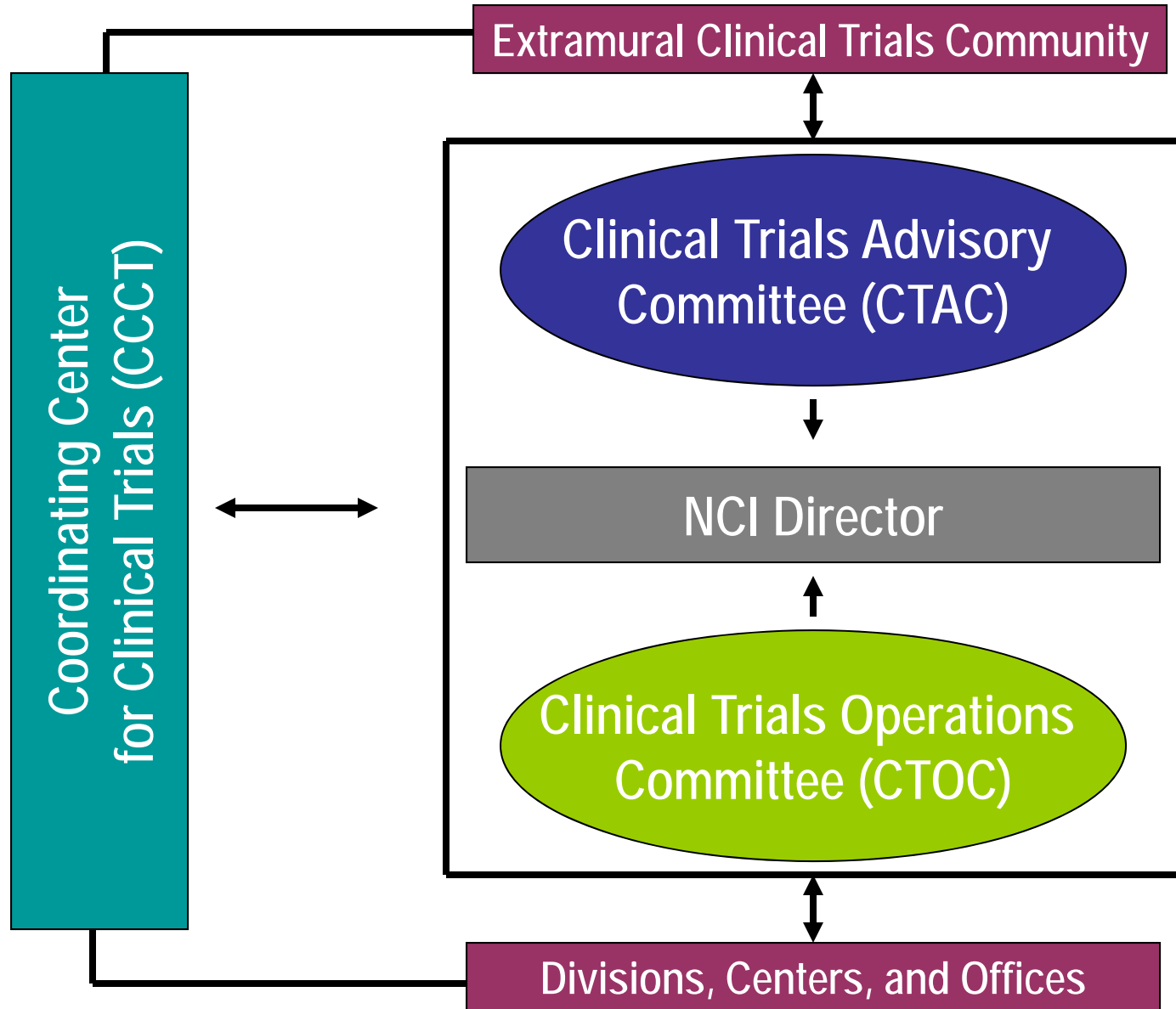
James H. Doroshov, MD

Lynn M. Matrisian, PhD

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**

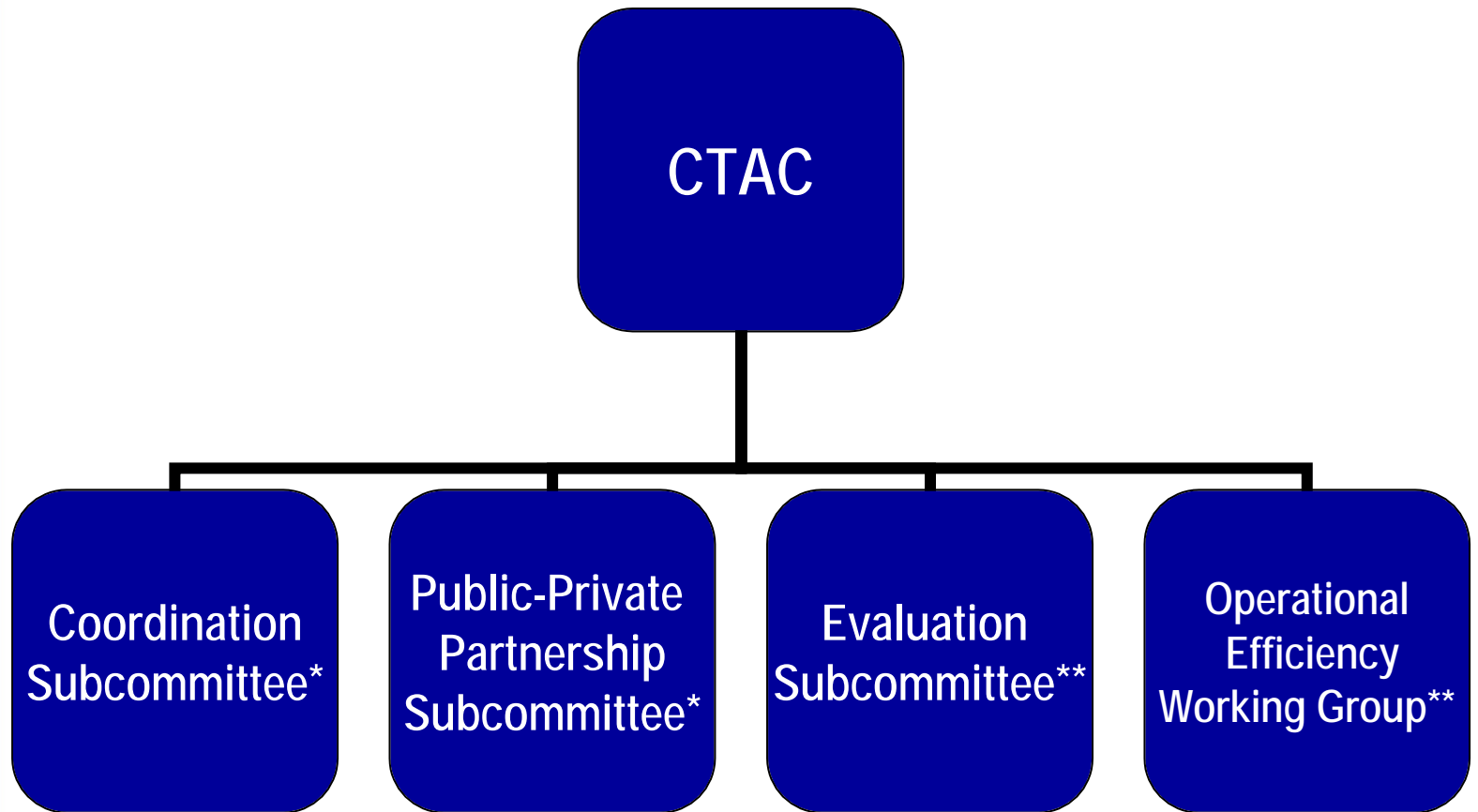
Integrated Management



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>

Clinical Trials Advisory Committee (CTAC)



*Ad hoc subcommittee

**Proposed

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

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**

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

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

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

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**

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

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

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

