

CTWG: A Decade of Progress

Review of Progress and Future Directions on the 10th Anniversary of the 2005 Clinical Trials Working Group (CTWG) Report

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July 8, 2015

June 2005 – CTWG Summary Vision

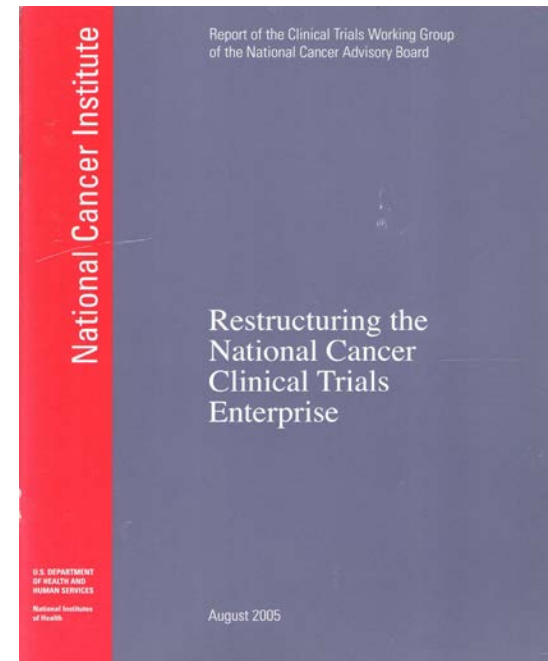
- Integrate components of current NCI clinical trials system into a cross-disciplinary, scientifically-driven, cooperative research effort
- Develop a coordinated network of institutions and clinical investigators to achieve adequate and timely accrual to trials of therapies intended for only a subset of patients
- Establish an open, collaborative system involving all stakeholders to enable the best decisions concerning which trials are most important to conduct in the publically funded clinical trials system
- Achieve increased integration of treatment protocols with modern molecular diagnostic and imaging techniques to enable evaluation of novel targeted therapies

Goals of Today's Presentation

- Summarize the CTWG implementation progress to date
- Assess the implementation status and role of future CTAC oversight
 - Achieved
 - Achieved; monitor activities
 - Partially achieved; monitor progress and/or may need some reassessment
 - Not achieved; needs reassessment
- Discussion
 - Are these the correct future CTAC oversight activities?
 - What other activities might be useful?

CTWG Initiatives- Common Themes

- Coordinated Clinical Trials Oversight – *Dr. Doroshow*
- Coordination – *Dr. Prindiville*
- Standardization – *Dr. Prindiville*
- Operational Efficiency – *Dr. Abrams*
- Prioritization – *Dr. Abrams*
- Scientific Quality – *Dr. Doroshow*



Coordinated Clinical Trials Oversight

Goal: Provide coordinated management and oversight for the NCI clinical trials enterprise

Coordinated Clinical Trials Oversight

Initiative 1: Establish a permanent federal body to provide *extramural* advice on the implementation of the CTWG initiatives and the ongoing conduct of clinical trials across NCI

Achieved

Initiative 1: Establish a permanent federal advisory body

- Clinical Trials and Translational Research Advisory Committee (CTAC) chartered in 2007
- Provides extramural advice and oversight for NCI clinical trials and translational research
 - Oversight of implementation of the CTWG and other working group recommendations
 - Strategic priorities and directions for clinical and translational research

CTAC Working Groups

- CTWG related
 - Guidelines Harmonization Working Group – 2009
 - Operational Efficiency Working Group – 2010
 - Cost-Effectiveness Analysis Working Group – 2010
 - CTWG Evaluation Working Group – 2011
 - NCTN Strategic Planning Working Group – 2014
 - *Clinical Trials Informatics Working Group – in process*
 - *National Clinical Trials Assessment Working Group – in process*
- Other clinical trials related including Recalcitrant Cancers Act
 - Pancreatic Ductal Adenocarcinoma (PDAC) Working Group – 2013
 - Small Cell Lung Cancer (SCLC) Working Group – 2014
 - SPORE Evaluation Working Group – 2014
 - *Progress in PDAC Research Working Group – 2015*
 - *Progress in SCLC Research Working Group – in process*

Coordinated Clinical Trials Oversight

Initiative 2: Establish a standing *internal* operations committee to provide ongoing integration, coordination and oversight of clinical trial activity across NCI

Achieved

Initiative 2: Internal operations committee

- NCI Clinical and Translational Research Operations Committee (CTROC) established in 2007
 - Internal NCI operations committee
 - Provides internal oversight for CTWG and other CTAC working group activities
 - Reviews clinical and translational research funding initiatives
 - BQSFP proposals for biomarker & Quality of Life (QOL) studies
 - Clinical Trials Planning Meetings
 - New and re-competing clinical/translational initiatives across NCI
 - Advises on clinical trials policies
 - Guides the Recalcitrant Cancer Research Act of 2012 activities

Coordination

Goal: *Improve coordination and cooperation among the functionally diverse components of the NCI-funded clinical trials system*

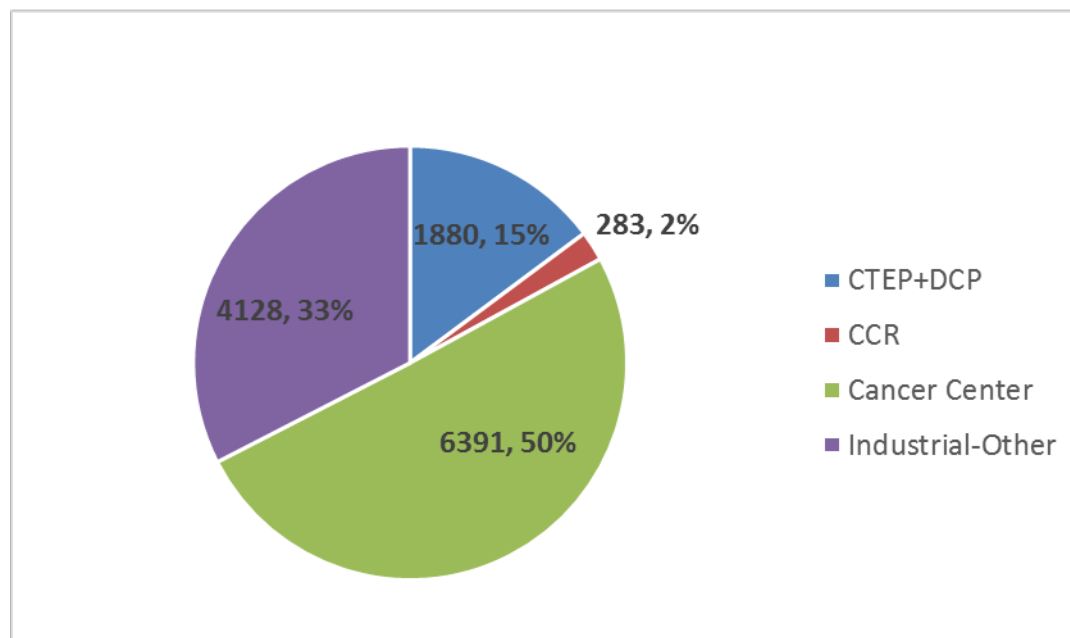
Coordination Initiatives

Initiative 1: Enhance information sharing concerning the status and results of NCI-funded clinical trials

