Transforming NCI’s Clinical Trials System

James H. Doroshow, M.D.
Deputy Director for Clinical and Translational Research
National Cancer Institute, NIH
Emphasized critical need for a public clinical trials system

4 goals for modernization with 12 recommendations

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

NCI is implementing a comprehensive approach to transforming its clinical trials system to create a highly integrated network that can address rapid advances in cancer biology based on:

- Recommendations from the IOM Report
- Previous reports (Clinical Trials & Operational Efficiency)
- Current stakeholder input
Extensive Review & Stakeholder Input on Revising NCI’s Clinical Trials System

- Cooperative Group Chairs & Group Biostatisticians
- NCI Advisory Boards
- Industry Partners
- Patient Advocates
- Cancer Center Directors
- NCI Mailbox
- IOM 2010
- CTWG 2005
- OEWG 2010
- ASCO Letter 2011
- NCI Website
- Academic & Community Sites/Investigators
- Professional Analysis STPI
- Oncology Professional Associations
Organizational Structure of Group Program: 2011

NCI Division of Extramural Activities (DEA) Review

Disease Committees
Operations
Stats & Data Mgt
Tumor Banks

NCI Disease Steering Committees – Evaluation/Prioritization of Group Trials

Central Access to NCI Clinical Trials Portfolio
(NCI Cancer Trials Support Unit – CTSU)

NCI Central IRB

Cancer Centers
Other Academic Centers
CCOPs & MB-CCOPs
Community Practices
International Members
**Recommendation 1**: Facilitate some consolidation of Group “front-office” operations by reviewing & ranking Groups with defined metrics on similar timetable & by linking funding to review scores

**Progress:**

- New Program with up to 4 adult & 1 pediatric Network Groups
- Peer-review focused on overall research strategy, collaboration, & operational efficiency
- Support for trials designed with integral molecular screening
- Integrated translational science & Lead Academic Participating Site awards
- Core RT/Imaging services
- Strategic planning & trial prioritization at national level
- Adult and pediatric Central IRBs; consent template
- Common IT data mgt system
- Centralized 24/7 patient registration

**New Program: NCI National Clinical Trials Network (NCTN)**

IOM Goal 1: Improve Speed & Efficiency of the Design, Launch, and Conduct of Clinical Trials
Recommendation 2: Require/facilitate consolidation of Group “back-office” operations & working with extramural community, make process improvement in operations & organizational management a priority

Progress

• Centralized 24/7 patient registration, regulatory support & site verification of trial participation by Cancer Trials Support Unit

• Implementation of timelines for study review & development with major time savings for trial activation

• Implementation of common IT data management system for trial development and conduct instituted for all new clinical trials activated in 2013
Cancer Trials Support Unit (CTSU) has expanded centralized administrative & regulatory functions for clinical trials

- Over 57,000 patients enrolled via CTSU since 2002
- Cross-Group accrual available for all phase 3 & select phase 2 tx trials
- Expansion of services to other NCI trial networks & collaborative trials
- Provides a range of critical services in support of the national system
  - Patient registration
  - Accrual reimbursement
  - Protocol Coordination
  - Clinical Data Operations
  - Regulatory Support Service
  - Financial Management
  - Site Auditing
  - Site QA
  - CTSU Help Desk
  - CTSU Web Site
  - Education & Trial Promotion

As of 2011, 24/7 enrollment for all Group Tx trials
Implementation of Operational Efficiency Timelines

Protocol terminated if absolute timelines not achieved
Breakdown of Study Development Stages

Early Phase Trials

<table>
<thead>
<tr>
<th>Stage</th>
<th>Pre-OEWG data</th>
<th>Post-OEWG data</th>
<th>Median days</th>
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<tr>
<td>LOI submission to LOI approval</td>
<td>110</td>
<td>78</td>
<td>60</td>
</tr>
<tr>
<td>LOI approvals to protocol submission</td>
<td>60</td>
<td>60</td>
<td>303</td>
</tr>
<tr>
<td>Protocol submission to trial activation</td>
<td>247</td>
<td></td>
<td>90</td>
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</table>

