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# Operational Efficiency Working Group (OEWG) Report

## National Cancer Advisory Board

**Gabriel Hortobagyi, MD**
**James H. Doroshow, MD**
**Co-Chairs**

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**Bethesda, MD**

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

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# OEWG Background

- **Clinical Trials Working Group Report Operational Efficiency Initiative 2**

  *Identify the institutional barriers that prolong the time from concept approval to accrual of first patient, and develop solutions for overcoming these barriers*

- **Clinical Trials Advisory Committee Charge**

  *Establish an Operational Efficiency Working Group (OEWG) to recommend strategies and implementation plans for reducing the time for activation of Cooperative Group and Cancer Center trials*

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# OEWG Membership…
# 63 Clinical Trial Stakeholders

- 10 Cooperative Group Chairs
- 8 Cancer Center Directors
- Clinical Investigators
- Statisticians
- Protocol/Trial Specialists
- Community Oncologist
- NCI Clinical Trials Leadership and Staff
  - DCTD, CTEP, DCP, CCR, NCICB, CCCT, Cancer Centers
- Pharma/Biotech
- Patient Advocates
- FDA
- CMS
- CTSU

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# Trial Categories Addressed by OEWG

- Cooperative Group Phase III Trials
- Cancer Center Investigator-Initiated Trials
- IDB Early Drug Development Phase II Trials
  - N01 Contract Holders
  - Cooperative Groups
- Cancer Center Activation of Cooperative Group Trials

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# Topics Outside OEWG Purview

- Industry sponsored trials
- OHRP regulated issues
- CMS coverage determinations
- State laws and requirements
- Congressional funding mandates

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# OEWG Deliberations

- Agreement on key barriers to timely trial activation
- Commitment to achieve new target timelines for steps in trial activation
- Developed new process maps for trial activation
- Identified external factors outside of NCI or investigators' control that delay activation
- Established firm dates to terminate protocol development if all issues are not resolved
- Developed recommendations and associated implementation plans to achieve target timelines

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# Operational Efficiency Working Group

- **Cooperative Group Phase III Trials**
  - Current State
  - Proposed OEWG Timeline
  - Recommended Process Improvements

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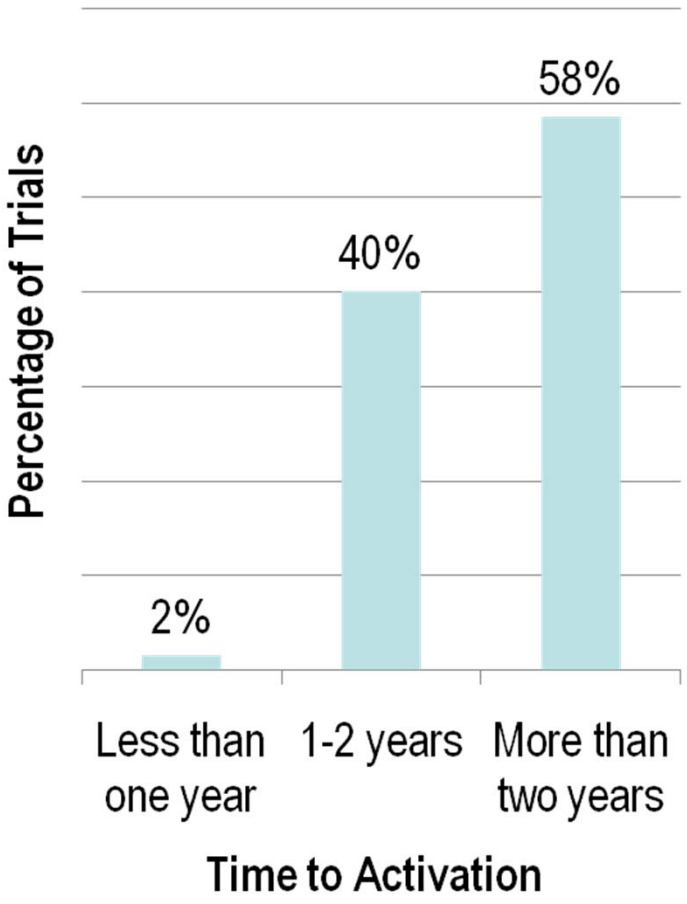
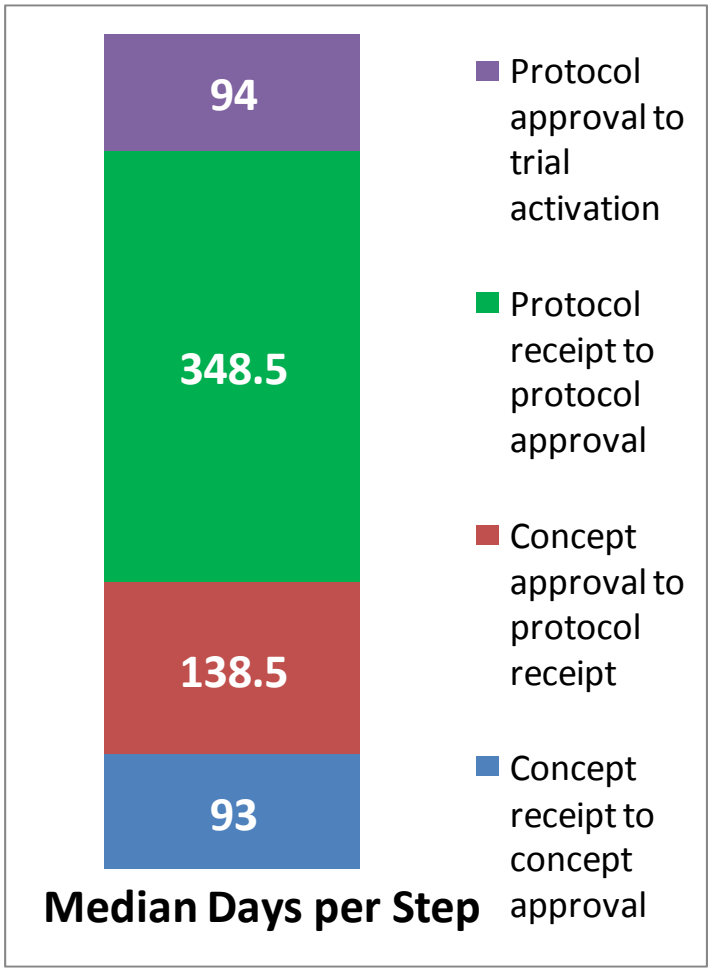
# Time to Activation – Current Status (2006 – 2008)