Partially achieved; monitor progress

Initiative 1: Clinical Trials Reporting Program (CTRP)

- Comprehensive database of NCI interventional trials (national, peer-reviewed, institutional, and industrial) open to accrual on or after January, 2009



Total # Trials: 12,682
July 6, 2015



CTRP Development Timeline

- 2008 ● Development initiated
- 2009 ● Registration piloted at NCI-supported Cancer Center early adopters
- 2009 ● Capability to provide data for ClinicalTrials.gov registration
- 2010 ● Registration initiated at all Cancer Centers
- 2011 ● AACI & NCI agree on reporting objectives and timeline
- 2012 ● Amendment and trial status update reporting begins (March)
- 2012 ● Quarterly accrual data reporting begins (October)
- 2013 ● CTRP data submission added to Cancer Center terms of award
- 2014 ● Comparison of Cancer Center CTRP data with Data Table 4 Reports
- 2015 ● Cancer.gov clinical trials search page data source is CTRP

CTAC Clinical Trials Informatics Working Group

- Advise on future CTRP enhancements
 - Generation of Cancer Center Data Table 4 Reports from CTRP data
 - Inclusion of clinical trial results reporting
 - Inclusion of observational trials
 - Inclusion of clinical trial ancillary and correlative studies
 - Direct channels for external stakeholders to query CTRP data
 - Structured eligibility searching based on individual patient characteristics

Coordination Initiatives

Initiative 2: Facilitate collaboration and cooperation across the NCI-funded clinical trials system

Achieved; monitor activities

Initiative 2: Facilitate collaboration and cooperation

- Guidelines Harmonization Working Group (July 2009)
- Guideline Revisions
 - *SPORE*
 - Scored “Scientific Collaboration” section emphasizing collaboration in moving along a translational pathway across mechanisms
 - *Cancer Centers*
 - Expanded emphasis on cross-mechanism collaboration including leadership and accrual to NCTN trials
 - *NCTN*
 - Reward cross-Group accrual
 - Encourage cross-Group leadership of trials
 - Enables PIs outside the NCTN Groups (ie., SPORES, Cancer Center and CCR) to submit concepts which, if approved by the Steering Committee, will be conducted in the NCTN

Initiative 2: Facilitate collaboration and cooperation

- Initiated NCTN Group/NCI Leadership Management Committee in 2014
- Proposed Committee activities
 - Establish operating policies/procedures
 - Resolve operational issues
 - Plan new initiatives
 - Identify need for new tools, services and core resources
 - Address recommendations for changes in NCTN program
 - Recommend deployment of special funding resources (e.g. biospecimen collection, rare cancer trials)

Initiative 2: Facilitate collaboration and cooperation

- Cancer Clinical Investigator Team Leadership awards
 - Designed to incentivize outstanding mid-career clinical investigators at NCI Cancer Centers by providing partial salary support
 - Program initiated in 2009 – 68 awards to date
 - Awardee activities include:
 - Serving as Principal Investigators on collaborative clinical trials
 - Participating in NCTN Group activities
 - Serving on Steering Committees/Task Forces

Coordination Initiatives

Initiative 3: Enhance interactions with FDA and CMS to promote coordination of regulatory and reimbursement policies with the scientific enterprise

Partially achieved; needs some reassessment

Initiative 3: Enhance interactions with FDA and CMS

- Activities of NCI-FDA Interagency Oncology Task Force
 - Joint Fellowship Program to educate investigators about regulatory review
 - Initiatives to advance the regulatory science of protein-based multiplex assays
- NCI/FDA/industry/academia meetings on the use of molecular diagnostics for clinical decision-making
- NCI/FDA coordination in development and launch of major target-based clinical trials
 - ALCHEMIST, Lung-MAP, MATCH, ALK

Initiative 3: Enhance interactions with FDA and CMS

- Other joint NCI/FDA activities
 - Collaboration on development of chimeric monoclonal antibody dinutuximab for pediatric use
 - Development of the Patient Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)
 - FDA/NCI standing meetings
 - Discuss new agents and diagnostics; industry representatives included as relevant (monthly)
 - FDA/NCI meetings to discuss drug approvals, study design and regulatory issues (bi-monthly)
 - FDA staff are liaisons to several Disease-Specific Steering Committees
 - Joint FDA-CCR investigators

Initiative 3: Enhance interactions with FDA and CMS

- Reimbursement activities

- 2005-2006 NCI/CMS collaboration to apply “coverage with evidence development” for non-routine costs incurred in 9 NCI-sponsored trials
- CMS more recently applied “coverage with evidence development” for investigational use of FDG-PET and NaF-PET imaging
- As of 2014, Affordable Care Act mandates reimbursement for routine/standard of care costs but not investigational costs in association with clinical trials
- NCI participating in August 2015 ASCO meeting to provide definitive information concerning which costs are covered by CMS in association with clinical trials and which are not

Coordination: CTAC Future Activities

- Monitor progress of CTRP through Clinical Trials Informatics Working Group
- Periodic updates on the extent, character and impact of collaborations among Cancer Centers, SPOREs and the NCTN/ETCTN
- Periodic updates on the extent, character and impact of collaborations among the NCTN Groups and on the activities of the NCTN Leadership Management Committee
- Periodic updates on interactions with FDA
- Decide if and how the impact of the Cancer Clinical Investigator Team Leadership awards on career status of awardees should be assessed
- Decide if there is a need to explore approaches to improve interactions with CMS and/or other federal agencies

Are these the correct future CTAC oversight activities?

What other activities might be useful?

Standardization

Goal: *Standardize tools and procedures for trial design, data capture, data sharing, and administrative functions*

Standardization Initiatives

Initiative 1: Create interoperable, standards-based information technology tools to facilitate the collection, management and analysis of clinical trial data.

