

CTAC NCTN External Evaluation Working Group Recommendations

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March 8, 2017

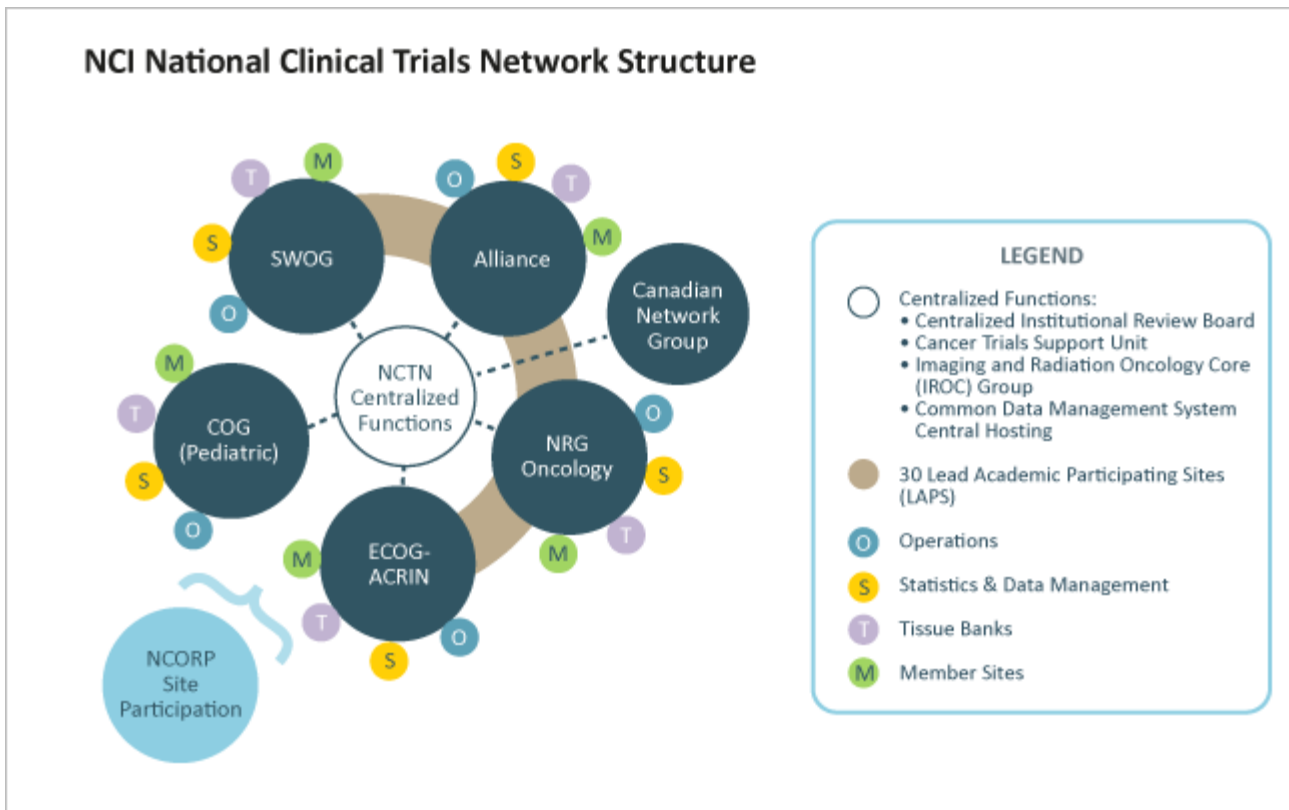
Overview of Report and Presentation

- Introduction & Background
- Overall Recommendation
- Evidence in Support of Reissuance
- Recommendations for NCTN improvement
 - Near-Term
 - Longer-Term
- Suggested Topics for Future Analysis

NCI National Clinical Trials Network -- March 1, 2014

- Five US groups (4 adult & 1 pediatric) and 1 Canadian Collaborating group
- 30 Lead Academic Participating Sites (LAPS) provide leadership in development, accrual & trial conduct of trials with the adult trial groups
- Seven Integrated Translational Science Awards (ITSAs) enhance incorporation of translational science into trials
- Disease-Specific Steering Committees evaluate large phase II and all phase III trial concepts
- Centralized functions for operational efficiencies & optimized use of scientific innovations

≈ 2400 enrolling sites across North America (plus international sites)



NCORP = NCI Community Oncology Research Program

NCTN Timeline

- **July 2012:** First NCTN RFAs released
- **March 2014:** NCTN grants awarded for 5 yrs.
- **2016:** NCI began considering renewal of NCTN
 - Requires external programmatic evaluation
- **July 2016:** NCTN External Working Group formed
 - Given the large investment in the NCTN by the NCI, the external review conducted under the auspices of CTAC

Purpose of the NCTN External Evaluation Working Group

- The **charge** to the Working Group:
 - Assess whether the **scientific contributions** of the NCTN **support program continuance**
 - If so, **develop recommendations for enhancing the scientific and operational functioning** of the NCTN