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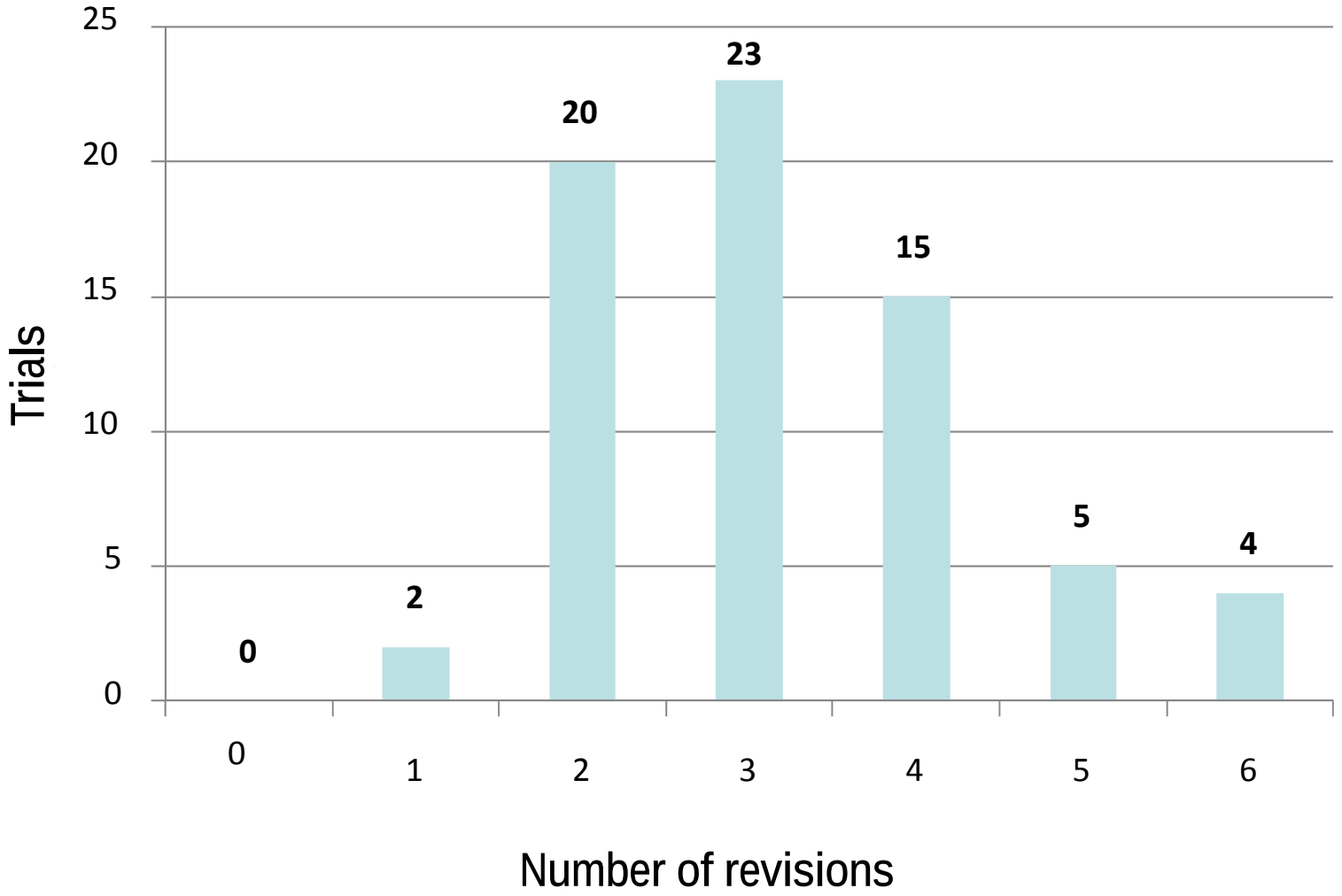
# Review/Revision of Protocols (2006 – 2008)



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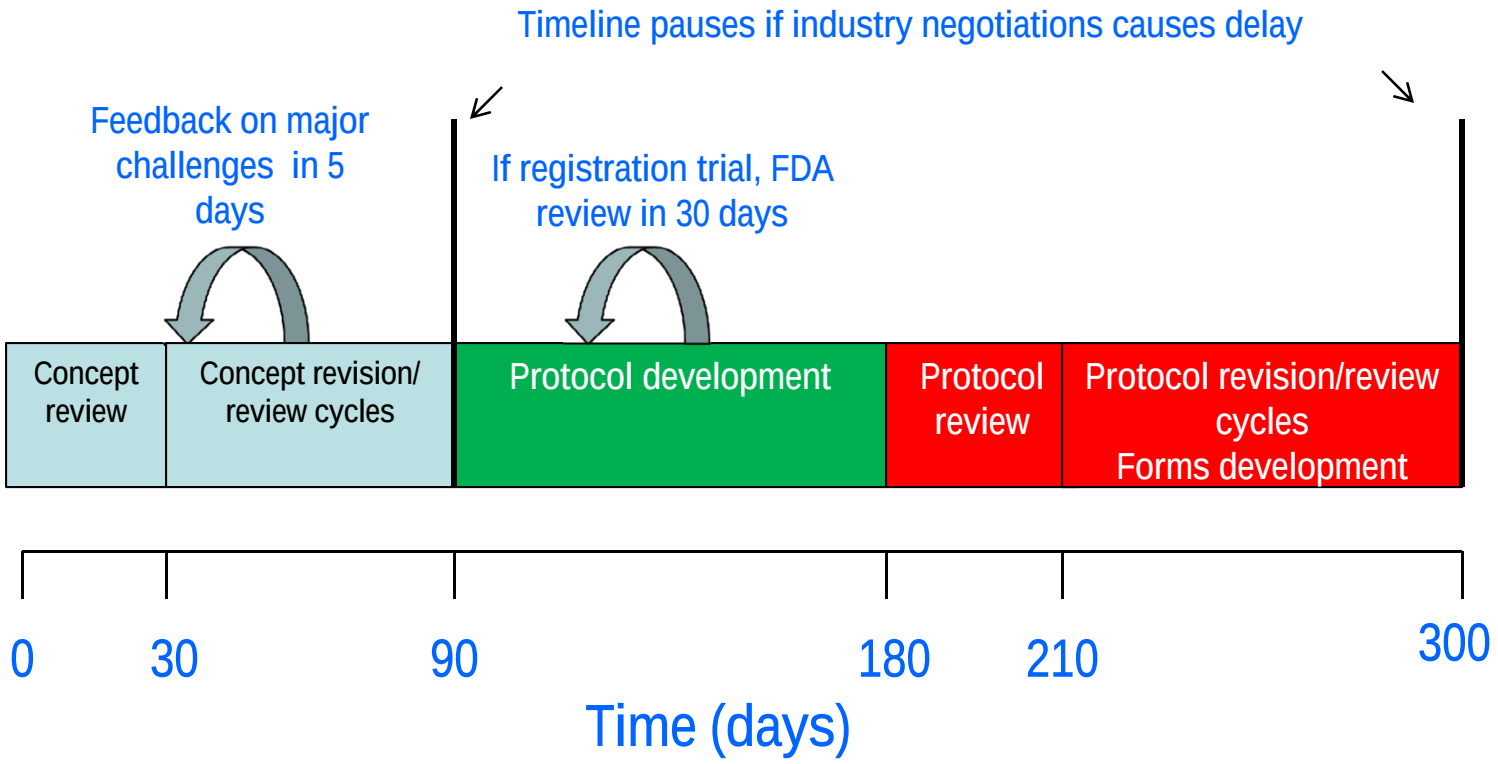
# Proposed OEWG Timeline – 300 days