Partially achieved; monitor progress

Initiative 1: Interoperable tools

- Plans developed to establish direct electronic links between the Clinical Trials Reporting Program (CTRP) and the CTEP, DCP and CCR data systems
- Cancer Centers can currently provide data to CTRP by direct electronic link if they have the internal capability
- Cancer Trials Support Unit (CTSU) provides common patient registration and menu of trials, regulatory support and site verification for NCI multi-center trials
- Medidata Rave Clinical Data Management System
 - Remote data capture
 - Common toxicity criteria
 - Discrepancy/delinquency analysis
 - Data communication/correction
 - Preparation of data for analysis
- Medidata Rave implemented by NCTN Groups, the ETCTN and the Adult Brain Tumor Consortium

Standardization Initiatives

Initiative 2: Develop standard Case Report Forms incorporating common data elements that utilize standard vocabularies

Partially achieved; monitor progress

Initiative 2: Develop Standard Case Report Forms

- Initial efforts to develop Common Data Elements (CDEs) and standard Case Report Form (CRF) modules
 - Broad scope in terms of target audiences and data management systems
 - Successfully created and curated a CDE repository
 - Agreement on and implementation of standardized CDEs not yet fully achieved
- Network Rave Data Standards (NRDS) initiative launched in 2015
 - Guided by NRDS Committee of NCTN, ETCTN and NCI representatives
 - Focused on NCTN and ETCTN trials that use Rave data management system
 - Goal to develop selected standardized CDEs that can be fully implemented
 - Agree on standard Questions and a standard set of Response Values
 - Pair each Response Value with a Coded CDE Value for building a CRF
 - Develop long term plan for standardized CDE expansion, maintenance and compliance

Standardization Initiatives

Initiative 3: Build a standard credentialing system for investigators and sites to avoid duplicative credentialing for every trial

Partially achieved; monitor progress

Initiative 3: Standardized Repository of Credentials

- **NCI Online Credentialing Repository (OCR)**
 - Software for a central repository for Form FDA 1572, Curriculum Vitae and Financial Disclosure Forms was developed in 2013 but has not yet been implemented
 - Joint effort between NCTN and NCORP to begin shortly to further develop and implement the NCI Online Credentialing Repository

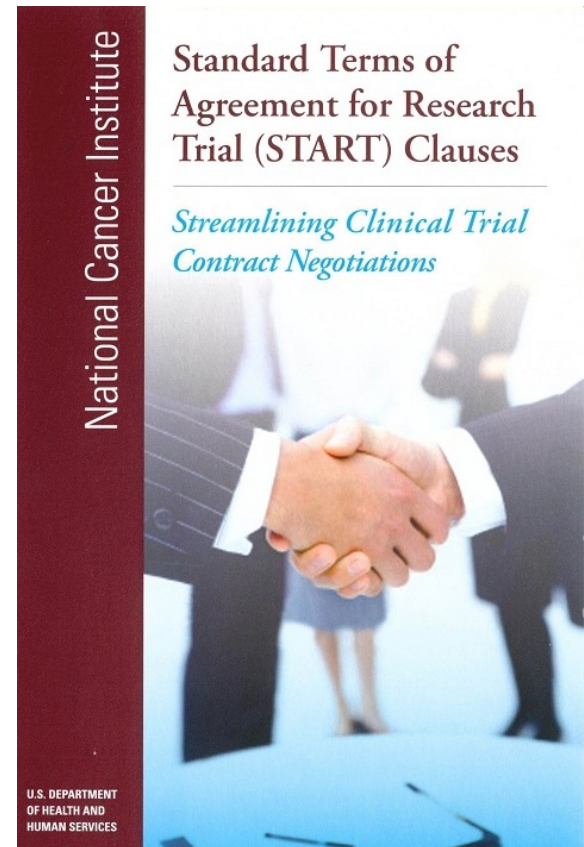
Standardization Initiatives

Initiative 4: Develop commonly accepted clauses for clinical trial contracts with industry to facilitate clinical trial initiation

Achieved; monitor activities

Initiative 4: Common Clauses for Clinical Trial Contracts

- NCI-CEO Roundtable on Cancer developed Standard Terms of Agreement for Research Trials (START) clauses
- Clinical trial agreements between industry & academic medical centers
- Separate clauses for company-sponsored and investigator-initiated trials
- Intended as a starting point for negotiations



http://www.cancer.gov/about-nci/organization/ccct/other-programs/StartClauses_info.pdf

Initiative 4: Common Clauses for Clinical Trial Contracts

- Evaluation of utilization and impact of START clauses in 2010 (45 Cancer Centers & 9 CEO Roundtable Life Science Consortium companies)
 - START clauses perceived as acceptable “middle ground”
 - Benchmarking tool for guidelines/templates and/or “fall back” positions
 - Identified negotiation time as issue and provoked dialog and action
 - All participants began actively monitoring negotiation time
 - Perception that negotiation time is no longer a substantial issue

Standardization: CTAC Future Activities

- Monitor progress via the CTAC Clinical Trials Informatics Working Group
 - Establishing direct electronic links between internal NCI clinical trials data systems and CTRP
 - Developing Common Data Elements (CDEs) and standard Case Report Form (CRF) modules through the Network Rave Data Standards (NRDS) initiative
 - Developing an online central repository of investigator credentials
- Is any further NCI action needed to facilitate the timely negotiation of clinical trials agreements between academic centers and industry?

Are these the correct future CTAC oversight activities?

What other activities might be useful?

Operational Efficiency

Goal: *Increase the rate of patient accrual and reduce operational barriers to timely trial initiation*

