



Transforming the NCI Clinical Trials System

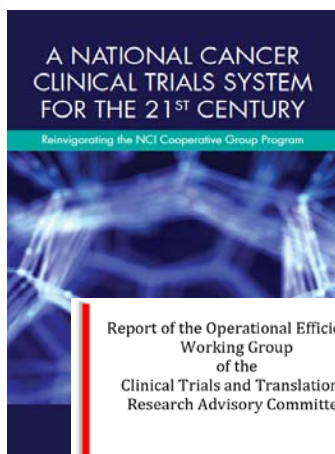
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DCTD, NCI



CTAC Meeting
July 13, 2011

Reviews of NCI's Clinical Trials System



Report of the Operational Efficiency
Working Group
of the
Clinical Trials and Translational
Research Advisory Committee

Compressing the Timeline for Cancer
Clinical Trial Activation

March 2010



Report of the
Clinical Trials Working Group
of the
National Cancer Advisory Board

Restructuring the
National Cancer Clinical Trials
Enterprise

June 2005



➤ *Emphasized need for public clinical trials system*

➤ *Consensus achieved on 4 goals for transforming the system:*

- Improve speed/efficiency of development & conduct
- Incorporate innovative science and trial design
- Improve trial prioritization, support, & completion
- Incentivize participation of patients & physicians

➤ *In response, NCI is transforming its clinical trials system to create a highly integrated network to address rapid advances in cancer biology based on:*

- Recommendations from the IOM Report
- Previous reports (CTWG & Operational Efficiency)
- NCAB, BSA and CTAC
- Current stakeholder input

ASCO Recommendations

- Enhance inclusion of innovative and clinically meaningful science and decrease duplication across all NCI-supported clinical trials
 - Improve connections between NCI translational and early-phase clinical trial mechanisms
 - National Clinical Trials Network (NCTN) (revised Cooperative Groups) should be open to scientific concepts from outside the Groups or other NCI-supported mechanism

ASCO Recommendations

- Prioritize trials that are practice-changing with meaningful clinical benefit
 - Federal system should focus on multi-modality treatments, adjuvant therapy, combinations of novel agents, screening and prevention strategies and therapies for rare diseases
- Improve Timelines of Concept Development and Scientific Review
 - Value-added review – not minor changes
 - Clarify roles of SC/Task Forces to streamline review

ASCO Recommendations

- Promote efficiency across the Network
 - Standardization of protocols, CRFs, ICDs, auditing, etc., should be emphasized with minimal deviation
 - Use the CIRB as the IRB of record for NCTN trials
 - NCTN should be the chief vehicle for phase 2 and 3 trials, and all NCI-funded mechanisms should be held accountable for their participation in NCTN trials

ASCO Recommendations

- Increase funding for NCI-supported Clinical Trials
 - For trials prioritized by NCTN, funding should be sufficient to reimburse research costs
 - Expand BISQFP (Biomarker, Imaging, Quality of Life, and Cost Effectiveness Analyses Funding Program)
- Ensure a national infrastructure to enable physician participation
 - Review criteria should recognize role of Groups in training and career development
 - Review criteria for other NCI-supported mechanisms (i.e., SPORES, Ca Centers) should provide credit for the scientific leadership provided by their faculty to the NCTN

Scientific Rationale for Transforming Current System

GROUP CONSOLIDATION & CREATING A NETWORK

- Ability to **prioritize molecular characterization resources & develop molecularly-driven trial designs** is critical for success of multisite clinical trials: these trials often require screening of large patient populations
 - Prioritization is facilitated by fewer groups with multi-disease capabilities and screening is facilitated by larger, multi-disease groups
- Need to **improve prioritization of phase 3 portfolio across disease entities** as trial costs (due to size and/or complexity) increase with limited resources
 - Prioritization is facilitated by fewer groups with multi-modality capability
- **Removes disincentives to study less common diseases** b/o accrual risks
 - Larger, multi-modality, multi-disease groups help to remove disincentives