(Timeline excludes IRB, contracting, drug supply)

Protocol terminated if not activated in two years

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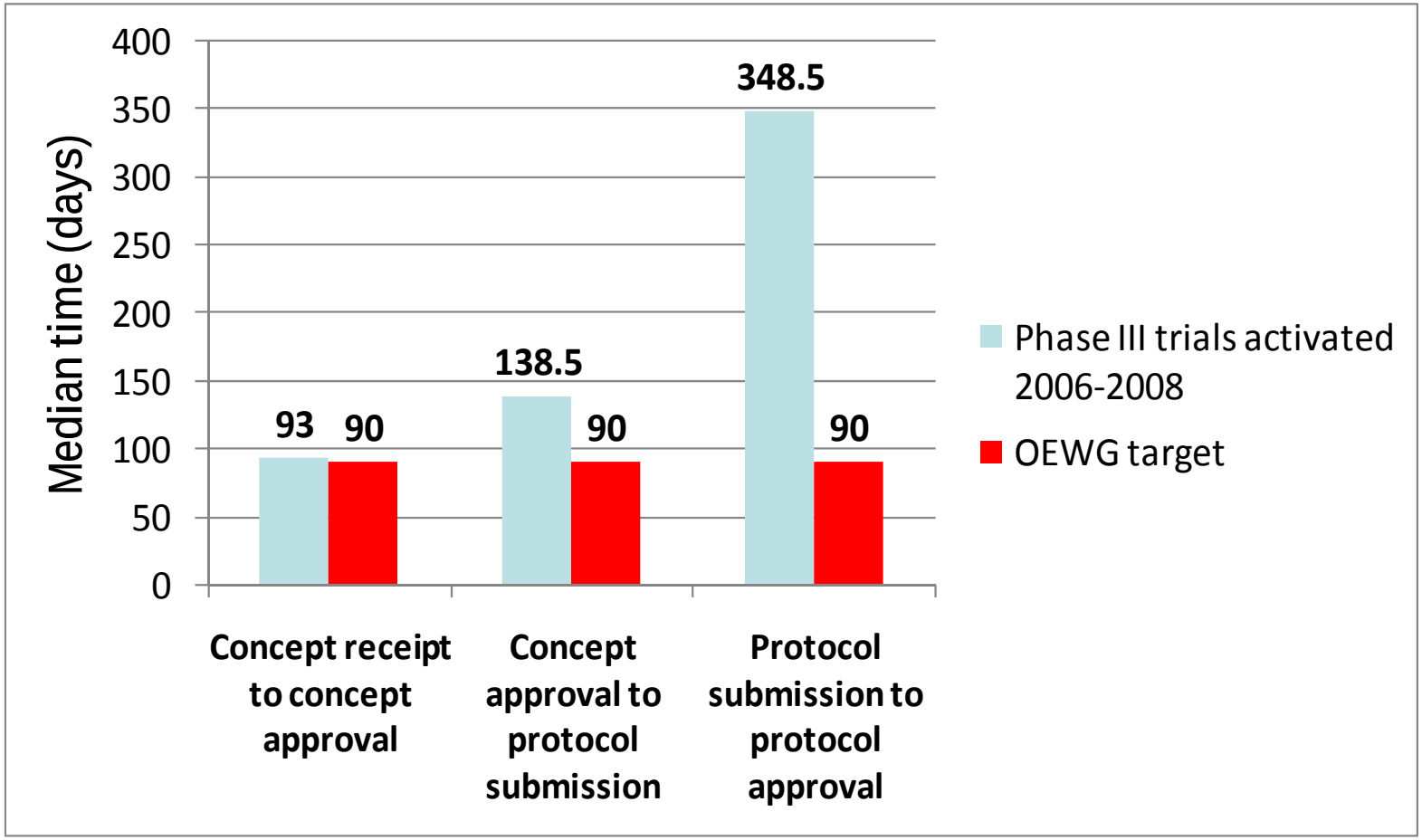
# Time to Trial Activation… Current vs OEWG Target




*Current median time includes CIRB approval, industry negotiations, and FDA approval*

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# Cooperative Group Process Improvement

***Recommendation 1: Group-specific Action Plan to achieve OEWG target timeline***

*Implementation Plan*

- Potential staffing changes
  - Physician Senior Protocol Officers
  - Non-physician Trial Development Managers
  - Specialist medical writers
- Trial development steps performed in parallel
- Direct, coordinated interactions to resolve issues
- Project management/protocol tracking tool