Operational Efficiency Initiatives

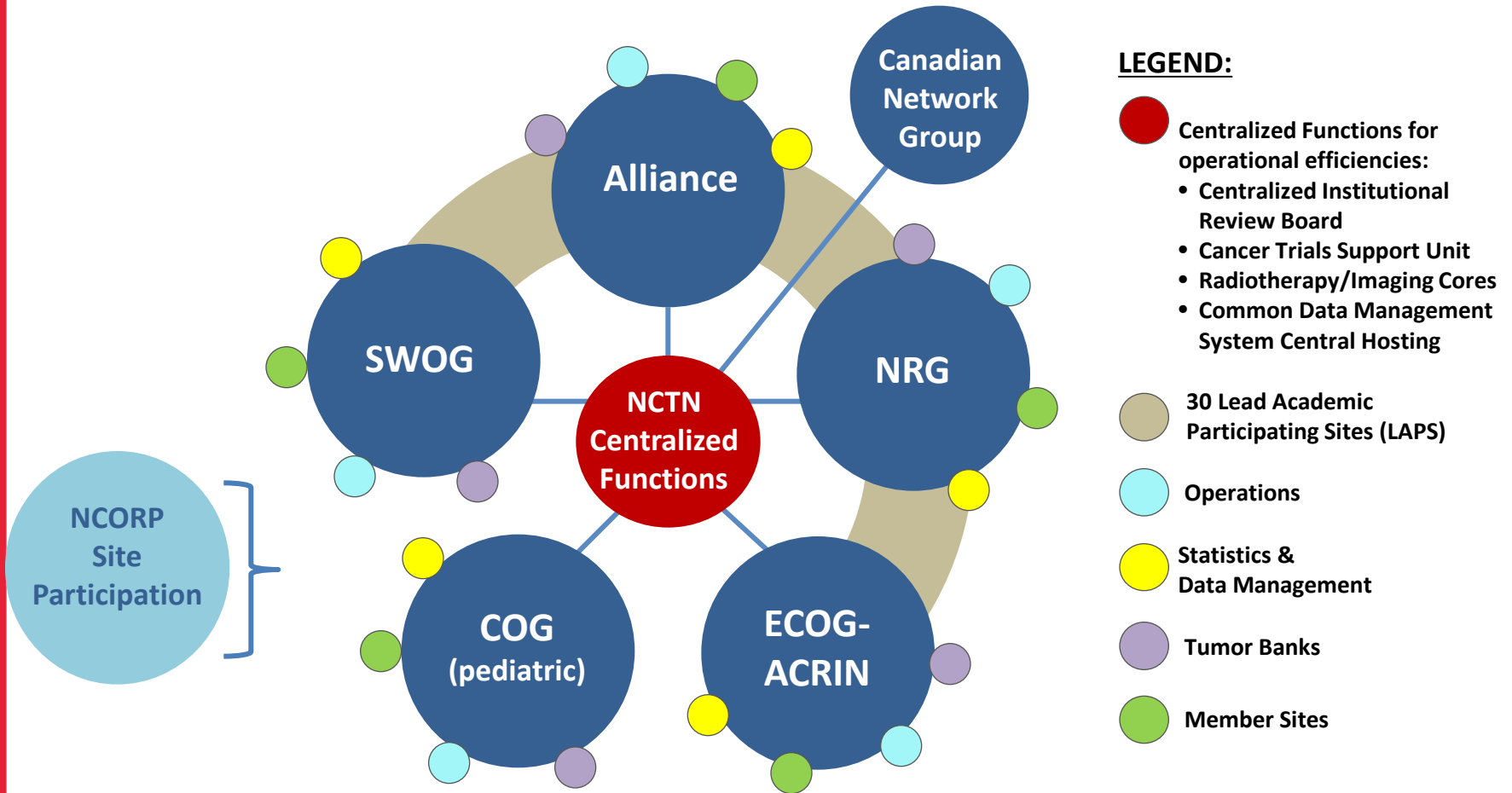
Initiative 1: Restructure the NCI's dedicated clinical trials programs to improve patient accrual and cost-effectiveness

Achieved; monitor activities

Initiative 1: Restructure the NCI's dedicated clinical trials system - NCTN

- Restructured National Clinical Trials Network (NCTN) launched March 2014
 - Consolidation into 4 adult Groups and 1 pediatric Group
 - Increased per case funding for high accruing Lead Academic Participating Sites
 - Tiered accrual reimbursement
 - Intervention
 - Screening
 - Advanced imaging
 - Biospecimen collection
 - Infrastructure costs linked to level of accrual to trials led by Group
 - Scientific leadership funding for Lead Academic Participating Sites linked to level of accrual

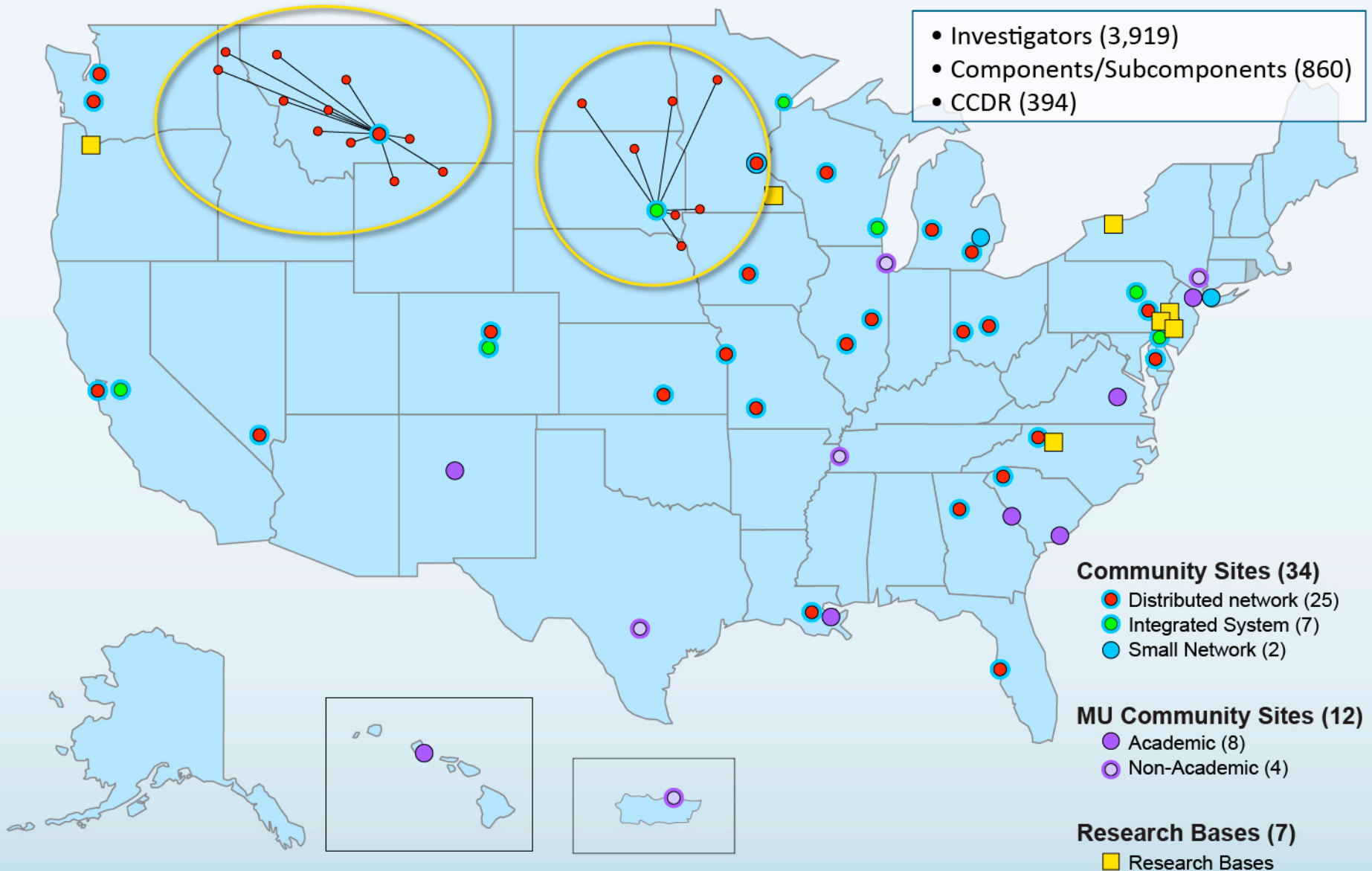
NCTN Structure - Optimize Scientific Opportunities