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

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)**

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

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

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

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

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.

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

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**.

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.

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

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

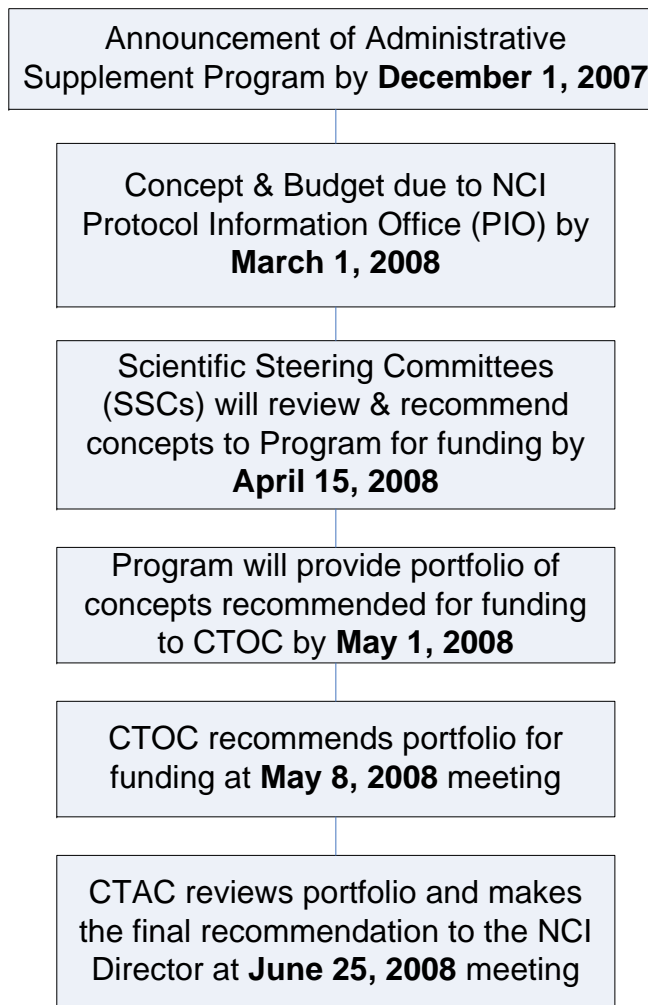
Implementation of the Program – FY08

- **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**

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