Target = 60 days

Target = 90 days
Timeline Comparison Early Phase Trials
Historical vs Post-OEWG (Apr 2010 – Aug 2012)

Time to Trial Activation - Early Phase Studies

Probability Trial Not Activated

Days from LOI Submission

OEWG  post-OEWG  pre-OEWG
Timeline Comparison Phase 3 Trials
Historical vs Post-OEWG (Apr 2010 – Aug 2012)

Time to Trial Activation - Phase 3 Studies

Days from Concept Submission

Probability Trial Not Activated

OEWG  post-OEWG  pre-OEWG

+ Censored
Common IT Data Management System (CDMS)

- **Electronic tool(s) or processes that support**
  - Data collection: Remote Data Capture (RDC)
  - Data coding: Standard libraries - Common Toxicity Criteria
  - Data management: Discrepancy, delinquency, communication, correction & preparation of data for analysis

- **Core benefits of CDMS on NCI-supported multicenter trials**
  - Reduces training costs & cost of overall cost of data management
  - Reduces risk of data delinquency and/or discrepancy
  - Reduces time/effort to correct/complete data
  - Reduces delays in obtaining Science and Safety results & improves trial management & decision-making

- **Other Benefits to NCI-supported multicenter trials**
  - Supports/complements transformation of Groups into new ‘Network’ program
  - Meets FDA & other Federal requirements for e-data capture, security & transfer
  - Promotes data sharing
  - Sets stage for further infrastructure improvements such as integration with expedited Serious AE reporting, remote auditing, electronic filing for FDA reports
Medidata RAVE® Toxicity (Adverse Event) Page

Record all Grade 3 or higher AEs. Record only Unexpected Grade 2 AEs. Record Grades 1 and higher for all events listed in protocol section 8.1.1. Record each event only one time per cycle of treatment, identifying the highest grade of the event.

<table>
<thead>
<tr>
<th>Adverse Event Text Name (CTCAE v4.0)</th>
<th>MedDRA Adverse Event Code (v12.0)</th>
<th>Adverse Event Grade</th>
<th>Adverse Event Description</th>
<th>CTC Adverse Event Attribution Scale</th>
<th>Has an adverse event been reported?</th>
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</thead>
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<tr>
<td>Anemia</td>
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<td>Yes</td>
</tr>
<tr>
<td>Bone marrow hypopcellular</td>
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<tr>
<td>Disseminated intravascular coagulation</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Febrile neutropenia</td>
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<tr>
<td>Hemolysis</td>
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<td></td>
</tr>
<tr>
<td>Hemolytic uremic syndrome</td>
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</tr>
<tr>
<td>Leukocytosis</td>
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<td>Lymph node pain</td>
<td></td>
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<tr>
<td>Spleen disorder</td>
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<tr>
<td>Thrombotic thrombocytopenic purpura</td>
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</tr>
</tbody>
</table>
Recommendation 3: HHS should lead a trans-agency effort to streamline and harmonize government oversight and regulation of cancer clinical trials

Progress

- Established interagency agreement with FDA for rapid review of approved Group phase 3 tx trials at concept stage
- Developed coordinated processes for development/review of trials under FDA Special Protocol Assessment (SPA)
- Developed adult & pediatric NCI Central IRBs with major improvement in review timelines & AAHRRP accreditation
- Working with CDRH/FDA to coordinate early review of investigational devices (biomarkers)
Enrollment of Institutions/IRBs reviewing Group Studies: Facilitated Review

- Number of Signatory Institutions Enrolled 330
  - Number of Institutions using Adult CIRB only 183
  - Number of Institutions using Pediatric CIRB only 42
  - Number of Institutions using both Adult & Pediatric CIRB 105

- Total Number of Enrolled Signatory Institutions, Affiliates, and Components 1,023

- Number of NCI Designated Cancer Centers 43
- Number of CCOPs 35
- Number of MBCCOPs 10

As of 4/30/2012
NCI CIRB: Changes in Initial Review Timeline

Timeline for Adult CIRB Approval of Initial Reviews (Median Number of Days)