Initiative 1: Restructure the NCI's dedicated clinical trials system - NCORP

- Restructured NCI Community Oncology Research Program (NCORP) launched August 2014
 - Community & Minority/Underserved Sites
 - Base infrastructure funding for all Sites
 - Increased per credit funding for high accruing Sites
 - Tiered accrual credits
 - Treatment, prevention, cancer control, screening & post-treatment surveillance
 - Health-related quality of life & advanced imaging
 - Biospecimen collection
 - Research Bases
 - Infrastructure funding linked to accrual to studies led by Research Base
 - Tiered for intervention, health-related quality of life & supplementary studies
 - Basic per case funding for Institutional Members

NCORP Community Site, MU Community Site and Research Bases Geographic and Organizational Diversity



Initiative 1: Restructure the NCI's dedicated clinical trials system - ETCTN

- Restructured Experimental Therapeutics Clinical Trials Network (ETCTN) launched February 2014 into integrated Phase 1 & 2 Cooperative Agreements
- Adapts to the new era of targeted therapies where separation of phase 1 and 2 activities is much less distinct
- Integrates pharmacology-focused phase 1 and disease-focused phase 2 investigators resulting in the flexibility required to nimbly test new agents
- New addition of competitive Phase 2 supplements to current Phase 1 Cooperative Agreement awardees
- Supplements to Cancer Centers not affiliated with an ETCTN awardee
 - Support for accrual to early phase trials in rare tumors
 - Pilot program of competitive supplements to lead early phase trials (Early Therapeutics Opportunity Program)

NCI Team Science- Drug Development Project Teams

Clinical
(Experimental
Therapeutics Clinical
Trial Network)



**NCI Team
Science -
Drug Project
Teams**



**Centralized
Support**



Translational



**Cancer
Biology**

Project Team Agents

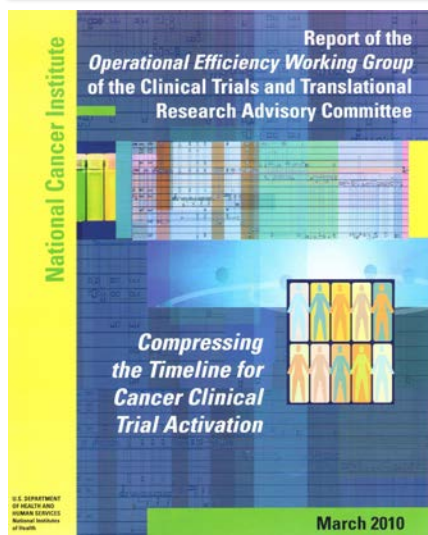
Agent	NSC/IND	MOA	CRADA*	Project Team
AT13387	749712/109876	Hsp90i	11/02/2009	Completed
AZD9291	781254/-----	EGFRi, T790M	09/29/2014	Completed
CO1686	783605	EGFRi, T790M	05/21/2015	Completed
VX-970	780162/-----	ATRI	05/29/2014	Completed
PDL1 MPDL3280 MEDI4736	783608 778709	Immune Checkpoint inhibitor	07/15/2015*	Project Team underway
T-VEC		Oncolytic viral immunotherapy		In preparation

Operational Efficiency Initiatives

Initiative 2: Identify and address barriers to timely trial initiation

Achieved; monitor activities

Initiative 2: Identify and address barriers to timely trial initiation



- Operational Efficiency Working Group (OEWG) – March 2010
- Set targets for opening NCI-sponsored trials
 - 300 days for NCTN phase 3 trials
 - 210 days for ETCTN phase 1 and phase 2 trials
 - 180 days for investigator-initiated Cancer Center trials
- Set absolute deadlines for cancelling an unopened CTEP trial
 - 24/**now 18** months for NCTN phase 3 trials
 - 18/**now 15** months for ETCTN phase 1 and phase 2 trials
- Recommended 14 initiatives for achieving target trial activation times

Initiative 2: Actions to achieve OEWG protocol development timelines

- NCI

- Hired Project Managers & Protocol Editors to facilitate protocol development
- NCI/Group conference calls to resolve critical issues
- Developed website for tracking protocol development status

- NCTN Groups

- Hired staff to oversee & expedite protocol development
- Eliminated or parallel-tracked protocol development steps
- Established processes that promote all parties working concurrently and interactively to develop a protocol

Initiative 2: Progress in achieving OEWG targets reported June 2013

- NCTN phase 3 trials
 - 45% reduction (727 to 395 days) in median time to open trials
 - All trials opened within 500 days, well short of absolute deadline
- ETCTN phase 1 and phase 2 trials
 - 18% reduction (541 to 442 days) in median time to open trials
 - Protocol submission to trial activation remains least efficient
 - Local institutional scientific review
 - IRB approval
 - FDA review
 - Contract negotiations
 - Drug supply issues
- Published results - JNCI, 2013: 105 (13)

Operational Efficiency Initiatives

Initiative 3: Analyze the status of patient accrual to NCI clinical trials and develop strategies to improve accrual rates and patient & public awareness and understanding of clinical trials

Partially achieved; monitor progress

Initiative 3: Analyze the status of patient accrual to NCI clinical trials and develop strategies to improve accrual rates

- During 2000-2010, 21% of phase 3 treatment trials and 21% of cancer prevention and control trials failed to reach 90% of targeted accrual due to inadequate accrual rates
- In 2010, NCI and ASCO convened a Clinical Trials Accrual Symposium resulting in recommendations for accrual best practices and future areas of research to improve accrual
- In 2015, NCI assembled a Network Accrual Core Team to address
 - Improved messaging for promoting trials
 - Developing templates for trial education
 - Standardizing trial tools and processes
 - Coordinating accrual enhancement efforts across NCTN