Scientific Rationale for Transforming Current System

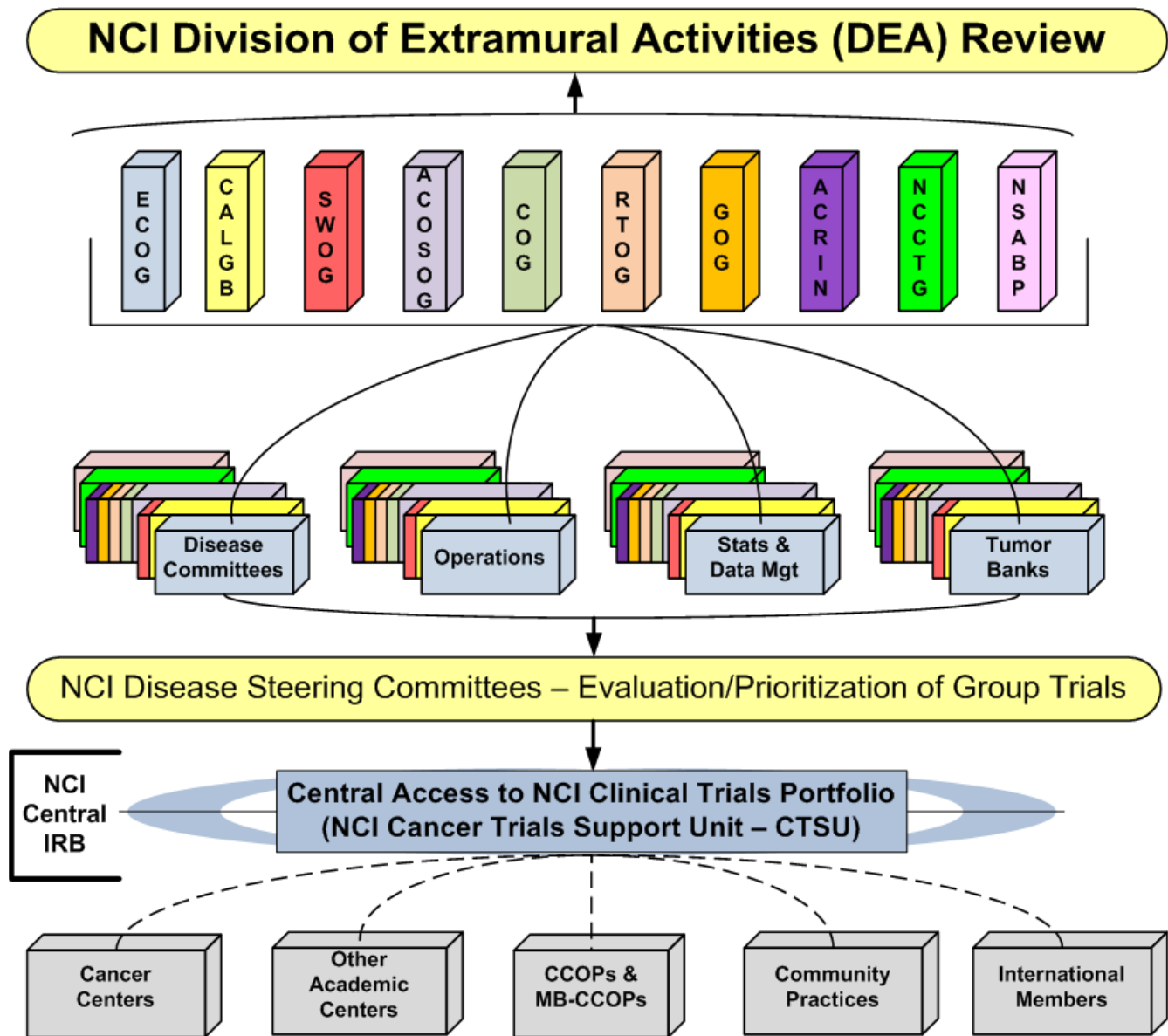
GROUP CONSOLIDATION & CREATING A NETWORK

- **Shared IT infrastructure** with common front end for clinical data management and for tissue resource management will be more manageable with fewer independent entities
- **Harmonized procedures** for scientific/administrative oversight for therapeutic trials and quality of life/cancer control studies is more feasible with fewer groups
- Scientific interactions around **imaging facilitated by integrating ACRIN**
- Optimal use **tissue specimens by creating an integrated national banking resource**
- Open access to a National Clinical Trials Network for **clinical/translational investigators not currently involved** in Group platform will assure best competition of ideas/movement high priority science into trials