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# Cooperative Group Process Improvement

***Recommendation 2: CTEP Action Plan to achieve OEWG target timeline***

*Implementation Plan*

- Project Managers
  - Manage overall protocol review, revision and approval process
  - Facilitate interactions between CTEP and the Groups
- Coordinated CTEP/DCTD scientific/clinical review to identify all issues at time of initial concept and protocol review
- Prompt communication of critical issues in advance of formal written review
- Streamlined methods for communicating comments
- Distinguish advisory comments from those requiring response
- Project management/protocol tracking tool

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# Cooperative Group Process Improvement

***Recommendation 3: Collaborative Group/CTEP process for concept and protocol revision***

*Implementation Plan*

- Direct, coordinated interactions to resolve issues
- High priority on devoting time to issue resolution
- Fundamental aspects of study design resolved at concept stage
- Interactions at protocol stage focused on mechanics of completing a protocol embodying an agreed concept
  - Prompt communication and resolution of major differences
  - Minimal time spent discussing non-critical differences of opinion
  - Minimization of time and effort for routine or pro forma revisions
- Rapid arbitration for any issues not resolved quickly

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# Cooperative Group Process Improvement

***Recommendation 4: Develop approaches to reward performance against timelines***

*Implementation Plan*

- Establish comprehensive, reliable system for reporting timeline performance for each step in trial activation
- Collect timeline performance data for at least one year and assess accuracy and value of the data and reports
- Analyze performance data by individual Groups and across the Group system compared to target timelines
- Joint Group/CTEP deliberations concerning
  - Linking incentives to Group-specific timeline performance
  - Incorporating performance against timeline targets in Subcommittee H review
- CTEP to include timeline performance in annual staff performance evaluations

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# Operational Efficiency Working Group

- **Cancer Center Investigator Initiated Trials**
  - Proposed OEWG Timeline
  - Recommended Process Improvements

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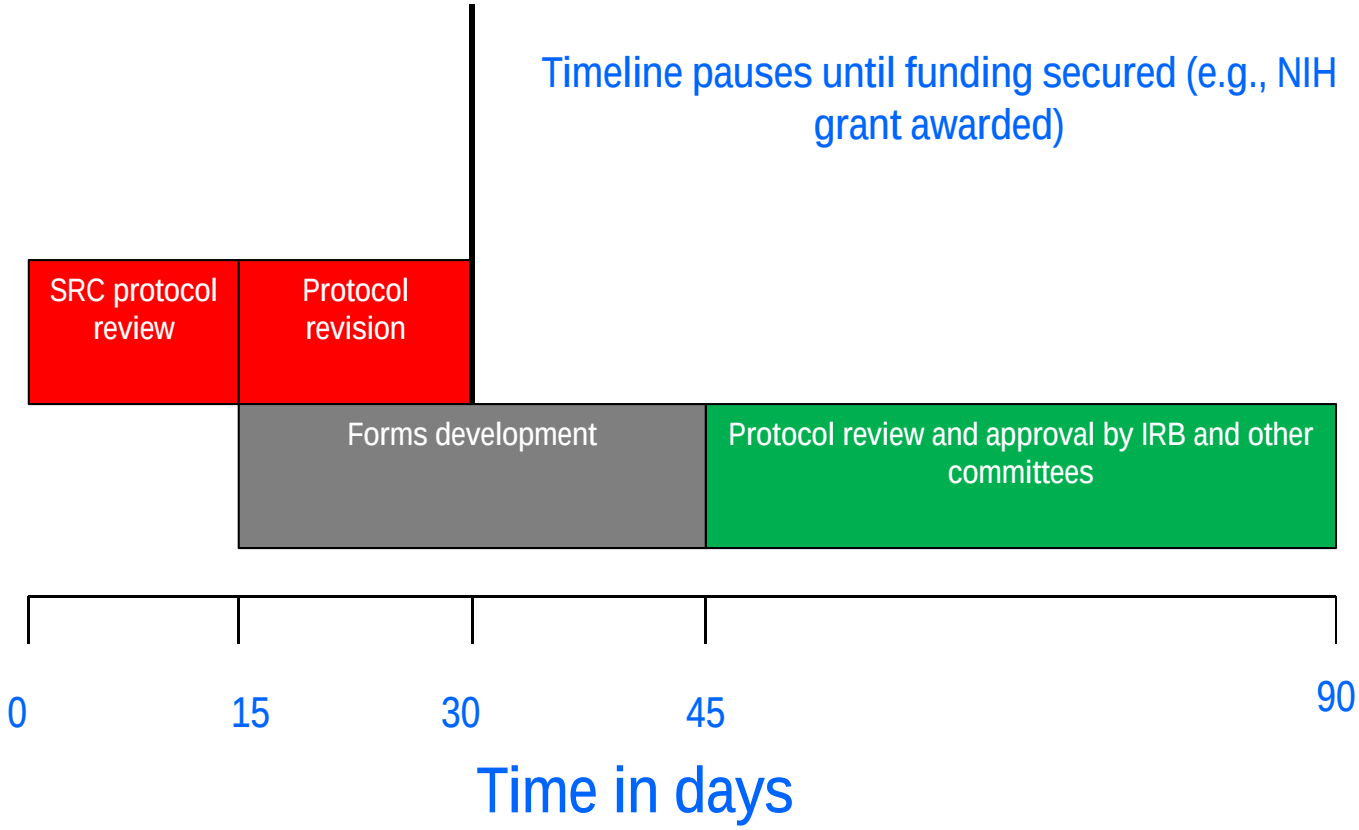
# Proposed OEWG Timeline – 90 days




(Timeline excludes writing of protocol, contracting, institutional financial review, drug supply)

Performance benchmark for trial activation = 180 days

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# Cancer Center Process Improvement

***Recommendation 5: Center-specific Action Plan to achieve OEWG target timeline***

*Implementation Plan*

- **Potential Action Plan Elements**
  - Specialist medical writers
  - Direct coordinated interactions to resolve differences
  - Project management /protocol tracking tool
- **Center-Specific Timeline Targets**
  - OEWG target modified to reflect specific Cancer Center environment
  - Targets analyzed for reasonableness by Cancer Center Directors/NCI
  - Timeline data reported annually against target
  - Centers performing below expectations report annually on actions taken
- **Funding Sources**
  - Explicitly allow use of CCSG funds for protocol development
  - Provide supplemental funds to implement Action Plan