Operational Efficiency Initiatives

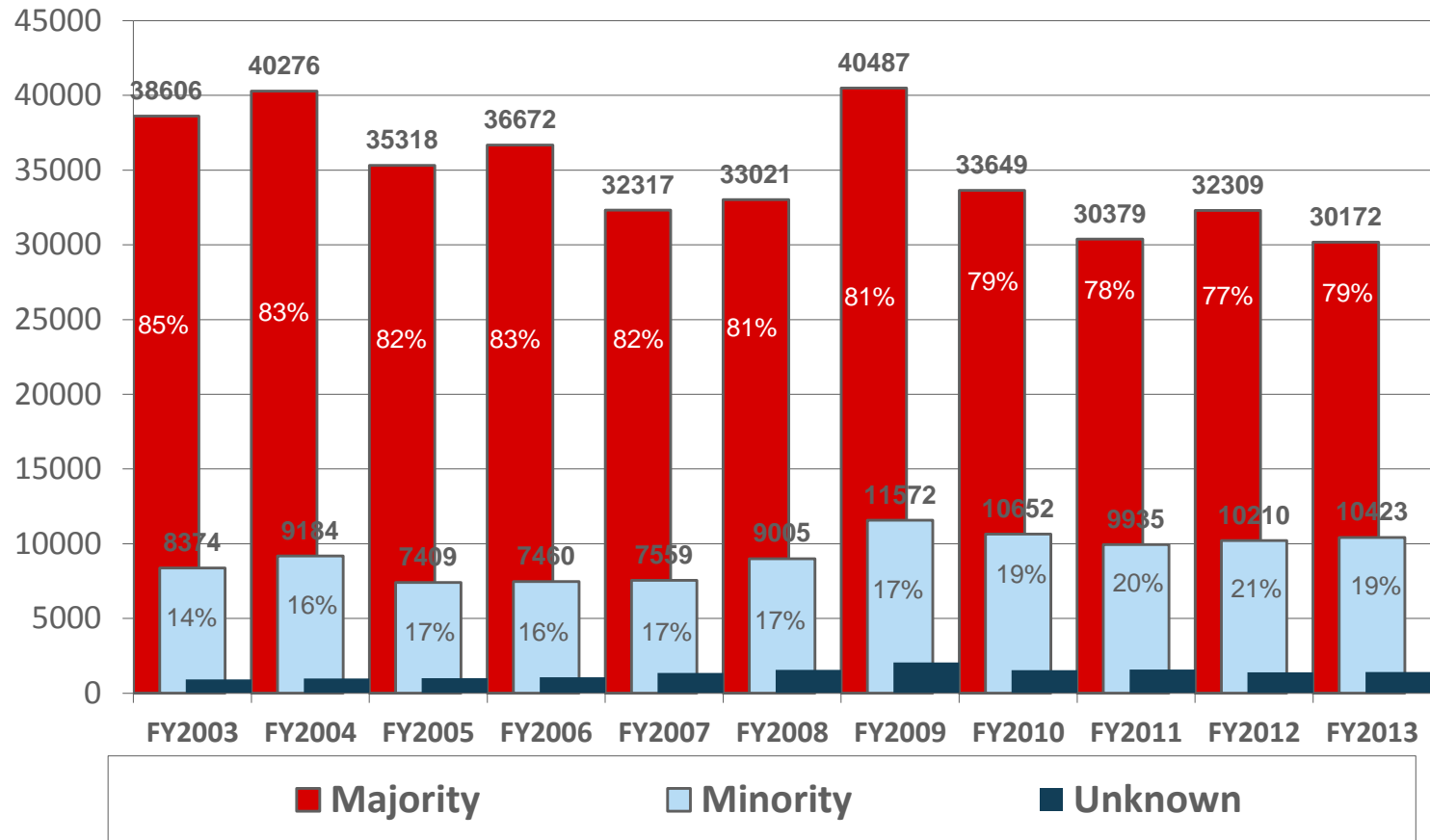
Initiative 4: Increase minority patient access to clinical trials to improve the participation of underserved and underrepresented populations

Not achieved; needs reassessment

Initiative 4: Increase participation of minority and underserved populations in clinical trials

- Pilot program of administrative supplements to promote minority accrual to clinical trials provided 2006 – 2010
 - Minority-Based Community Clinical Oncology Program - 7 awards
 - Community Clinical Oncology Program – 1 award
 - Patient Navigator Research Program – 3 awards
 - Cancer Disparities Research Program – 3 awards
- Review by NCI in 2011 concluded that overall minority accrual trends were unchanged and therefore the program should not be continued in its original form

Minority Enrollment to NCI Cooperative Group Clinical Trials



Worta McCaskill-Stevens et al, NCI Community Oncology Research Program, unpublished data

Operational Efficiency Initiatives

Initiative 5: Promote adoption of the NCI Central Institutional Review Board facilitated review process

Achieved

Initiative 5: Central Institutional Review Board (CIRB)

- Actions taken to promote acceptance of CIRB
 - Modified operating procedures to improve efficiency and compliance
 - Obtained AAHRPP accreditation
 - Adopted an independent review model allowing sites to rely solely on the CIRB for all IRB regulatory requirements
 - All NCTN and NCORP sites expected to be members of and rely on the CIRB for all trials reviewed by the CIRB
 - CIRBs established for Pediatric, Cancer Control/Prevention and early phase (ETCTN) trials
 - FDA issued formal guidance in 2006 endorsing and encouraging use of centralized IRBs
 - OHRP proposed rulemaking in 2011 generally supportive of the centralized IRB concept although not advocating a definitive policy change

Initiative 5: Promote acceptance of NCI Central Institutional Review Board (CIRB) review by sites

- As of May 2015, 1552 institutions are enrolled in the NCI CIRB compared to 330 institutions in April 2012
- CIRB widely viewed by participating sites as substantially preferable to local IRB review

Operational Efficiency: CTAC Future Activities

- Receive periodic updates on the timeliness of NCTN, NCORP and ETCTN trial activation and decide if target timelines should be further reduced
- Receive periodic updates on the status of actual versus expected accrual rates for NCTN, NCORP and ETCTN trials and decide if additional improvement is needed
- Decide if and how the results of NCTN, NCORP and ETCTN *completed* clinical trials contribute to progress in cancer treatment, prevention and symptom management (how should this be assessed?)
- Decide if any additional opportunities to improve the operational efficiency of NCTN, NCORP and ETCTN trials should be explored
- Identify additional actions that might enhance access to clinical trials for minority and underserved populations

Are these the correct future CTAC oversight activities?

What other activities might be useful?