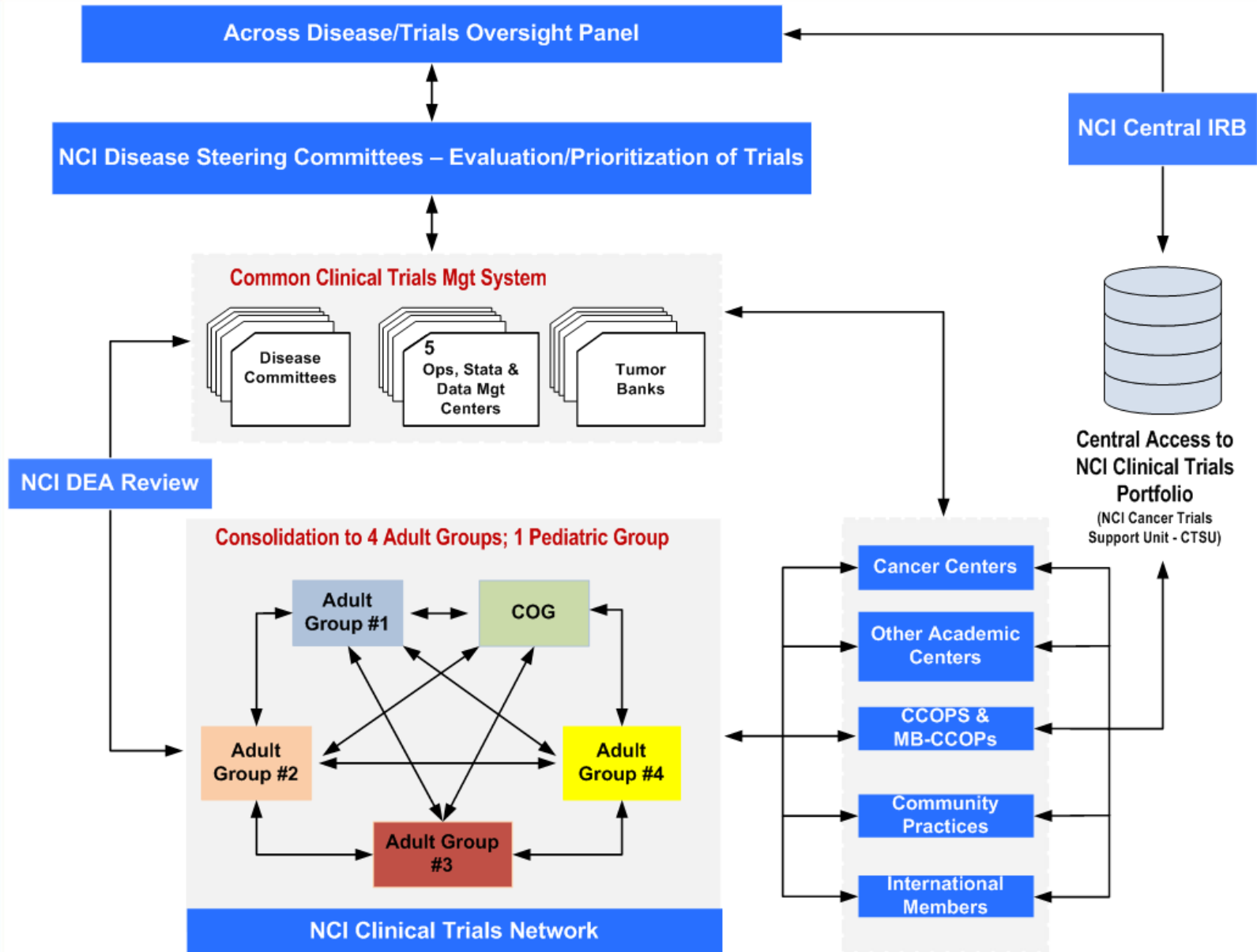
NCI Recommendations

- **Integration into not more than 4 Adult Groups and 1 Pediatric Group with multi-modality capacity in a broad range of diseases all fully committed to a national clinical trials network**
- **Potential strategies to assist integration:**
 - NIH grants now permits multiple PIs which may help with leadership transition
 - Incentivize the transition with provision of additional resources
 - Allow distributed data mgt & operations to avoid disruptions of ongoing trials
 - Combine (rather than disband) overlapping disease committees to include all current participants
- **Re-configure NCI review of the clinical trials program with emphasis on incentives for a national system**

Organizational Structure of the Program: 2011



Proposed New Organizational Structure for the NCI Clinical Trials Network



NCI's Response to Recommendations

Progress:

➡ As recommended by IOM, support up to 4 Adult and 1 Pediatric Group; Engaged in discussion with Group Chairs about potential consolidation activities & incentivize the transition with provision of additional resources

1st steps to consolidation/transition:

RTOG-NSABP; ACOSOG-CALGB-NCCTG; ECOG-ACRIN
GOG recently announced negotiations with NSABP-RTOG

➡ Consideration of modified site U10 program and proposed new funding model based on increased per case reimbursement for high-accruing sites

➡ Planning NCI external peer-review of Groups in same review cycle & new review criteria on collaboration/evaluation as partners in National Clinical Trials Network; use of NIH/NCI multiple PI construct for program grants

NCI's Response to Recommendations

Progress:

- ➔ Instituted comprehensive, central 24/7 patient registration for all adult Group trials, w/ regulatory & site verification of participation by Cancer Trials Support Unit (CTSU);
 - incorporation of COG into system in near future
- ➔ Implemented OEWG timelines for concept evaluation, protocol development, trial activation
- ➔ Working with Groups on a single, harmonized approach to clinical trial management, including protocol authoring, case report forms, standardized data collection & management
- ➔ Working on establishing ongoing collaborative management team to manage program as a national program

Components of New Review Process for Transformed System

Re-configure NCI external peer-review of clinical trials program grants with emphasis on incentives for a national system – all trials on the CTSU will be open to all sites and sites can credit any Group to which they belong

- **Components of review for the NCTN system**
 - Disease-specific SCs evaluate/prioritize specific trials
 - **Reconfigures NCI/NIH external peer review of new system**
 - Criteria for scientific evaluation will no longer focus on trials put forward by disease committees; emphasis will shift to evaluating role of Group in NCTN & overall scientific direction/quality
 - Operational Efficiency
 - Review criteria for collaborative management of the system
 - **Coordination with other NCI-funded programs**
CCOPs, Tumor Banks, Cancer Centers, SPORES, N01s/U01s, P01s