- Time from CIRB Receipt to Review
  - 2008: 29.0
  - 2009: 23.5
  - 2010: 17.0
  - 2011: 20.0
  - 2012: 9.0

- Time from CIRB Review to Approval
  - 2008: 94.0
  - 2009: 70.5
  - 2010: 20.5
  - 2011: 14.5
  - 2012: 11.0

- Time from CIRB Receipt to Approval
  - 2008: 126.0
  - 2009: 96.0
  - 2010: 43.0
  - 2011: 34.0
  - 2012: 21.0
NCI Adult & Pediatric CIRB Independent Model

- Received full accreditation by Association for Accreditation of Human Research Participant Protection Programs (AAHRPP) in December 2012

- New institutions being added and current institutional members of CIRB being transitioned to independent model

- Participation in NCTN trials will require use of CIRB (with waiver exemption possible for sites demonstrating similar local IRB review timelines)

- Being expanded to include study review of other NCI-supported clinical trials networks & potential expansion to other types of studies
  - Experimental Therapeutics Clinical Trials Network; other NCI Networks
  - DCP-supported cancer control & prevention studies
Recommendation 4: NCI should take steps to facilitate more collaboration among the various stakeholders in cancer clinical trials

Progress

• NCI has harmonized all guidelines for programs engaged in the conduct of clinical trials so that the appropriate incentives are in place for collaboration (SPORES, Cancer Centers, Groups)

• In collaboration with CEO Roundtable on Cancer, developed Standard Terms of Agreement for Research Trials (START) clauses for company and academic collaborations to speed clinical trial negotiations

• Revised IP option on all CTEP Cooperative Research and Development Agreements (CRADAs) relating to drug development (CTEP Intellectual Property Option to Collaborator; Pages 13404-13410 [FR DOC# 2011-5609]): Biomarkers/Tissues—no blocking IP; royalty-free non-exclusive licenses

• CRADA negotiations with Pharma: 6 month absolute deadline
**IOM Goal 2: Incorporate Innovative Science and Trial Design Into Cancer Clinical Trials**

**Recommendation 5:** NCI should mandate submission of annotated biospecimens to high-quality, standardized central biorepositories when samples are collected from patients in the course of Group trials and should implement new funding mechanisms and policies to support the management and use of those resources for retrospective correlative science.

**Progress**

- Revising RFA for U24 grants for National Specimen Banks for NCTN Groups to include common operating procedures for samples collected from patients Group and other NCI supported trials.

- Developing common process & procedures for requesting biospecimens banked from NCI clinical trials.

- Developing shared IT infrastructure to enhance specimen inventories.
Integrated National Biospecimen Banks for NCTN

Biospecimen Navigator

- Provide consolidated inventory of biospecimens across NCTN trials
- Connect biospecimen inventory data with associated trial data and (where possible) clinical data – as aggregate counts – to allow for assessment of biospecimen availability based on trial design / end points
- Provide tools and standards definitions to facilitate automated data loading from multiple systems
- Provide secure, role-based, highly functional user interface performing data queries & reporting to meet needs of various stakeholders
- Provide user interface & data model for tracking biospecimen requests, utilization, & scientific productivity
- Create an extensible system to serve similar biospecimen inventory / query & request tracking needs beyond NCTN Groups as needed
Recommendation 6
Cooperative Groups should lead the development and assessment of innovative designs for clinical trials that evaluate cancer therapeutics and biomarkers (including combinations of therapies).

Progress
• Initiated the Biomarker, Imaging, and Quality of Life Studies Funding Program to ensure that critical correlative studies could be incorporated in a timely manner into phase 3 and large, multi-institutional phase 2 trials during the process of concept development.