Prioritization

Goal: *Establish an open, collaborative process for examining clinical trial strategic directions, encouraging innovation, reducing duplication and overlap and prioritizing clinical trials based on the best science*

Prioritization Initiatives

- **Initiative 1:** Obtain broad extramural scientific and clinical input into strategic directions for CTEP-funded phase I and phase II trials

Achieved; monitor activities

Initiative 1: Extramural scientific and clinical input into strategic directions for CTEP-funded phase I and II trials

- Accomplishment highlights for Investigational Drug Steering Committee (IDSC) established in 2005
 - Guidelines for incorporation of biomarkers into early-phase clinical trials
 - Recommendations for design of early phase clinical trials
 - Recommendations on adoptive cell therapy using tumor-infiltrating lymphocytes
 - Recommendations concerning cross-validation of analytical chemical assays and development of pediatric formulations of adult drugs
 - Guidelines for management of cardiac and metabolic toxicities associated with cancer therapies
 - Recommended Career Development LOI (CrDL) program for new investigators
- Input obtained from IDSC concerning Drug Development Plans for 32 new CTEP agents
- 2014: Drug Project Teams with extramural expertise develop Drug Development Plans for presentation to the IDSC

NCI Experimental Therapeutics Program (NExT) established in 2009

- Designed to translate to the clinic promising new anti-cancer drugs, biologics, imaging agents and medical devices entering at any of six stages
 - Target validation
 - Exploratory screen development
 - Screening/Hit-to Lead
 - Lead development and optimization of lead candidates
 - Preclinical evaluation
- Projects evaluated by Special Emphasis Panel of non-NCI experts for scientific merit, feasibility, novelty, clinical need and match to NCI mission
- Approved projects have access to NCI resources including the Chemical Biology Consortium, the Developmental Therapeutics Program, and the Center for Cancer Research early clinical trials program

NExT Active Portfolio



- Overview
- Mission
- Contacts

ABOUT NExT

Last Updated: 09/25/14

NExT Pipeline

DISCOVERY



DEVELOPMENT

Click each module to view active project(s)

Click [here](#) for another view of the NExT discovery pipeline.

Click each stage to view an interactive list of active NExT projects

Prioritization Initiatives

▪

Initiative 2: Obtain broad scientific and clinical input from academic disease experts, practicing oncologists, patient advocates, and NCI staff into the development and selection of NCI-funded late phase trials

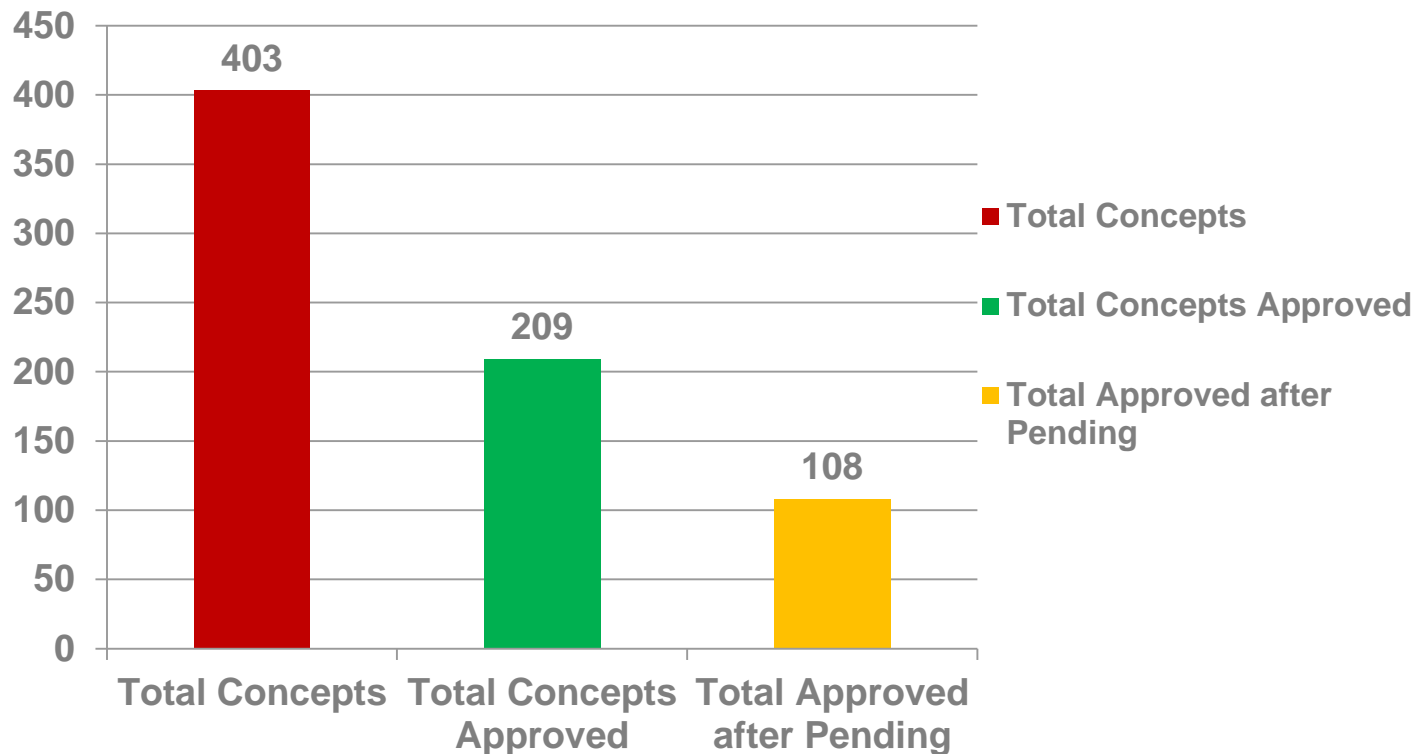
Achieved; monitor activities

Initiative 2: Broad input into the development and selection of NCI-funded late phase trials

- Scientific Steering Committees formed for 12 disease areas, symptom management/quality of life and imaging
 - Conduct extramural scientific evaluation of trial concepts
 - Recommend changes to trial concepts prior to approval
 - Develop topics for Clinical Trials Planning Meetings
 - Develop national strategic approach for each trial portfolio
- 31 Clinical Trials Planning Meetings in 12 disease areas and 3 in symptom management/quality of life
- Patient Advocate Steering Committee established to ensure patient advocates are effectively integrated into Scientific Steering Committees

Steering Committee Concept Approval Rates

- Overall, 403 concepts reviewed, 209 approved (52%) as of April 30, 2015



Ongoing Assessment of Steering Committee Approved Trials and Establishment of Strategic Priorities for Each Portfolio