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# Cancer Center Process Improvement

***Recommendation 6: Streamline university contracting and financial review processes***

*Implementation Plan*

- **System level**
  - Educate universities on NCI Standardized Clauses for Clinical Trial Agreements
  - Develop standardized clauses for other types of agreements
  - Collaborate with CTSA program to streamline processes
- **Institution level activities**
  - Educate stakeholders on NCI Standardized Clauses for Clinical Trial Agreements
  - Establish master agreements with individual companies
  - Consider use of non-federal funds for university legal/contracting staff devoted to Cancer Center trials
  - Direct interactions among Center/university/hospital staff to resolve issues

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# Operational Efficiency Working Group

- **IDB Early Drug Development**
  **Phase II Trials**
  - Current State
  - Proposed OEWG Timeline
  - Recommended Process Improvements

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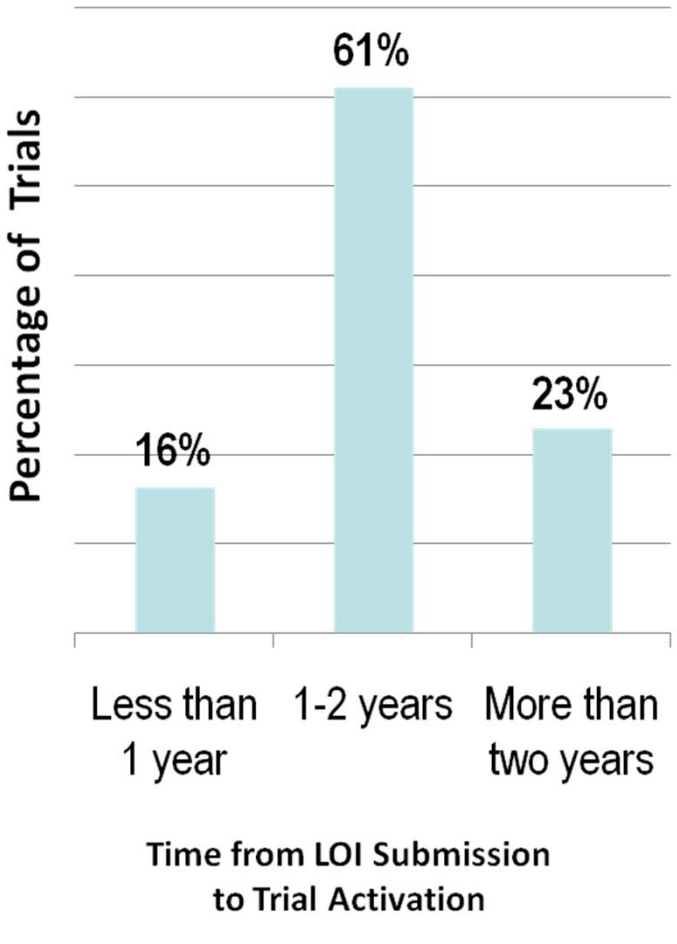
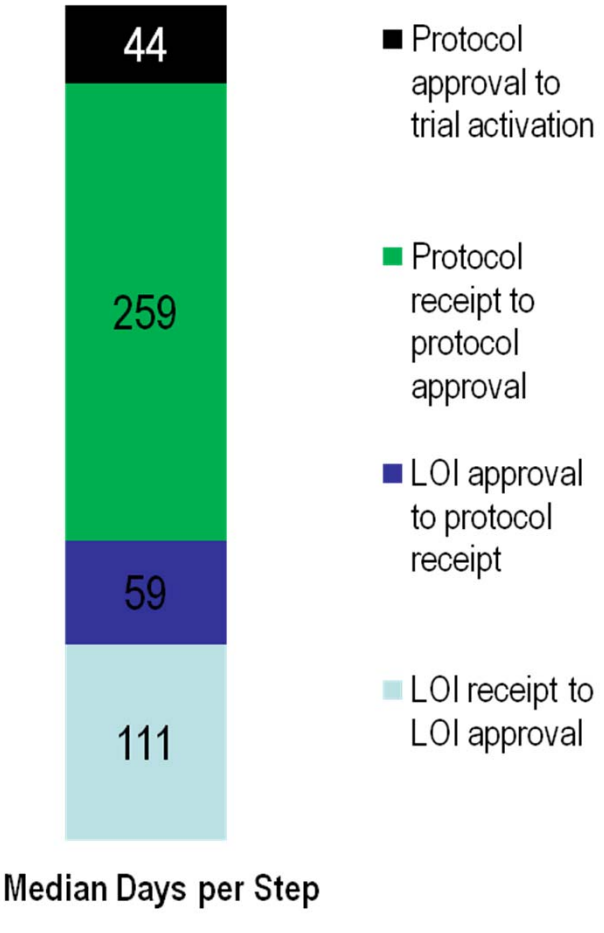
# Time to Activation - Current State
## (2006 – 2008, N01 & Cooperative Groups)