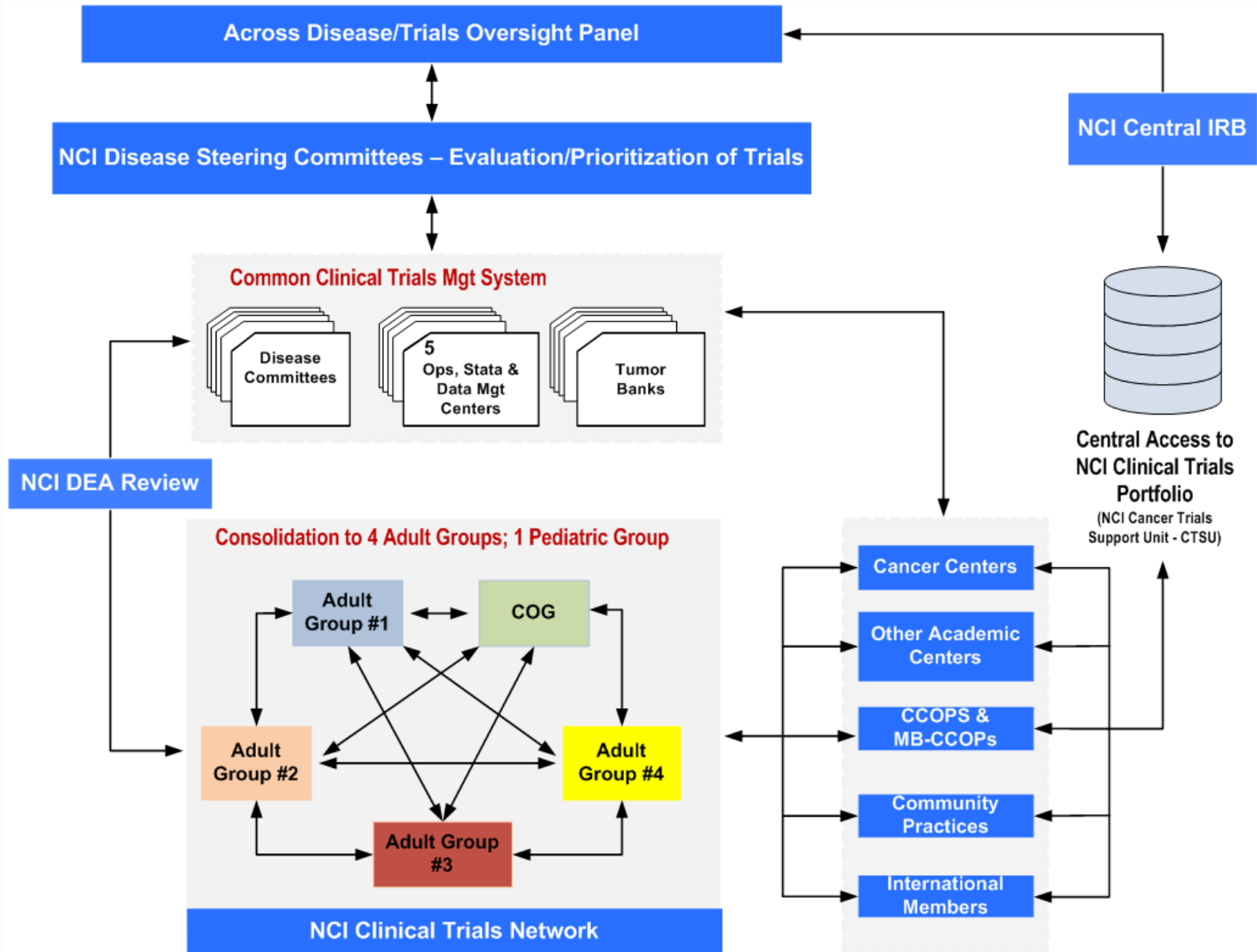
Questions for CTAC

- Does CTAC believe the changes in review criteria will foster a collaborative network?
- Are there other measures/resources NCI should consider to make the Network available to non-Group investigators?

Tentative Timeline for Change

Dec 2010 – Jul 2011:	Gather information/input from stakeholders & community for New FOA & Guidelines; develop Concept
Aug 2011:	NCI Divisional/CTROC Concept Review
Sept 2011:	NCI Scientific Program Leadership Concept Review
Nov 2011:	BSA Concept Review
Nov 2011 – July 2012:	NCI DEA & NIH Review of FOA & Guidelines
July 2012	New FOA Released/Published
Nov 2012	Receipt of Competing Applications for New FOA
Feb 2013	Review of Competing Applications by DEA
May 2013	NCAB Review
After Oct 2013	Rollout of Awards in FY2014

Proposed New Organizational Structure for the NCI's Clinical Trials Network



Improve Prioritization, Selection, Support, and Completion of Cancer Clinical Trials

NCI has re-evaluated and changed its role in the clinical trials system.

Progress

- Initiated Clinical Trials and Translational Research Advisory Committee: First federally-chartered NCI advisory group in a decade; in operation for >3 years with specific responsibilities for NCI's clinical trials programs; currently engaged in evaluation of implementation of CTWG recommendations
- Revamped prioritization process for large phase 2 and phase 3 treatment and control trials by creating disease- and modality-specific Steering Committees to ensure that most important trials are given highest priority
 - Steering Committees convene clinical trials planning meetings to identify critical clinical trial issues for future studies
 - While NCI has a voice on the Steering Committees, its role is to facilitate trial implementation, rather than to direct primary review

Disease-Specific Steering Committees: Prioritizing Clinical Trials

Steering Committee	Year Established	Co-Chairs Disease-Specific Steering Committees (SCs)
GI	2006	Dan Haller, MD & Joel Tepper, MD
Gyne	2006	David M. Gershenson, MD, Gillian Thomas, MD, & Michael Birrer, MD
Head & Neck	2007	David Adelstein, MD, David Brizel, MD, & David Schuller, MD
GU	2008	Eric Klein, MD, George Wilding, MD*, & Anthony Zietman, MD
Breast	2008	Charles Geyer, MD & Nancy Davidson, MD*
Thoracic	2008	David Harpole, MD, William Sause, MD, & Mark Socinski, MD
Leukemia	2009	Wendy Stock, MD & Jerry Radich, MD
Lymphoma	2009	Oliver Press, MD & Julie Vose, MD
Myeloma	2009	Morie Gertz, MD & Nikhil Munshi, MD
Brain	2010	Ian Pollack, MD & AI Yung, MD
Pediatrics (Heme & Solid Tumors)	2011	David Poplack, MD & Robert Arceci, MD (Leukemia & Lymphoma) Mark Bernstein, MD (Solid Tumors)