Topics Outside Working Group Scope

- Evaluation of specific disease areas or individual trials
 - Role of the CTAC Clinical Trials Strategic Assessment Working Group convening later in 2017
- Evaluation of individual NCTN groups or individual grantees of the other NCTN components
 - Role of peer-review conducted by the NCI Division of Extramural Activities

Members of the NCTN External Evaluation Working Group

Chair: Patrick Loehrer, Sr., MD, Indiana University

Members: Carol Brown, MD, Memorial Sloan Kettering CC
Ken Cowan, MD, PhD, University of Nebraska
Richard Gelber, PhD, Dana Farber Cancer Institute
J. Philip Kuebler, MD, PhD, Columbus Hematology Oncology Assoc.
Ralph Meyer, MD, McMaster University
Nikhil Munshi, MD, Dana Farber Cancer Institute
Edith Perez, MD, Genentech
Greg Reaman, MD, Food and Drug Administration
Nancy Roach, Fight Colorectal Cancer
Joel Tepper, MD, University of North Carolina

Executive Secretary: LeeAnn Jensen, PhD, National Cancer Institute

Members were chosen for their knowledge of NCI's late phase trials program, and were determined to be free from conflicts of interest related to the NCTN

NCTN External Evaluation Working Group (NEE WG) Timeline

- **December 16, 2016:** NEE WG Orientation Call
- **December 2016/January 2017:** Review Information
- **January 10, 2017:** NEE WG Call to Gauge Progress
- **January 26, 2017:** In Person NEE WG Meeting
- **February 2017:** Prepare NEE WG Report
- **March 8, 2017:** **NEE WG Report Presented to CTAC**

Areas of Evaluation

1. **Overall value and scientific impact** of the clinical trials and other research activities conducted by the NCTN (high level view)
2. Overall **effort integration and collaboration** within the network
3. Overall network **timeliness of clinical trial development and accrual rates and efficiency of operations**
4. **Interactions with other federal and non-federal organizations and programs**

Evaluation Source Materials Provided by NCI

- **Lists of trials activated March 2014 – October 2016**
 - IND status
 - Registration trials
 - Trials with translational studies
 - Trials with quality of life studies
- **Accrual to trials**
 - Accrual by trial phase, disease, and grant year
 - Cross-Group accrual
 - Accrual by role (LAPS, NCORP, Rostered sites, Cancer Centers)
- **Other information**
 - Trial Activation Timelines
 - IROC activities
 - ITSA activities

Evaluation Source Materials from Groups

- **Accomplishment highlights** 2014 – 2016 provided by each NCTN Group
- Key Group stakeholders were sent a **satisfaction survey** concerning various aspects of the NCTN (307 responses were received)
- **Group Chairs'** comments (anonymized) concerning NCTN strengths and weaknesses-**solicited by** the Working Group



Overall Working Group
Recommendation:

**“The NCTN Program
Should Be Continued”**



Evidence in Support of NCTN Renewal

Overall Value and Scientific Impact of NCTN (1)

Highly significant, practice-changing trials that could not be conducted without public funding

Examples include:

- Difficult randomized comparisons of types of radiotherapy, surgery or drug treatment versus no treatment,
- Studies of combined modality therapy,
- Studies evaluating agents from different companies (alone or in combination),
- Evaluations of inexpensive commercial agents,
- Studies where NCI supplies the manufactured drug,
- Studies designed to reduce the need for surgery or radiation,
- Studies of unique surgical approaches, e.g. laproscopic resection of rectal cancer,
- Studies in rare tumors,
- Studies in pediatric cancers, and
- Studies with behavioral interventions, such as for breast cancer recurrence

Overall Value and Scientific Impact of NCTN (2)

- Increased emphasis on smaller phase II studies examining biological principles has potential for leading to major advances
- Stakeholders surveyed considered NCTN trials to meet or exceed expectations for incorporating innovative science

Overall Value and Scientific Impact of NCTN (3)

Unique ability to conduct precision medicine trials accruing large numbers of patients nationally

- Lung Cancer Master Protocol (Lung-MAP)
 - 431 patients enrolled/1171 screened*
- Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials (ALCHEMIST)
 - 186 patients enrolled/1663 screened (pre-op and post-op)*
- NCI-Molecular Analysis for Therapy Choice (NCI-MATCH)
 - 480 patients enrolled/5003 screened*

*Accrual data as of 2/27/17

Integration and Collaboration across NCTN

- NCTN accrual is widely distributed across the U.S. roughly reflecting population density
- NCTN trials are open to all NCTN members, not just to members of the trial's lead Group
- NCTN accomplishments (noted by the Groups) include 31 trials with substantive cross-group collaborations
- Conduct of AYA* studies involving COG and the adult Groups facilitated by the NCTN
- >70% of stakeholders in survey considered:
 - LAPS, IROC, Tissue Banks, NCORP, and the CCTG to meet or exceed expectations
 - Collaboration across specialties and disciplines to meet or exceed expectations

