Changing the NCI’s Clinical Trials System to Meet the Needs of the 21st Century: Implementation of the Clinical Trials Working Group and the Institute of Medicine Recommendations

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Changing the NCI’s Clinical Trials System to Meet the Needs of the 21st Century

- CTWG – June 2005
- OEWG – March 2010
- IOM – April 2010

A comprehensive approach is needed to achieve a collaborative, public, national system that addresses the challenges and opportunities provided by our rapidly evolving understanding of cancer biology.
IOM Goals Build on CTWG and OEWG

IOM Goals: What do we need to change?

- Improve the speed and efficiency of the development and conduct of trials
- Incorporate innovative science and trial design into our studies
- Improve prioritization, support, and completion of trials
- Incentivize the participation of patients and physicians in clinical investigations

What have we changed to date?

Where do we go from here?
What have we changed to date?

- Developed operational efficiency standards for trial launch to achieve new target timelines for clinical trial activation
- Developed Standard Terms of Agreement for Research Trials (START) clauses for company and academic collaborations
- Enhanced & Speeded Up Central IRB functions (Jaci Goldberg)
OEWG Target Timeline for Group Phase III Trials – 300 days

Timeline pauses if industry negotiations cause delay

Feedback on major challenges in 5 days

If registration trial, FDA review in 30 days

Protocol terminated if not activated in two years
18 Concepts Proposing Phase III Trials Received Since April 1, 2010

- 3 concepts approved
- 6 concepts in review or in time-out (company &/or drug commitment)
- 5 concepts disapproved or withdrawn
- 4 concepts submitted to CTEP awaiting Steering Cmte. review

Approved Concepts (3): Target timeline for Concept approval –90 days if Group phase II $> 100$ pts or Group phase III

- Average number of days for concept approval by Steering Cmte. (without time-outs) = \textbf{41 days (n=2)}
- Average number of days for ph II concept approval w/o SC (without time-outs) = \textbf{40 days (n=1)}
- Average time-out length: NA (no time-outs among approved concepts)
- 0 concepts have exceeded the 90 day target
OEWG Target Timeline for Group Phase II Trials – 210 days

Timeline excludes contracting, drug supply, FDA

Protocol terminated if not activated in 18 months
21 Group LOIs received since April 1, 2010

- 5 Group LOIs approved; 2 protocols submitted
- 4 Group LOIs in review or in time-out
- 12 Group LOIs disapproved, withdrawn, or declined by Pharma

Approved LOIs (5): Target timeline for Group LOI approval – 60 days

- Average number of days for Group LOI approval – 42 days
- Average time-out length – 15 days (among the approved Group LOIs)
- 1 Group LOI has exceeded the 60-day target

Protocols (2): Target timeline for Protocol Submission – 90 days

- Average time from Group LOI approval to Protocol submission – 61 days
20 U01/N01 LOI’s received since April 1, 2010
– 8 U01/N01 LOI’s approved; 1 U01/N01 Protocol submitted
– 7 U01/N01 LOI’s in review or in time-out (drug commitment or grant approval)
– 5 U01/N01 LOI’s disapproved or withdrawn

Approved U01/N01 LOI’s (8): Target timeline for LOI Approval – 60 days
– Average number of days for LOI approval (without time-outs) – 36 days
– Average time-out length – 32 days (all for drug commitment)
– No LOI’s have exceeded the 60 day target

6 other (P50, R01, R21, DoD) LOIs submitted
– 4 in review
– 2 withdrawn/disapproved
6 intramural LOI’s received since April 1, 2010
- 2 intramural LOI’s approved; 2 protocols submitted
- 2 intramural LOI’s in review
- 2 intramural LOI’s disapproved

Approved intramural LOI’s (2): Target timeline for LOI Approval – 60 days
- Average number of days for LOI approval (without time-outs) – 38 days
- Average time-out length – 2 days (drug commitment)
- No intramural LOI’s have exceeded the 60 day target

Protocols Submitted (2): Target timeline for Protocol Submission – 60 days
- Average time from LOI Approval to Protocol submission – 59 days
NCI Initiatives to Achieve OEWG Goals

• Kick-off meeting late March with Groups, Consortia, and Phase I/II UO1s and NO1s to establish common understanding and collaborative procedures

• Hire Project Managers to oversee OEWG processes

• Standardized CTEP consensus reviews and provide comments in Track Change® Mode
NCI Initiatives to Achieve OEWG Goals (cont.)

• Modified/developed internal SOPs to streamline processes and improve communication
• Identified at-risk trials (First quarter of CY11)
• Established teleconference calls to discuss/resolve outstanding issues
• Developed secure, role-based, web-portal to share tracking reports with intramural and extramural investigators and support staff
• Two OEWG working groups meet monthly via conference calls to discuss OEWG processes:
  – OEWG Cooperative Groups Working Group
  – OEWG Early-Phase Clinical Trials Working Group
Changing the NCI’s Clinical Trials System
Improving Efficiency

First 6 months of implementation (targets and absolute drop dead dates): Hitting timeline targets; 60% improvement
The application is primarily for NCI CTep internal and external collaborators to access data reports generated from the CTep Enterprise System.

Version 1.0:
The first version of the application will allow users to generate Protocol Development Timeline (PDT) reports to track the amount of time it takes to develop a protocol from Concept or LOI receipt to Protocol Activation. The PDT reports will be available in 4 different formats for comparison and analysis. The users of the application should have an ACTIVE CTepIAM account.
What have we changed to date?