Over 180 Concepts evaluated since inception of SCs (6/30/2011)

*Cancer Center Directors

Other Related Steering Committees: (Non-disease Focus)

- **Investigational Drug Steering Committee**
 - Co-Chairs: Pat LoRusso, DO, & Dan Sullivan, MD
- **Clinical Imaging Steering Committee**
 - Co-Chairs: Steven Larson, MD and Etta Pisano, MD
- **Symptom Management & Health-Related Quality of Life Steering Committee**
 - Co-Chairs: Deborah Bruner, RN, PhD & Michael J. Fisch, MD, MPH
- **Patient Advocate Steering Committee**
 - Co-Chairs: Regina Vidaver & Nancy Roach

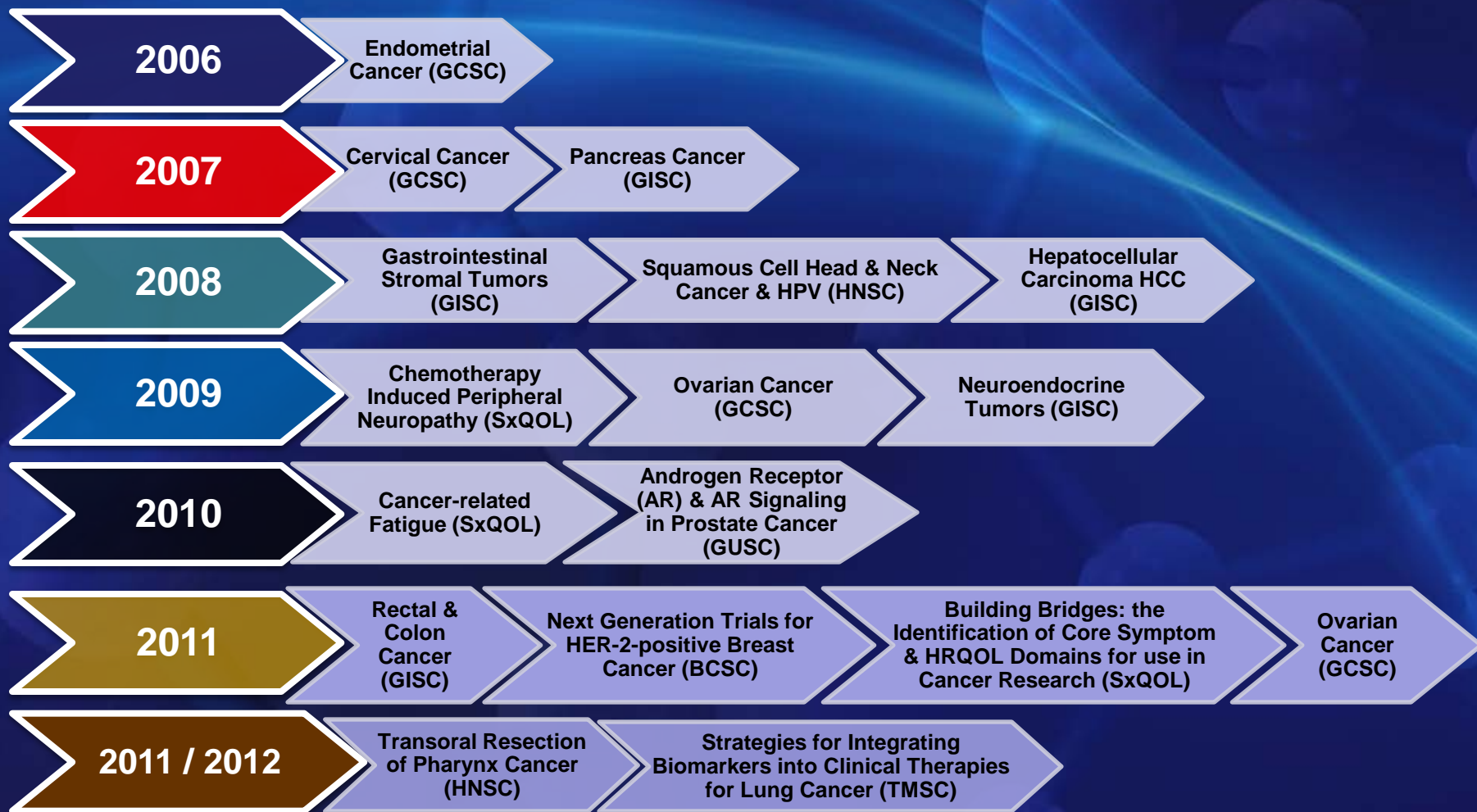
Scientific Steering Committee

Concept Evaluation (as of 06/30/2011)