*Adolescent and Young Adult

Timeliness and Efficiency

- Actual “screening on study” accrual exceeds NCTN target
 - NCTN target: **2,500-3,000** patients per year
 - Actual accrual average*: **4,168** patients per year
- Intervention/cohort accrual close to NCTN target
 - NCTN target: **17,000-20,000** patients per year
 - Actual accrual average*: **16,430** patients per year
- Total NCTN yearly accrual similar to accrual in 2012-2013
- Timelines for phase II and phase III trial activation met absolute deadlines
- Majority of stakeholders surveyed believed CTSU, CIRB, and Medidata Rave have increased operational efficiency

*2014-2016 average (2016 projected)

Interactions with Federal and Non-Federal Organizations and Programs

Federal:

- Collaborative studies (e.g., MATCH, LUNG MAP, TailoRx)
- Other interactions (e.g., FNIH Biomarkers Consortium, Project DataSphere)
- 24 NCTN trials with DCP-approved Quality of Life endpoints and/or assessments*
- Over 200 externally funded (R01, R21, DoD, LLS, ACS) grants support translational studies embedded in NCTN trials or using biospecimens from NCTN trials

Non-Federal:

- Nine registration/licensing trials open as of 10/31/16*
 - 7 drugs
 - 6 pharmaceutical companies



Recommendations for Near-Term NCTN Improvement

Goal of NCTN Program (from 2012 RFAs)

The overall goal for the entire NCTN Program is to conduct definitive, randomized, late phase clinical treatment trials and advanced imaging trials across a broad range of diseases and diverse patient populations as part of the NCI's overall clinical research program for adults and children with cancer.

Recommendations Related to Scientific Impact

- Revise NCTN goal statement
 - NCTN trials *“should impact the morbidity and mortality of cancer and improve patient outcomes”*
 - Since not all trials are *“definitive”* and *“randomized,”* delete these terms
 - Omit phrasing, *“late phase”*
- Trial portfolio should include scientifically-innovative phase II, and clinically-impactful phase III trials
- High quality trials of agents, surgery, radiation and imaging are all of interest
- Some members thought that Groups should define unique areas of scientific excellence and/or expertise in their applications

Recommendations Related to Collaboration within NCTN

- Groups and NCI should more optimally collaborate to identify and prioritize the most important strategic issues
- Maintain a high level of cross-Group collaboration in study development and accrual
- Coordination among the Groups and with NCI in overall management of the NCTN is important
- Multidisciplinary integration and operational efficiencies within and between Groups should be encouraged
- Groups should specify the roles and responsibilities for patient advocates in Group activities

Recommendations Related to Efficiency

- Groups should address in their applications
 - Current internal timelines for trial development
 - Previous activities taken to improve timelines
 - Planned actions to make further improvements
- Groups should identify mechanisms supporting:
 - Career development and opportunities for new investigators
 - Leadership training for Group and Committee chairs
 - Increased diversity in leadership, especially regarding age, gender and inclusion of community physicians
- Groups should develop and share plans to increase emphasis on and facilitate minority/underserved accrual

Recommendations Related to External Collaboration

- Highlight NCI's commitment to collaborations in NCTN trials with
 - Pharmaceutical and biotech companies
 - Other federal programs such as PCORI, FDA, DoD and VA
 - International clinical trials groups



Recommendations for Longer-Term NCTN Improvement

Recommendations for Longer-Term NCTN Improvement

- Too early to evaluate some NCTN components but should be done prior to subsequent NCTN renewal
 - Integrated Translational Science Awards
 - IROC Credentialing Standards
 - Lead Academic Participating Centers
- The NCTN should promote best practices for Group operations
 - Groups and NCI to identify and agree on best practices
 - NCI to include these best practices in future NCTN Program Guidelines
 - Groups should commit to implementation of these practices

Timeline for NCTN Renewal

- **March 8, 2017:** *NEE WG Report Presented to CTAC*
- **April 2017:** *Scientific Program Leaders Concept Review*
- **June 2017:** *Board of Scientific Advisors Concept Review*
- **September 2017:** *New Funding Announcement Released*
- **January 2018:** *Applications Due*
- **March 1, 2019:** *New Award Date*



Suggested Topics Needing Further Analysis

Suggested Topics for Further Analysis

These topics either

- Not directly related to NCTN renewal or
- May need additional consideration by CTAC or NCI.

Suggested Topics for Further CTAC Analysis

- Scientific Steering Committee operating processes
- Integration of translational research in NCTN studies
- Stakeholders' concerns regarding
 - Number and type of NCTN trials
 - Access to new agents and modalities
 - Balance between CTEP's and extramural investigators' roles in the management of operational and scientific activities
- Help for community sites transitioning to new model emphasizing phase II and precision medicine trials
- Comprehensive analysis of NCTN screening and accrual efficiency

Suggested Topic for NCI to Address

- **Inadequate NCTN funding**

- Working Group identified insufficient funding for various activities, notably for:
 - Volume of patients screened for precision medicine trials
 - Accrual to trials
 - Biospecimen collection
 - Correlative studies
 - Extra costs for participating in NCTN registration trials
- Recommend NCI investigate approaches for addressing these funding concerns



Questions?

Motion for
Approval of the
Report?