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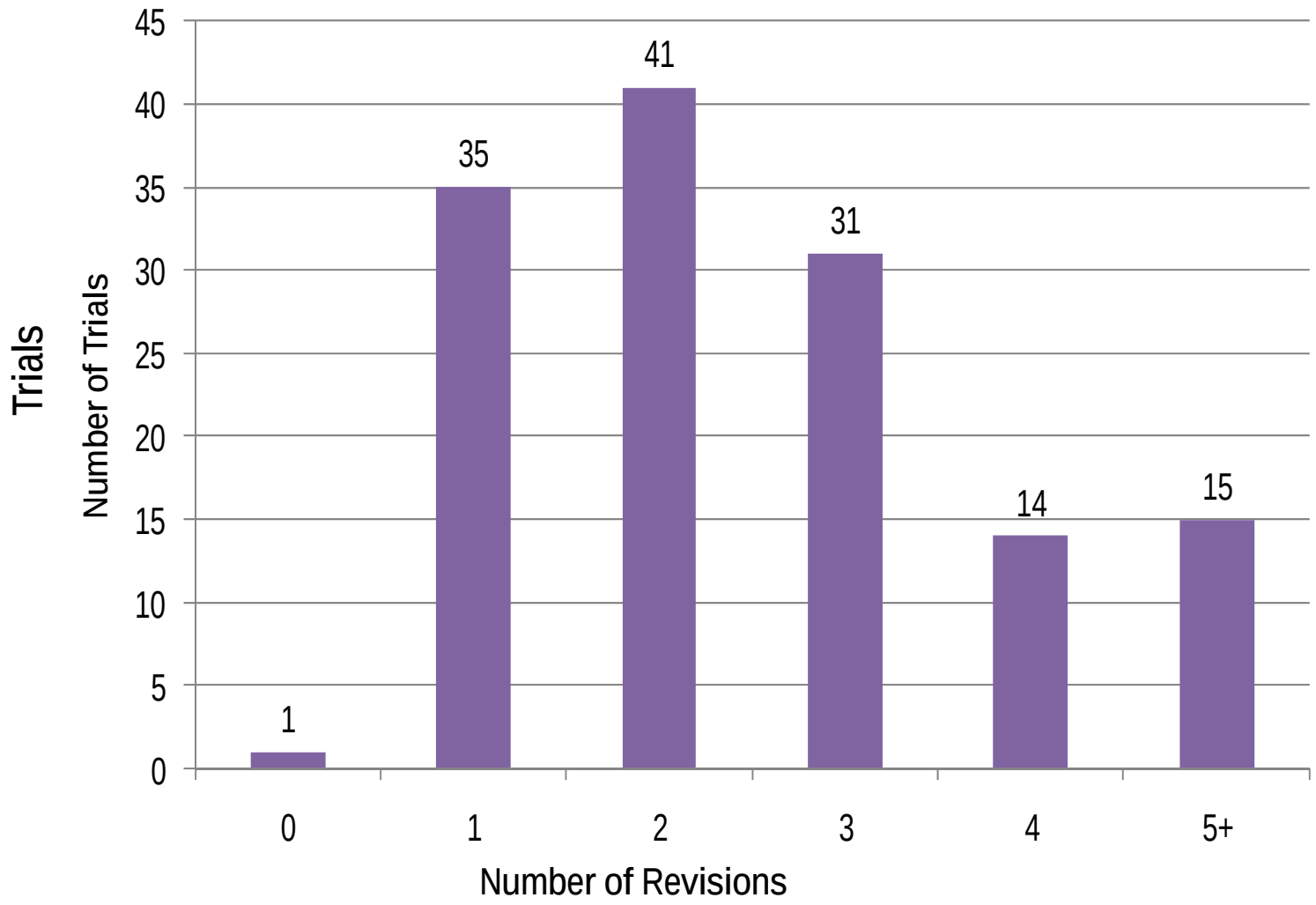
# Review/Revision of Protocols



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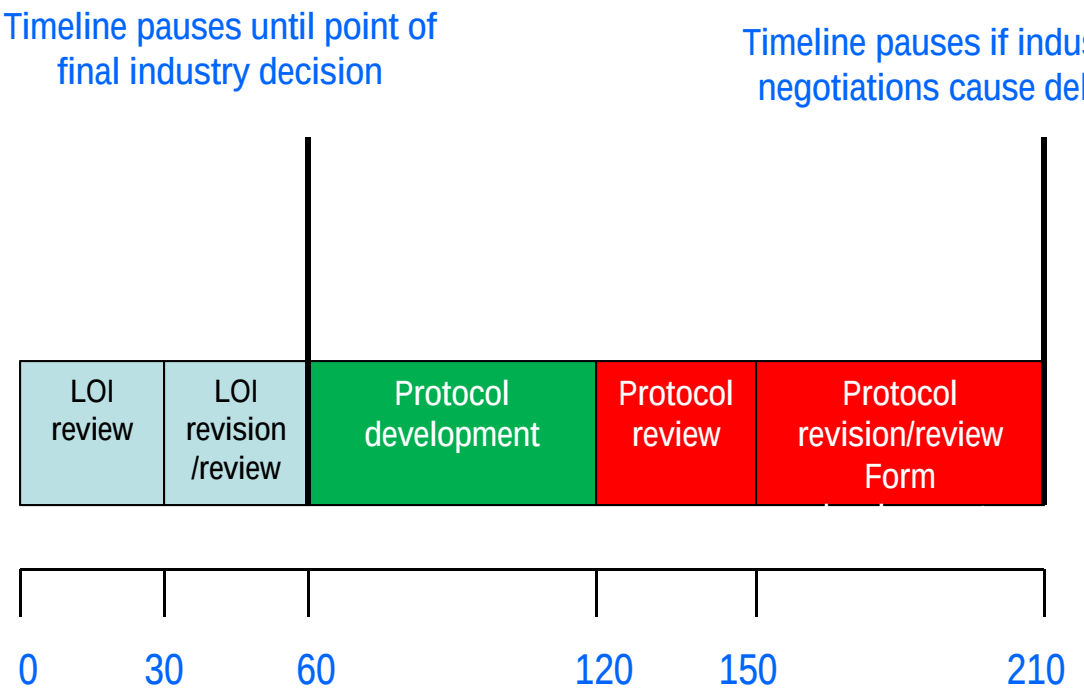
# Proposed OEWG Timeline – 210 days




(Timeline excludes contracting, drug supply, IRB, FDA)