Steering Committee	Year Established	Number Evaluated	Approved	OPEN to Accrual
GISC	2006	33	15	12
GCSC	2006	35	24	19
HNSC	2007	9	4	4
SxQOL SC	2007	39	17	9
GUSC	2008	14	6	3
BCSC	2008	17	6	4
TMSC	2008	15	4	2
LKSC	2009	4	2	0
LYSC	2009	9	4	0
MYSC	2009	3	1	0
BMSC	2010	4	2	0
Peds LL SC	2011	2	0	0
		184	85* (46%)	53

* Total Approved Concepts = 90 (5 withdrawn after approval)

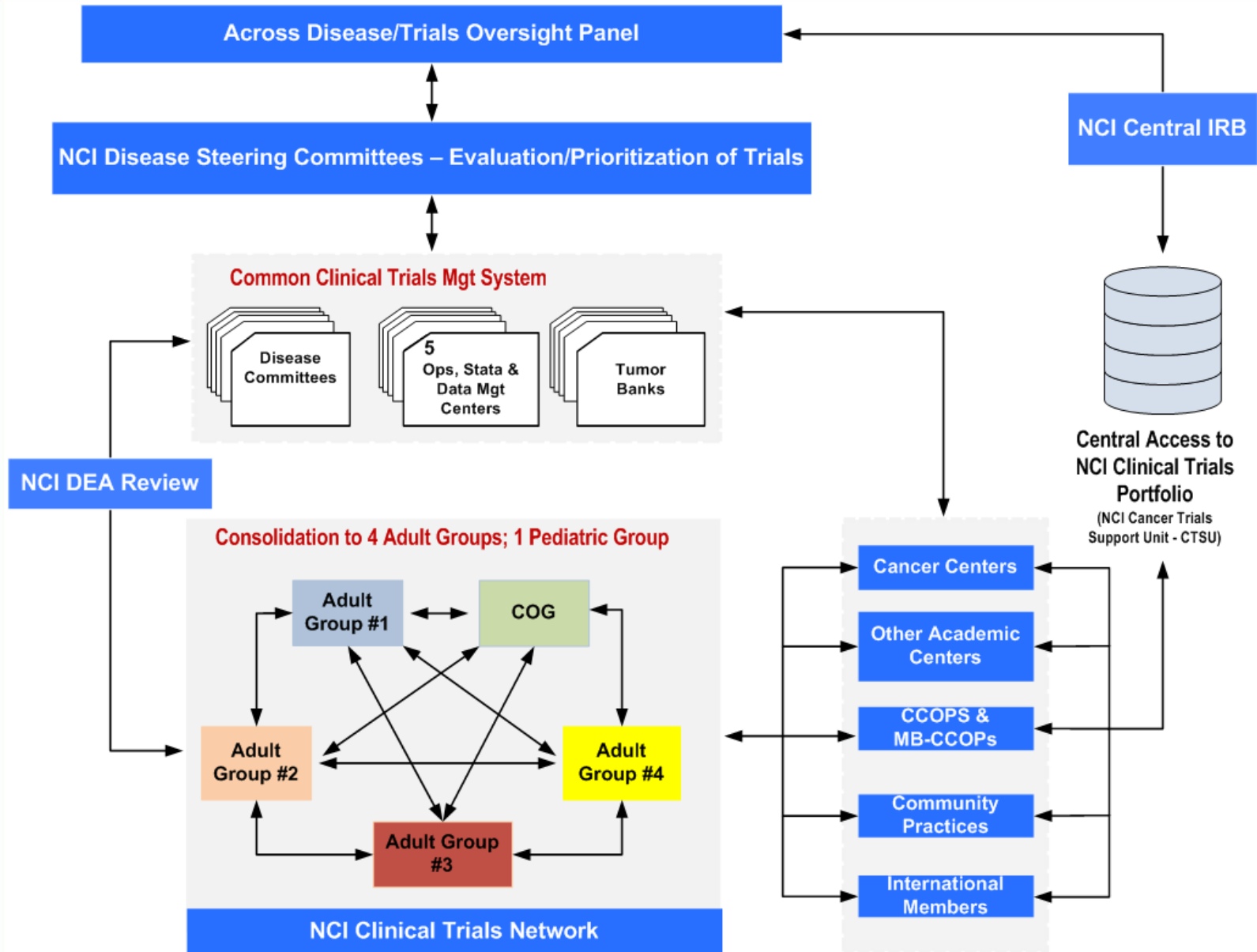
Clinical Trials Planning Meetings (CTPMs)