• From mid-2008 thru 12/27/12, 24 of 88 concepts submitted incorporating integral and integrated biomarker, imaging, QOL, and CEA studies have been supported for a total commitment of $30,538,091.
<table>
<thead>
<tr>
<th>Cooperative Group/CCOP</th>
<th>Funded Study Type</th>
<th>Cancer Site</th>
<th>Assay/Test/Assessment</th>
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</thead>
<tbody>
<tr>
<td>SWOG</td>
<td>Integral Biomarker</td>
<td>Breast</td>
<td>OncoType DX</td>
</tr>
<tr>
<td>COG</td>
<td>Integrated QOL</td>
<td>Peds ALL</td>
<td>vincristine-associated neuropathy &amp; motor function</td>
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<tr>
<td>COG</td>
<td>Integral &amp; Integrated Biomarkers</td>
<td>Peds AML</td>
<td>FLT3/ITD, KIT, MRD, WT1, RUNX1, TET2, MLL-PTD, c-CBL, CEBPα, CD74, PSMB5</td>
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<tr>
<td>RTOG/ACRIN</td>
<td>Integrated Imaging</td>
<td>Glioblastoma</td>
<td>MRI</td>
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<tr>
<td>RTOG</td>
<td>Integral Biomarker</td>
<td>Esophageal</td>
<td>HER2</td>
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<tr>
<td>NCCTG</td>
<td>Integral Biomarker</td>
<td>Glioma</td>
<td>translocation of 1p:19q</td>
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<tr>
<td>CALGB</td>
<td>Integral &amp; Integrated Biomarkers</td>
<td>Lung</td>
<td>COX-2, urinary PGE-M</td>
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<tr>
<td>COG</td>
<td>Integral Biomarker</td>
<td>Peds AML</td>
<td>FLT3/ITD, MRD, CEBPα</td>
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<tr>
<td>NSABP</td>
<td>Integrated QOL</td>
<td>Breast</td>
<td>fatigue, behavioral &amp; health outcomes</td>
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<tr>
<td>GOG</td>
<td>Integrated QOL</td>
<td>Uterine</td>
<td>PROMIS 7 (HRQOL)</td>
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</table>
IOM Goal 2: Incorporate Innovative Science and Trial Design Into Cancer Clinical Trials

- NCI worked with Investigational Drug Steering Committee on evaluation of innovative clinical trial designs as well as other key issues related to cancer therapeutics:
  


  ✓ “Approaches to phase I clinical trial design focused on safety, efficiency, and selected patient populations: a report from the clinical trial design task force of the NCI investigational drug steering committee. Clin. Cancer Res. 16: 1726-1736, 2010
• NCI is revising Early Therapeutics Clinical Trials System:
  ✓ Team Science focused approach for Early Experimental Therapeutics Program
  ✓ Molecular profiling of patient tumors from early experimental therapeutics clinical trials
  ✓ Enhanced collaboration, both within NCI/DCTD (PD Lab, CRADA collaboration, CDP, CIP, RRP) and with other NCI-sponsored programs, including SPORES, Centers, mouse models consortia, grantees (P01s)
  ✓ Streamline the timeline for study development by identifying processes that can be better synchronized and/or performed simultaneously; provide core services
IOM Goal 3: Improve Prioritization, Selection, Support, and Completion of Cancer Clinical Trials

Recommendation 8: NCI should re-evaluate its role in the clinical trials system

Progress

• Initiated Clinical Trials and Translational Research Advisory Committee (CTAC) with specific responsibilities for evaluating NCI’s clinical trials programs strategic vision

• CTAC Strategic Planning Working Group: Evaluate the overall effectiveness of studies conducted by NCTN

• Revamped prioritization process for phase 3 and large phase 2 treatment & control trials through disease and modality-specific Steering Committees to ensure most important trials are given highest priority

• NCI represents Institute priorities for the public program on the Steering Committees and facilitates implementation of prioritized clinical trials
## NCTN Program Cooperative Agreements: 6 Funding Opportunity Announcements Released