Protocol terminated if not activated in 18 months

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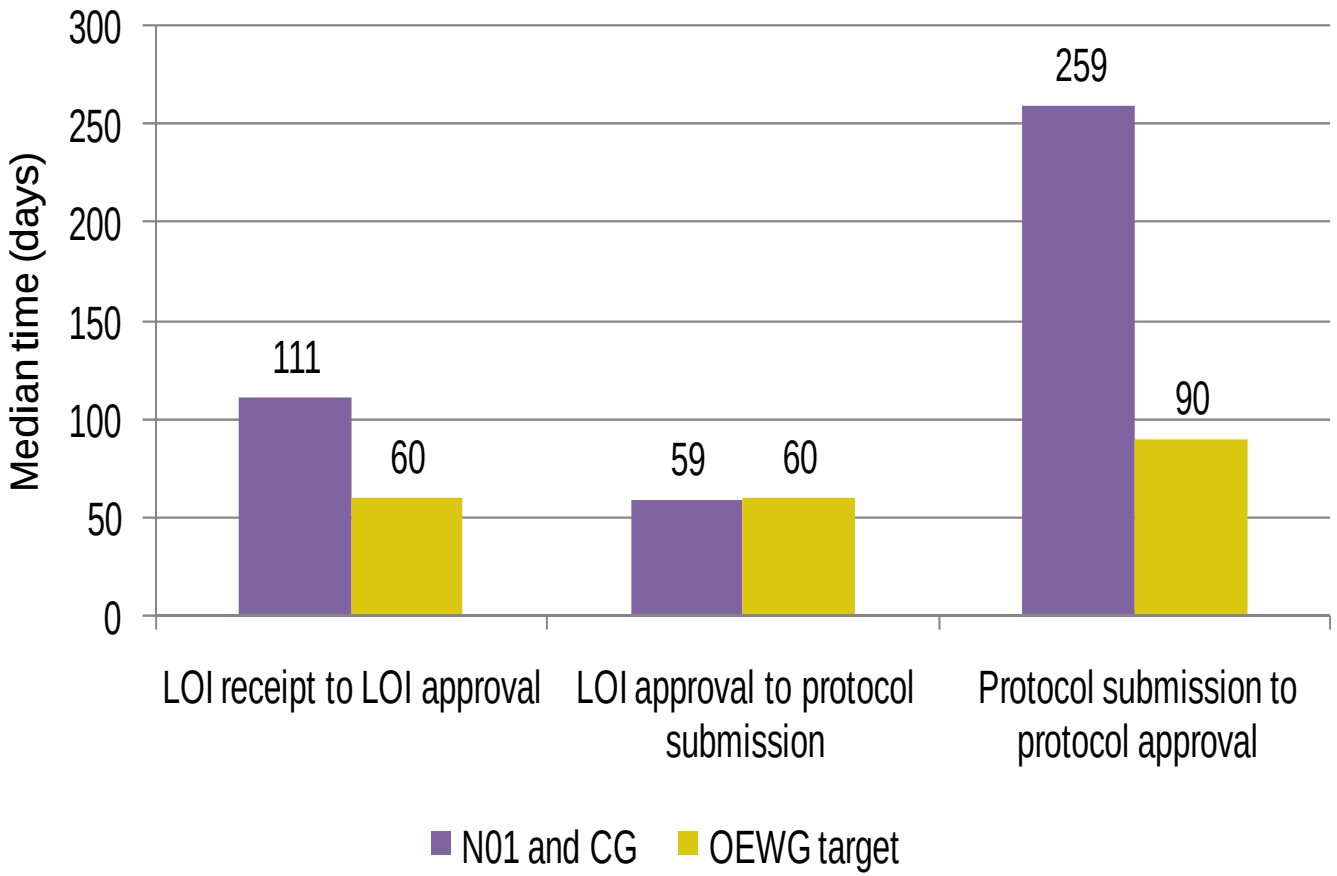
# Time to Trial Activation… Current vs OEWG Target




*Current median time includes IRB approval and industry negotiations*

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# Early Drug Development Phase II Trial Activation Process Improvement

***Recommendation 7: CTEP Action Plan to achieve OEWG target timeline***

*Implementation Plan*

- Project managers
  - Manage overall protocol review, revision and approval process
  - Facilitate interactions between CTEP, PIs, and industry
- Teleconferences to resolve issues for “on hold” LOIs
- Prompt communication of disapprovals in advance of review letter
- Streamlined methods for communicating comments
- Distinguish advisory comments from those requiring response
- Project management/protocol tracking tool

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# Early Drug Development Phase II Trial Activation Process Improvement

***Recommendation 8: Collaborative Group/N01/CTEP process for LOI and protocol revision***

*Implementation Plan*

- Direct, coordinated interactions to resolve issues
- High priority on devoting time to issue resolution
- Fundamental aspects of study design resolved at LOI stage
- Interactions at protocol stage focused on mechanics of completing a protocol embodying an agreed LOI
  - Prompt communication and resolution of major differences
  - Minimal time spent discussing non-critical differences of opinion
  - Minimization of time and effort for routine or pro forma revisions
- Rapid arbitration for any issues not resolved quickly

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# Process Improvements Applicable Across Trial Categories

- Standardization of Tools and Templates
- Cancer Center Trial Prioritization
- Enhanced Biomarker Funding and Capabilities

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# Standardization of Tools and Templates

***Goal: Facilitate rapid assembly of protocols***

***Recommendation 9: Form working group involving NCI, Group and Center staff to coordinate standardization efforts***

*Implementation Plan*

- Compile inventory of protocol templates, data elements, case report form modules, etc. from Groups and Centers and NCI
- Analyze inventory to identify current standards, best-in-class products, redundant development efforts and unmet needs
- Analyze status and output of existing standardization efforts
- Identify tools and templates where standardization is mandatory and those where recommended or optional
- Identify needed standards for interoperability
- Develop a coordinated process for implementing standards

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# Cancer Center Trial Prioritization

***Goal: Optimize use of resources by reducing the number of protocols in development***

***Recommendation 10: Perform rigorous review of clinical trial concepts in advance of protocol development***

*Implementation Plan*

- Concept review process specified in CCSG guidelines
  - Approval/disapproval by disease group or Center-wide
  - Uniformity of reviews across diseases
  - Content of a concept document
  - Criteria by which concepts are reviewed
- NCI should not mandate the specific process or criteria
- Applicable to all trials – investigator-initiated, Cooperative Group and N01

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# Enhanced Biomarker Funding & Capabilities

***Goal: Facilitate rapid activation of trials involving critical biomarker studies***

***Recommendation 11: Enhance funding and capabilities for use of biomarkers in NCI-funded clinical trials***

*Implementation Plan*

- Expand the Biomarker, Imaging and Quality of Life Studies Funding Program (BIQSFP) to large randomized Phase II trials
- Create program to fund biomarker studies for early-phase trials
- Require clinical trial concepts/LOIs to describe proposed integral or integrated biomarker studies
- Provide funding for development, validation, and conduct of clinical grade assays
- Develop standards for qualifying sites to conduct imaging studies associated with clinical trials

