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# Proposed Evaluation Plan for Assessing Implementation of the Clinical Trials Working Group (CTWG) Recommendations

CTWG Evaluation Working Group
Interim Report

Clinical Trials and Translational Research Advisory Committee

March 3, 2011

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# Interim Report Context

- Goal of overall CTWG evaluation
  - Assess performance and impact of implemented CTWG initiatives on the effectiveness of the overall NCI clinical trials enterprise
- Goals of the CTWG Evaluation Working Group
  - Refine the proposed evaluation plan
  - Establish a timeline for implementation
- Goals of today's discussion
  - Present interim findings of the Working Group
  - Obtain CTAC guidance to inform the final plan

# CTWG Evaluation Process

- Completed baseline study October 2008
  - Determined feasibility of data collection
  - Reported on certain measures of the state of system (data from 2005-2006)
  - http://transformingtrials.cancer.gov/initiatives/ctwg/evaluation
- Baseline study included measures and methodologies for a proposed future evaluation plan
- CCCT constituted the CTWG Evaluation Working Group under CTAC to advise on the proposed evaluation plan

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# Working Group Process to Date

- Orientation teleconferences (November-early December)
- Face-to-face meetings to refine the proposed measures and methodologies (mid December)
- NCI stakeholders reviewed results of Working Group meetings and further refined the measures and methodologies (December 22)
- Co-Chairs reviewed and refined revised Evaluation Plan (January)
- Teleconferences with Working Group members to review and refine revised Plan approved by the Co-Chairs (late January and early February)

# Working Group Membership

Extramural Members

- Peter Adamson (Co-chair)
- Dan Sargent (Co-chair)
- Deb Bruner
- Deborah Collyar
- Arlene Forastiere
- Steve Grubbs
- David Parkinson
- Joel Tepper
- George Weiner
- George Wilding

NCI Members

- Jeff Abrams
- Debbie Jaffe
- Lori Minasian
- Meg Mooney
- James Zwiebel

Facilitators

- CCCT: Sheila Prindiville/ Elizabeth Dean
- STPI: Judy Hautala/Brian Zuckerman/Rachel Parker

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# Evaluation Plan Overview

- Four primary evaluation components
  1. System Outcomes
     1A. Trial quality
     1B. Scientific importance and clinical relevance of trial results
     1C. Efficiency of trial initiation and conduct
  2. Collaboration
  3. Disease Steering Committees
  4. Investigational Drug Steering Committee
- Limited to trials under purview of the Scientific Steering Committees and contained in current CTEP/DCP databases

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# 1A. System Outcomes: Trial Quality Quantitative Measures

- Percentage of trials that complete accrual
  - New definitions of 'complete' may be needed for Phase I/II adaptive designs
- For trials that do **not** complete accrual, collect data on reasons; examples include:
  - Sufficiently positive results at an interim analysis
  - Stopped for safety concerns
  - Subjects accrue to competing trials
  - Patients did not complete study
  - Sponsor withdraws from trial
  - Loss of drug supply
  - Study not feasible/too complex
  - Study loses relevance because of scientific advances
- Percentage of trials that definitively answer primary question (either positively or negatively)

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# 1A. System Outcomes: Trial Quality Quantitative Measures (cont.)

- Percentage of trials whose results are published in peer-reviewed journals
  - Impact factor of journals
  - Time lag for publication
- Linkage between early-stage and Phase III trials
  - For Cooperative Group Phase III trials, determined from protocol background section
  - For industry Phase III trials, solicit information from study chair (identified in clinicaltrials.gov)

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# 1B. System Outcomes: Scientific Importance & Clinical Relevance - Qualitative Analysis

- Qualitative interpretation and expert judgment required
- Potential Measures
  - Do trial results provide a definitive answer (yes or no) to the primary question as opposed to being inconclusive
  - Were results novel when trial completed or superseded by other results
  - Are trial results sufficiently meaningful to warrant practice changes (e.g., two-week extension of survival likely not meaningful)
  - Did results, even if scientifically important, result in real-world practice changes
  - Did trial meet important secondary aims (‘important‘ defined as ‘if met, would warrant stand alone publication’)

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# 1B. System Outcomes: Scientific Importance & Clinical Relevance - Qualitative Analysis

- Convene initial expert group
  - Develop refined set of measures
  - Establish preliminary criteria for judging the selected measures
- Pilot the proposed measures and criteria on all Phase III trials completed in a recent year (e.g., 2009 or 2010)
  - Determine feasibility of approach
  - Refine measures and criteria
- Annual evaluation of trials completed in past year
- Periodic review of whether trial results impacted real-world practice

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# 1B. System Outcomes: Clinical Relevance Quantitative Measures