- NCTN Strategic Planning Working Group – 2014
 - Cross-portfolio and portfolio-specific recommendations for improving NCTN clinical trials enterprise
 - Recommended implementing strategic priority setting and periodic strategic assessment for each Steering Committee’s trial portfolio
- Cross-Disease Prioritization Working Group – 2014
 - Priority ranking by extramural experts of resource-intensive Scientific Steering Committee approved trials in times of resource constraint
 - March 2014 pilot judged process feasible and scientifically robust
- *Steering Committee Strategic Research Priorities – 2015*
- *CTAC National Clinical Trials Assessment Working Group – 2015*
 - Next strategic assessment of trial portfolios – late 2015 to early 2017

Prioritization: CTAC Future Activities

- Periodic updates on IDSC activities and its interaction with newly reorganized ETCTN
- Periodic updates on the success of NExT supported drugs, biologics, imaging agents and medical devices in progressing from early to late phase development
- Oversee the Scientific Steering Committees
 - Assess the active trial portfolios (National Clinical Trials Assessment Working Group)
 - Review strategic research priorities
 - Assess operating policies and procedures
 - Assess value of Clinical Trials Planning Meetings
- Oversee any required cross-disease prioritization of approved concepts due to resource constraints

Are these the correct future CTAC oversight activities?

What other activities might be useful?

Scientific Quality

Goal: *Enhance the scientific quality of NCI-funded clinical trials by improving prioritization, funding and standardization of associated biomarker and quality of life studies*

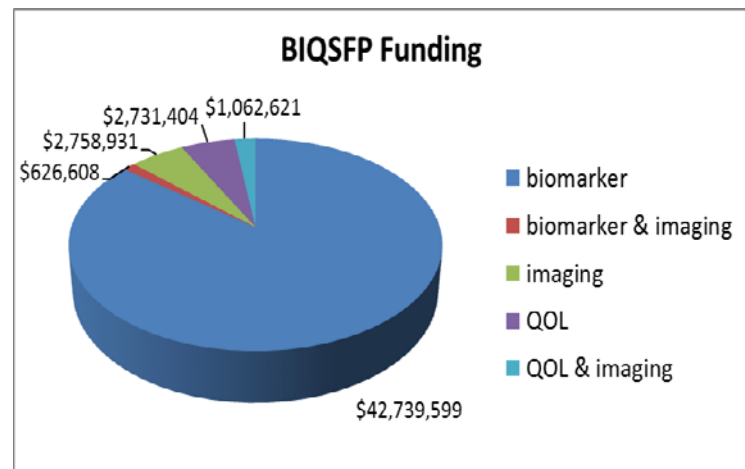
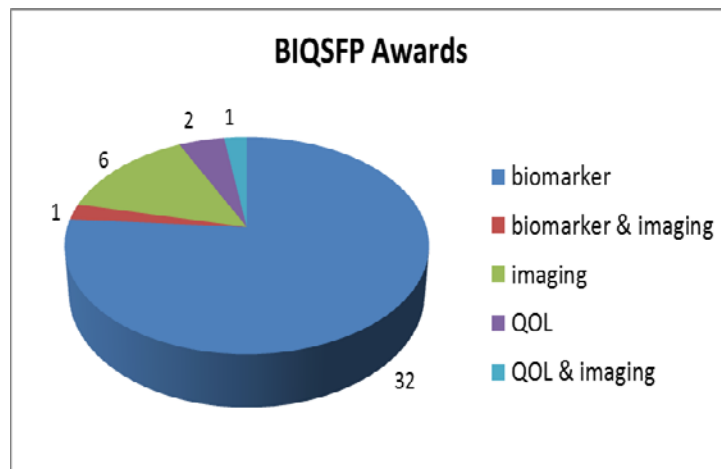
Scientific Quality Initiatives

Initiative 1: Assure that adequate funding is available for clinical trials involving biomarkers, imaging, and quality of life

Achieved; monitor activities

Initiative 1: Adequate funding for clinical trials involving biomarkers, imaging and quality of life

- Biomarker, Imaging and Quality of Life Studies Funding Program (BIQSFP) established in 2008 to fund integral and integrated biomarker studies for clinical trials
- 42 studies funded for a total of \$50 million as April 2015



- Study characterization
 - 52% integral, 33% integrated, 15% both integral and integrated
 - 16 disease sites – pediatric leukemia most common with 9 studies

Scientific Quality Initiatives

Initiative 2: Establish quality control standards for laboratory assays and imaging procedures used in association with NCI-funded clinical trials

Achieved; monitor activities

Initiative 2: Quality control standards for laboratory assays and imaging procedures for NCI-funded clinical trials

- Program for the Assessment of Clinical Cancer Tests (PACCT)
 - Developed in vitro assay and imaging test performance standards for integral and integrated assays conducted in association with trials
- Integral assay requirements
 - CLIA Certificate of Compliance and standard operating procedures for in vitro assay laboratories
 - Adherence to image acquisition, analysis and interpretation guidelines
 - Accuracy, precision, reproducibility, specificity and sensitivity data
- Integrated assay requirements
 - Well characterized analytical and clinical performance on specimens similar to those from the clinical trial
 - Controls adequate to ensure reproducibility and transferability
 - Statistical design sufficient to establish correlation with clinical parameter(s)
- Clinical Assay Development Program
 - Support for assay development

Scientific Quality: CTAC Future Activities

- Periodic updates on BQSFP funded projects including the outcomes of trials incorporating BQSFP funded tests
- Periodically assess the status of assay and imaging standards and decide if additional NCI action is needed
- Advise if BQSFP policies and procedures should be re-examined to determine if it remains optimally structured

Are these the correct future CTAC oversight activities?

What other activities might be useful?

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- Integrate components of current NCI clinical trials system into a cross-disciplinary, scientifically-driven, cooperative research effort
- Develop a coordinated network of institutions and clinical investigators to achieve adequate and timely accrual to trials of therapies intended for only a subset of patients
- Establish an open, collaborative system involving all stakeholders to enable the best decisions concerning which trials are most important to conduct in the publically funded clinical trials system
- Achieve increased integration of treatment protocols with modern molecular diagnostic and imaging techniques to enable evaluation of novel targeted therapies

NCI Clinical Trials – the Next Decade

- CTAC Summary Vision - 2015
 - What are the new scientific opportunities that offer the most clinical promise?
 - What are the most important scientific priorities for NCI supported clinical trials over the next decade?
 - What are the major challenges in addressing these opportunities and priorities?
- What operational/structural improvements are needed to achieve a new, 2015 summary vision?
- How can CTAC best assist the NCI in the continuing process of anticipating scientific change and focusing government-supported clinical trials and translational research to meet new scientific priorities?