<table>
<thead>
<tr>
<th>Network Component</th>
<th>Mechanism (Duration)</th>
<th>Est. Max. # Grants</th>
<th>Frequency New Application Accepted?</th>
<th>Multiple PI Option?</th>
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<tr>
<td>Group Operations Centers</td>
<td>U10 (5 Yrs)</td>
<td>5</td>
<td>Every 5 Years</td>
<td>Yes</td>
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<tr>
<td>Group Statistical &amp; Data Mgt Centers</td>
<td>U10 (5 Yrs)</td>
<td>5</td>
<td>Every 5 Years</td>
<td>Yes</td>
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<tr>
<td>Lead Academic Participating Sites</td>
<td>U10 (5 Yrs)</td>
<td>30 to 40</td>
<td>Possible Additional Date After 2 Years within 5 Year Period</td>
<td>Yes</td>
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<tr>
<td>Integrated Translational Science Awards</td>
<td>U10 (5 Yrs)</td>
<td>5 to 7</td>
<td>Every 5 Years</td>
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<tr>
<td>RT and Imaging Core Services</td>
<td>U24 (5 Yrs)</td>
<td>1</td>
<td>Every 5 Years</td>
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<tr>
<td>Canadian Collaborating Network</td>
<td>U10 (5 Yrs)</td>
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<td>Every 5 Years</td>
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<td>Event</td>
<td>Date</td>
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<td>--------------------------------------------------</td>
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<td></td>
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<tr>
<td>NCI Board of Scientific Advisors Review</td>
<td>Nov 2011</td>
<td></td>
<td></td>
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<tr>
<td>New FOAs &amp; Guidelines Released</td>
<td>July 23, 2012</td>
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<td>Letter of Intents Due</td>
<td>December 15, 2012</td>
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<td>Receipt Competing Applications Due</td>
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<td>National Cancer Advisory Board Review</td>
<td>October 2013</td>
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<td>Rollout of Awards in FY2014</td>
<td>March 2014 (tentative)</td>
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</tbody>
</table>
Vision for Transformed Network

- Provide essential infrastructure for NCI trials in treatment, control, screening, diagnosis, & prevention across all NCI clinical research programs

- Launch trials rapidly and complete accrual according to defined guidelines through integrated national network of performance sites

- Promote user-friendly, harmonized processes to extramural community (investigators, patients, advocates, & industry)

- Provide functional platform to perform large scale testing of increasingly smaller subsets of molecularly-defined cancers & focus on questions not well supported in a commercial environment
Additional Slides
Integrated National Biospecimen Banks for NCTN

Biospecimen Navigator

Shared Standards and Governance
Shared semantics/vocabulary, data formats, web service definitions, IT tooling, etc.

Data Submitters
- Banks
- Groups
- SDCs

Data Uploads

CGB Navigator Solution
- Data Upload Services/Endpoints (e.g., SFTP, DBI, SOAP, REST, etc.)
- Back Room Staging Database
  Houses raw uploads (un-conformed, pre-audit data)
- Data Quality Firewall
  Data quality checks, failure notifications to data submitters, quality statistics
- Front Room Querying Database
  Houses conformed, merged, cleansed data suitable for dissemination any querying by analytic tools; derived datasets for optimized query performance

Data Inquiries

Scientific Community

CGB Navigator Query Tools and Services
High-performance, user-friendly environment for obtaining integrated biospecimen inventory information
User Interface Design Concept - Investigator Page