- Percentage of NCI-funded trials that support NDA/sNDA submission and FDA approval (both initial and for new uses)
- Percentage of NDA/sNDA submissions and FDA approvals that are supported by one or more NCI-funded trials
- Percentage of NCI-funded clinical trials that lead to CMS decision to reimburse for the intervention
- Need to develop measures for interventions that do not require FDA approval or a CMS coverage determination

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# 1C. System Outcomes: Efficiency of Trial Initiation & Conduct - Quantitative Measures

- Efficiency of trial initiation
  - Time from LOI receipt to trial opened for accrual (CTEP early drug development trials)
  - Time from concept submission to Steering Committee to trial opened for accrual (CTEP late-phase and DCP symptom management trials)
- Efficiency of trial conduct
  - Percentage of trials meeting originally projected accrual
  - Percentage of trials with substantive amendments (exclusive of those resulting from new drug safety information)
  - Average number of substantive amendments per trial not resulting from new safety information

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# 2. Collaboration: NCI Program Guideline Analysis

- Identify types of collaboration defined within the Cooperative Group, SPORE, and Cancer Center guidelines
- For each type of collaboration identify incentives and disincentives such as:
  - Whether there are scored review criteria associated with collaboration
  - Whether funds from the base award can be used to conduct collaborative activities
  - Whether supplemental funds are available for collaboration

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# 2. Collaboration: Quantitative Measures

- Percentage of CTEP funded Phase II clinical trials (and patients on trials) that involve collaboration in accrual across multiple institutions
- Percentage of Phase III clinical trials (and patients on trials) that involve collaboration in accrual across multiple Cooperative Groups
- Extent of industry collaboration
  - Number of investigational agents provided to CTEP (total, number of new agents added/year)
  - Number of companies collaborating with CTEP (total, net number of new companies added/year)

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# 3. Disease Steering Committees: Evaluation Methodology

- Quantitative and qualitative approaches
- Evaluation on an individual Steering Committee level
- System Outcome measures stratified by Steering Committee
- Database analyses of timeline performance in approving concepts
- Qualitative analysis via stakeholder interviews
  - Steering Committee members (including Group disease committee chairs)
  - NCI staff
  - Group leadership
  - Investigators who submitted concepts
  - Other extramural trialists

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# 3. Disease Steering Committees: Evaluation Topics & Sample Measures

- Timeline Performance
  - Time from initial concept receipt to final decision
  - Time from initial concept receipt to trial opened for accrual
- Prioritization
  - Transparency, fairness, quality, and efficiency
- Concept Development
  - Role of Task Force/Steering Committee deliberations
- Portfolio Management
  - Role of Steering Committee in providing strategic guidance for future trials in disease area
- Collaboration
  - Collaboration among Steering Committees and with IDSC

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# 4. Investigational Drug Steering Committee Evaluation Methodology

- Predominantly qualitative approaches
- Expert panel review of IDSC impact
- Database analyses of timeline performance in approving concepts
- Qualitative analysis via stakeholder interviews
  - IDSC members
  - Investigators who submitted LOIs
  - NCI staff
  - Industry
  - Steering Committee members
- Bibliometrics and document review

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# 4. Investigational Drug Steering Committee Evaluation Topics

- Clinical Development Plan (CDP) quality pre- and post-IDSC review (expert panel and stakeholder interviews)
- Process for developing CDPs (stakeholder interviews)
- Quality/balance of CTEP early drug development trial portfolio (expert panel)
- Transparency and quality of early drug development trial prioritization (stakeholder interviews)
- Collaboration in accrual to CTEP EDD trials (database analyses)
- Collaboration among IDSC members (stakeholder interviews)
- Impact of IDSC Reports/Guidelines (database/document analyses and stakeholder interviews)

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# Discussion Questions for CTAC

- Should the evaluation be a high priority for initiation in 2011?
- Are the proposed areas of evaluation (System Outcomes, Collaboration, Steering Committees, IDSC) on target?
- Are there alternatives to expert judgment for assessing the scientific importance and clinical relevance of trial results?
- Are there alternatives to stakeholder interviews for addressing Steering Committee and IDSC performance?
- Is the extent of qualitative measures appropriate to achieve the goals of the evaluation?
- Should CTAC form a standing subcommittee to monitor the evaluation process?

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# Next Steps

- Incorporate CTAC guidance from today into the final Evaluation Plan
- Working Group to prioritize proposed data elements for addition to current databases
- NCI to determine feasibility of incorporating the proposed data elements into current databases
- Final report presented at July 2011 CTAC meeting
- Proceed with Evaluation Plan implementation according to timeline in Final Report