- Biomarker, Imaging, and Quality of Life Studies Funding Program (BIQSFP): a novel mechanism to facilitate the early development of integral components of phase 2 and 3 clinical trials
- Developed standards for biomarker assays used in clinical trials
- Consolidating Cooperative Group biospecimen banks into a national banking system that supports Cooperative Group and other NCI-supported clinical trials
- Developed the Clinical Assay Development Program and Patient Characterization Center: Operational 1/11
- Novel designs for phase 1/2 trials to better predict successful phase 3 trials (Adjei et al, Clin Cancer Res 2009)
What have we changed to date?

- **Scientific Steering Committees**

- **Developing a unified clinical trials informatics system**
  - Comprehensive database (Clinical Trials Reporting Program)
  - Standardized case report form modules
  - Credentialing repository (launched 2010)
  - NCI will be the first Institute to provide a robust, standardized, off-the-shelf clinical trials management (software) system to all of its grantees that includes a standardized “look and feel” as well as protocol development and data collection modules

- **Reimbursement for phase 2 trials increased**
# Disease-Specific Steering Committees: Prioritizing Clinical Trials

<table>
<thead>
<tr>
<th>Steering Committee</th>
<th>Year Established</th>
<th>Co-Chairs</th>
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<tbody>
<tr>
<td>GI 2006</td>
<td>Dan Haller, MD &amp; Joel Tepper, MD</td>
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<tr>
<td>Gyn 2006</td>
<td>David Gershenson, MD, Gillian Thomas, MD, &amp; Michael Birrer, MD</td>
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<tr>
<td>Head &amp; Neck 2007</td>
<td>Arlene Forastiere, MD, David Schuller, MD, &amp; Andy Trotti, MD</td>
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<td>GU 2008</td>
<td>Eric Klein, MD, George Wilding, MD, &amp; Anthony Zietman, MD</td>
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<tr>
<td>Breast 2008</td>
<td>Charles Geyer, MD &amp; Nancy Davidson, MD</td>
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<tr>
<td>Thoracic 2008</td>
<td>David Harpole, MD, William Sause, MD, &amp; Mark Socinski, MD</td>
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<tr>
<td>Leukemia 2009</td>
<td>Wendy Stock, MD &amp; Jerry Radich, MD</td>
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<td>Lymphoma 2009</td>
<td>Oliver Press, MD Julie Vose, MD</td>
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<tr>
<td>Myeloma 2009</td>
<td>Morie Gertz, MD, &amp; Nikhil Munshii, MD</td>
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<tr>
<td>Brain 2010</td>
<td>Ian Pollack, MD &amp; W.K. (Al) Yung, MD</td>
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**Pediatrics:** TBD - 2010

Approximately 98 Concepts evaluated since inception of SCs with an approval rate of 56% to 60%; see [http://ccct.nci.nih.gov](http://ccct.nci.nih.gov) for other SSC & rosters
IOM Goal 4: Patient and Physician Participation

What have we changed to date?

- **Cancer Clinical Investigator Team Leadership Award**
  - CTWG initiative to enhance recognition for mid-level clinical investigators at academic institutions who promote successful clinical research programs
  - Program launched in 2009 with 11 awardees receiving partial salary support for up to $50,000 per year for two years
  - 12 awardees in 2010

- **Guidelines Harmonization Working Group (GHWG)**
  - Chair: Jim Abbruzzese
  - Common clinical trials program guidelines to promote collaboration
  - Incentives
2010 Clinical Investigator Team Leadership Awardees

- Dr. Rafat Abonour, Indiana University
- Dr. Jeffrey Bradley, Washington University
- Dr. Steven Cohen, Fox Chase Cancer Center
- Dr. Linda Duska, University of Virginia
- Dr. Naomi Haas, University of Pennsylvania
- Dr. Elisabeth Heath, Wayne State University
- Dr. Susan Kelly, University of Texas MDACC
- Dr. Smitha Krishnamurthi, Case Western Reserve University
- Dr. Suresh Ramalingam, Emory University
- Dr. David Rizzieri, Duke University
- Dr. Cheryl Saenz, University of California-San Diego
- Dr. Sheri Spunt, St. Jude Children's Research Hospital
Organizational Structure 2005: Pre-CTWG

NCI Division of Extramural Activities (DEA) Review

- ECOG
- CALGB
- SWOG
- ACOSOG
- COG
- RTOG
- GOG
- ACRIN
- NCCTG
- NSABP

- Disease Committees
- Operations
- Stats & Data Mgt
- Tumor Banks

- Cancer Centers
- Other Academic Centers
- CCOPs & MB-CCOPs
- Community Practices
- International Members
Organizational Structure of the System: 2010

NCI Division of Extramural Activities (DEA) Review

- ECOG
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- GOG
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- NSABP

Disease Committees
Operations
Stats & Data Mgt
Tumor Banks

NCI Disease Steering Committees – Evaluation/Prioritization of Group Trials

NCI Central IRB

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

- Cancer Centers
- Other Academic Centers
- CCOPs & MB-CCOPs
- Community Practices
- International Members
Changing the NCI’s Clinical Trials System
What Else Do We Need To Do?

• Consolidation: How to restructure current system into a harmonized network; Size? Working parameters?

• How to incentivize cooperation and greater participation in the NCI’s clinical trials system?

• How to optimally provide access to needed molecular tools to answer critical scientific questions?

• How best to facilitate interactions with FDA and CMS to bring the most effective treatments to patients rapidly?

• How best to extend benefits of clinical trials participation to underserved populations?