Interactive Query Interface

User Profile

Project / Request Status

Search History

Interactive Search Refinement

Aggregate result counts by Group / Protocol

Reporting Tools & Summary Statistics
<table>
<thead>
<tr>
<th>Cooperative Group/CCOP</th>
<th>Funded Study Type</th>
<th>Cancer Site</th>
<th>Assay/Test/Assessment</th>
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<tbody>
<tr>
<td>RTOG</td>
<td>Integrated Biomarker</td>
<td>Pancreas</td>
<td>SMAD4</td>
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<td>ECOG</td>
<td>Integral &amp; Integrated Biomarker</td>
<td>Adult ALL</td>
<td>MRD</td>
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<td>Alliance</td>
<td>Integrated Imaging</td>
<td>Prostate</td>
<td>PET/CT</td>
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<tr>
<td>RTOG</td>
<td>Integral Biomarkers</td>
<td>Head &amp; Neck</td>
<td>P16 &amp; EGFR</td>
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<td>COG</td>
<td>Integral Biomarker</td>
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<td>DNA Sequencing</td>
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<td>Gastric</td>
<td>ERCC-1</td>
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<td>Integral Biomarker</td>
<td>Breast</td>
<td>Ki67</td>
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<tr>
<td>CALGB</td>
<td>Integral Biomarker &amp; Imaging</td>
<td>Esophageal</td>
<td>central pathology &amp; PET-CT</td>
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<tr>
<td>RTOG</td>
<td>Integral Biomarker</td>
<td>Oropharynx</td>
<td>p16</td>
</tr>
<tr>
<td>COG</td>
<td>Integral Biomarker</td>
<td>Peds ACL</td>
<td>galactomannan &amp; β-D-glucan</td>
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<td>COG</td>
<td>Integrated Biomarkers</td>
<td>Peds ACL</td>
<td>bacterial isolates from stool/perirectal swabs</td>
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<tr>
<td>COG</td>
<td>Integrated Imaging</td>
<td>Peds ALL (osteonecrosis)</td>
<td>MRI</td>
</tr>
<tr>
<td>SWOG</td>
<td>Integral &amp; Integrated Biomarkers</td>
<td>NSCLC</td>
<td>KRAS, EGFR</td>
</tr>
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</table>
IOM Goal 2: Incorporate Innovative Science and Trial Design Into Cancer Clinical Trials

Integration of NCI-Sponsored Programs Using Early Experimental Therapeutics Program: Network Collaborations of All Sites
IOM Goal 2: Incorporate Innovative Science and Trial Design Into Cancer Clinical Trials

- Major Components of Revised Early Experimental Therapeutics Program
Recommendation 7: NCI, in cooperation with other agencies, should establish a consistent, dynamic process to oversee development of national unified standards.

Progress

- Under auspices of Clinical and Translational Research Advisory Committee (CTAC), developed definitions of integral & integrated studies for biomarkers, imaging, and quality of life investigations associated with Group trials.

- Working with the NLM and the AACI to develop the Cancer Trials Reporting Program (CTRP) database to provide accrual information related to all NCI-supported clinical trials with full accrual reporting to begin in 2013.
## Steering Committee Leadership

### Disease Specific Steering Committee

<table>
<thead>
<tr>
<th>Steering Committee</th>
<th>Co-Chairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal (GISC)</td>
<td>Dan Haller, MD, Bruce Minsky, MD, &amp; Neal Meropol, MD</td>
</tr>
<tr>
<td>Gynecologic (GCSC)</td>
<td>David Gershenson, MD; Gillian Thomas, MD; Michael Birrer, MD</td>
</tr>
<tr>
<td>Head &amp; Neck (HNSC)</td>
<td>David Adelstein, MD; David Brizel, MD; &amp; Drew Ridge, MD, Ph.D</td>
</tr>
<tr>
<td>Genitourinary (GUSC)</td>
<td>Eric Klein, MD; Robert Dreicer, MD; &amp; Anthony Zietman, MD</td>
</tr>
<tr>
<td>Breast (BCSC)</td>
<td>Thomas Buchholz, MD; &amp; Nancy Davidson, MD</td>
</tr>
<tr>
<td>Thoracic (TMSC)</td>
<td>William Blackstock, MD; David Harpole, MD; &amp; Mark Socinski, MD</td>
</tr>
<tr>
<td>Leukemia (LKSC)</td>
<td>Wendy Stock, MD; &amp; Jerry Radich, MD</td>
</tr>
<tr>
<td>Lymphoma (LYSC)</td>
<td>Oliver Press, MD; &amp; Julie Vose, MD</td>
</tr>
<tr>
<td>Myeloma (MYSC)</td>
<td>Morie Gertz, MD; &amp; Nikhil Munshi, MD</td>
</tr>
<tr>
<td>Brain (BMSC)</td>
<td>Ian Pollack, MD; &amp; W.K. (Al) Yung, MD</td>
</tr>
<tr>
<td>Pediatric Leukemia &amp; Lymphoma</td>
<td>David Poplack, MD; &amp; Robert Arceci, MD</td>
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<td>(PLLSC)</td>
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<td>Pediatric &amp; Adolescent Solid</td>
<td>Mark Bernstein, MD; &amp; Kate Matthay, MD</td>
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<tr>
<td>Tumor (PASTSC)</td>
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# Steering Committee Leadership