Dual Function of Steering Committees

- Steering Committees evaluate and prioritize trial concepts received from Group and non-Group investigators for large phase 2 and phase 3 trials
 - Some SC's have created Task Forces to help with this evaluation
- Steering Committees strategize regarding the needs of clinical research in their domain and may form Task Forces, Working Groups and/or hold Clinical Trials Planning Meetings to encourage/develop trials to respond to unmet needs

Proposed New Organizational Structure for the NCI's Clinical Trials Program



NCTN Strategic Working Group

- Scientific Steering Committees are disease or modality focused.
- NCI, Group Chairs and CCOP Research Base PIs need feedback and assistance in assessing cross-disease/modality priorities
- This feedback should be provided by thought leaders from within and outside the Groups, and should be part of CTAC
- This is NOT another level of protocol-specific review
 - Strategy as opposed to tactics
 - Longer-term planning as opposed to short-term objectives

Responsibilities of the NCTN Strategic Working Group

Monitor and assess the scientific effectiveness of the individual Scientific Steering Committees by addressing the following questions and recommending improvements as needed:

- Is each Steering Committee making decisions that result, over time, in a portfolio that represents the most important and best-designed trials for its clinical domain?
- Are approval/disapproval decisions within each Steering Committee justified with clear and compelling rationales?
- Have changes required by Steering Committees' resulted in improved clinical trial designs?

Responsibilities of the NCTN Strategic Working Group (cont'd)

Monitor and assess the scientific conduct across Steering Committees and recommend improvements as needed:

- Are the standards used by Steering Committees to judge scientific merit and clinical importance/prioritization consistent across the Committees? If there is variation, is it justified by distinctive characteristics of the respective clinical domains?
- Does each Steering Committee conduct task forces, working groups or clinical trials planning meetings that effectively help to assess the unmet clinical research needs in their respective clinical domains? How effective are these complementary activities?

Responsibilities of the NCTN Strategic Working Group (cont'd)

Monitor and assess the balance, coherence and appropriateness of NCI's overall late stage clinical trials portfolio by addressing the following questions.

- Is the portfolio of Steering Committee-approved trials appropriately balanced across clinical domains in light of available resources, clinical needs and scientific opportunities?
- If not, how should the Steering Committees adjust their decision criteria and processes so as to achieve a more optimal balance system-wide?

Responsibilities of the NCTN Strategic Working Group (cont'd)

- Recommend new strategic priorities and directions for late stage clinical trials based on the current portfolio of trials, evolving clinical needs and emerging scientific opportunities
- Output would be:
 - Recommendations to individual Steering Committees
 - Recommendations to NCI and Groups about the entire portfolio in a disease area
 - Recommendations across diseases to NCI about the portfolio of the entire system
 - Report to CTAC about function/needs of the entire system

Proposed Categories of NCTN Strategic Working Group Membership

Non-NCI

Cooperative Group Chairs
Cooperative Group Statisticians
Cancer Center Directors
CCOP PIs
Patient advocates
Translational scientists (SPORE/PO1)
Cancer Control – Research Base PIs
Steering Committee Chairs
CTAC members

NCI

DCTD
DCP
CCCT

Vision of Transformed Network

- System provides essential infrastructure for Group trials in treatment, control, screening, diagnosis, & prevention; and is major enabler of e, definitive confirmation of cutting-edge discoveries across all of NCI's clinical research programs
- Trials approved by Steering Committees open rapidly opened and complete accrual according to defined guidelines by leveraging an integrated national network of performance sites
- User-friendly system with harmonized processes is available to the extramural cancer community: investigators, patients, advocates, and industry
- New system provides an optimal platform to perform large scale testing of increasingly smaller subsets of molecularly-defined cancers, and efficiently answers critical questions not well supported in a commercial environment