## Non-Disease Specific Steering Committee

<table>
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<th>Steering Committee</th>
<th>Co-Chairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigational Drug SC (IDSC)</td>
<td>Lillian Siu, MD &amp; Miguel Villalona, MD</td>
</tr>
<tr>
<td><strong>Symptom Management &amp; Health Related QoL SC (SxQOL SC)</strong></td>
<td>Deborah Bruner, RN, PhD &amp; Michael Fisch, MD, MPH</td>
</tr>
<tr>
<td>Patient Advocate SC (PASC)</td>
<td>Elizabeth Frank &amp; Mary Jackson Scroggins</td>
</tr>
<tr>
<td>Clinical Imaging SC (CISC)</td>
<td>Steve Larson, MD &amp; Neil M. Rofsky, MD</td>
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## Concept Evaluation Summary ~ (as of 12/31/2012)

<table>
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<tr>
<th>Steering Committee</th>
<th>Total Concept Evaluated</th>
<th>Total Concept Approved</th>
<th>Total OPEN to Accrual</th>
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<td>GCSC</td>
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<td>PLLSC</td>
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<tr>
<td>PASTSC</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>293</strong></td>
<td><strong>144 (49%)</strong></td>
<td><strong>93 (65%)</strong></td>
</tr>
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</table>
Recommendation 9: NCI, Groups, and physicians should take steps to increase the speed, volume, and diversity of patient accrual and to ensure high-quality performance at all sites participating in Group trials.

Progress

- Modernizing clinical trials IT infrastructure by implementing common clinical data management system to be used across NCI-supported clinical trials system.

- Enhancing trial participant diversity through support for Minority-based Community Clinical Oncology Programs, Patient Navigator Research Program, & other NCI programs.

- Working with patient advocates in concept development and accrual planning, along with Groups, Disease Steering Committees, and Patient Advocate Steering Committee.
Update of NCI Informed Consent Document (ICD) Template to address concerns regarding patient understanding of clinical trials presented to them by their treating physicians.

Process put in place to assess status current ICDs in NCI trials & address concerns of stakeholders across the oncology community.

'Snapshot' Audit: Length of Phase 3 CTEP Tx Trials
97 studies - Range: 5 to 35 pages - Median: 16 pages

Series of Working Groups to address key aspects of the ICD created in order to update and streamline/shorten the NCI ICD Template.

Anticipated implementation date in 2nd Quarter 2013.
Update NCI Consent Template: Working Group Co-chairs & Federal Regulatory Advisors

- **Working Group 1** (Background, required tests, intervention sections):
  - Shlomo Koyfman, MD – clinical investigator
  - Joan Westendorp, RN, MSN, OCN, CCRA – protocol coordinator

- **Working Group 2** (Risks and benefits sections):
  - Roy Smith, MD – former CIRB Chair
  - Michael Paasche-Orlow, MD, MA, MPH – ICD expert

- **Working Group 3** (Alternatives, privacy, injury, cost, rights, signature):
  - Edward Goldman, JD – ICD expert
  - Nancy Morton, MT, MPH – protocol coordinator

- **Working Group 4** (Possible attachments):
  - Barbara LeStage, MPH – patient advocate
  - Mary McCabe, RN, MA – ICD expert

- **Working Group 5** (Companion studies):
  - Lisa Carey, MD – clinical investigator
  - Laura Beskow, MPH, PhD – translational investigator

- **FDA Advisors**: Sandra Casak, MD; Ruthann Giusti, MD; Joanne Less, PhD; Shan Pradhan, MD; Sara Goldkind, MD, MA

- **OHRP Advisors**: Jerry Menikoff, JD, MPP, MD; Julie Kaneshiro, MA; Lisa Rooney, JD; Lisa Buchanan, MA
New NCI ICD Template Features

- Text examples for different types & phases of studies
  - *Includes chemoprevention and imaging trials*

- Section page/length limits

- Text provided for mandatory specimen collection, within primary consent, and optional specimen collection, located before signature line

- Contact information for study doctor
  - *Easy to find for study participants with one location to ask questions, discuss concerns, report side effects or injuries*

- More text examples for optional studies, e.g., imaging correlatives

- Text for biobanking, optional research biopsy, and future studies

- Complies with new FDA regulation, 21 CFR 50.25(c)

- Meets new CTEP electronic submission requirements, FDA mandate
New NCI ICD Template – Risk Presentation

• Recommendations for risks section
  – *Risks described from study participant perspective*
    • Easy to understand, meaningful
    • Changes in specific lab values not included
  – *Similar frequency categories as previous Templates*
    • Clearer definition of frequency – “x out of one hundred” rather than percentage
  – *Format risks into tables – “Tables of Possible Side Effects”*
    • Use different tables for experimental and standard arms; grouping by regimen
    • List risks by body system, keeping description at a general level using lay terms
  – *Three tasks for DCTD/CTEP*
    • Translate DCTD/CTEP’s risk profiles of IND agents into more general lay terms
    • Develop repository of “Tables of Possible Side Effects” for CTEP IND agents
    • Develop repository of “Tables of Possible Side Effects” for commonly used commercial drugs and regimens
Recommendation 10: NCI should allocate a larger portion of its research portfolio to the Clinical Trial Group Program to ensure that the Program has sufficient resources to achieve its unique mission.

Progress

- NCI developed targeted initiatives that have increased reimbursement to sites for patients on large phase 2 studies & additional funding provided for select phase 3 trials based on complexity as well as the funding for critical biomarker, imaging & QOL studies.

- Changes in the funding model for new RFA:
  - Increased reimbursement for high-performing sites (~aimed at 40% accrual)
  - Need for additional infrastructure support with proposed RFA budget increased to support better reimbursement but lower level of accrual
  - Increase in core resources for genomic correlative studies
IOM Goal 4: Incentivize the Participation of Patients and Physicians in Clinical Trials

Recommendation 11: All stakeholders should work to ensure that clinical investigators have adequate training and mentoring, paid protected research time, the necessary resources, and recognition.

Progress

- NCI created Clinical Investigator Team Leadership Award to promote collaborative science & recognize outstanding clinical investigators with annual awards made since 2009.

2012 Awardees

Dr. Lyudmila Bazhenova
Dr. Lisa Bomgaars
Dr. Alberto Broniscer
Dr. Daniel DeAngelo
Dr. Konstantin Dragnev
Dr. Shirish Gadgeel
Dr. Shannon Puhalla
Dr. Bart Lee Scott
Dr. B. Douglas Smith
Dr. Jonathan Strosberg
Dr. Antoinette Tan
Dr. Jason Zell

UC San Diego Moores Cancer Center
Baylor College of Medicine, Lester and Sue Smith Clinic at Texas Children’s CC
St. Jude Children’s Research Hospital
Dana-Farber Cancer Institute
Dartmouth-Hitchcock Norris Cotton Cancer Center
Wayne State University Karmanos Cancer Institute
University of Pittsburgh
Fred Hutchinson Cancer Research Center; University of Washington
Johns Hopkins University, Sidney Kimmel Comprehensive Cancer Center
H. Lee Moffitt Cancer Center
Cancer Institute NJ/UMDNJ-Robert Wood Johnson Medical School
UC Irvine Chao Family Comprehensive Cancer Center
Recommendation 12: Health care payment policies should value the care provided to patients in clinical trials and adequately compensate that care.

Progress

- NCI continues to work with the NIH as well as across HHS Agencies and with other federal Agencies to help define and shape national policy on clinical trials and reimbursement as well as to educate patients and payers regarding the benefit of clinical trials.

- Working with FDA to facilitate incorporation of genomic tests into definitive clinical trials and the development of companion diagnostics.