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# Process Improvements to Enhance Overall Clinical Trials Program

- Robust OEWG discussion of several improvements in the NCI clinical trials program not directly linked to activation time
  - Cancer Center Participation in Cooperative Group Trials
  - Cancer Center Clinical Trials Strategic Review
  - Clinical Research Mentorship and Training
- Developed recommendations and implementation plans for improvements in each of these areas

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# Process Improvements to Enhance Overall Clinical Trials Program

- **Enhance Cancer Center Participation in Cooperative Group Trials**
  - Cooperative Group leadership and accrual scored CCSG review criteria
  - NCI officially recognizes investigators for leadership in the design and conduct of Cooperative Group trials
  - Enhance the stability and size of accrual funding
  - Create incentives for institutions to include Cooperative Group accrual as a “service” criterion for tenure and promotion
- **Cancer Center Clinical Trials Strategic Review**
  - Requirement for Comprehensive Cancer Centers
  - Allocate clinical trial resources based on scientific/clinical advances, basic/translational/clinical research strengths and patient population
- **Enhance Clinical Research Mentorship and Training**
  - Flexibility in use of CCSG funds for mentorship and training
  - Clinical research training required for Comprehensive Cancer Centers
  - Create new training awards, programs and tools

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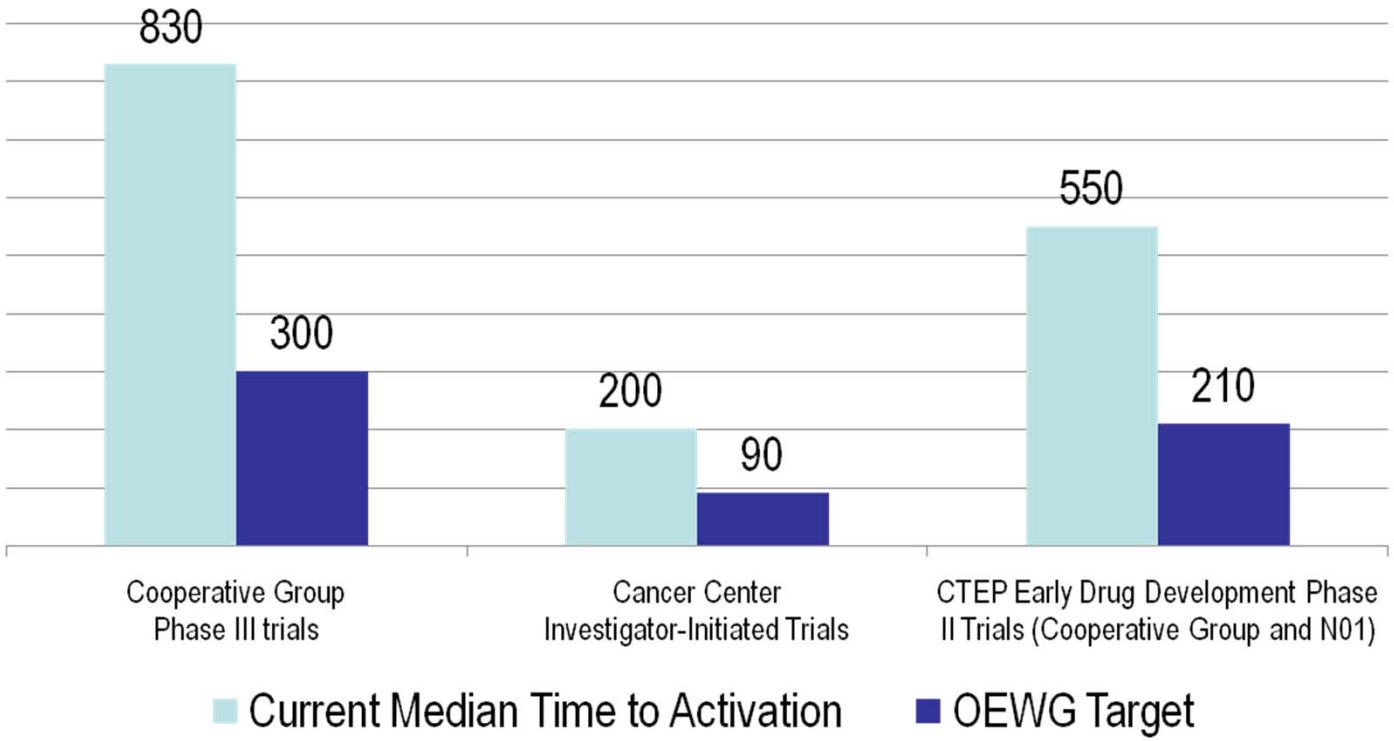
# Goal is aggressive but necessary…




*(Current median time includes IRB approval, industry negotiations, and FDA approval)*

Commitment will result in significant progress but success will not be fully achieved without incremental funding

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# OEWG ARRA Funding and Beyond

- **ARRA administrative supplements**
  - Develop Cooperative Group, Cancer Center, NCI Action Plans
  - Dedicated protocol development staff (protocol writers, trial development managers, etc)
  - Acquisition and deployment of project management/protocol tracking software tools
- **Long Term**
  - Economic incentives for Cooperative Groups and Cancer Centers to meet the new timelines
- **Ultimate Vision**
  - A coordinated, collaborative, interactive process for timely development, review, revision, and approval of all NCI-supported clinical trials
  - Commitment will result in significant progress but success will not be achieved without devoted incremental funding

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# OEWG Next Steps

- Prepare Phase I OEWG Final Report
- Launch OEWG Phase II addressing rate of accrual and time to trial completion

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# Appreciation

**Thanks to:**

- **OEWG members**
- **NCI professional staff**
- **Science Technology Policy Institute: Judy Hautala, Oren Grad, Brian Zuckerman**

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# Questions for NCAB Discussion…

- Will the recommendations results in fewer trials, but with higher priority?
- Will the timelines be embraced by the drug companies and are they sufficiently aggressive?
- How could NCI best facilitate the development and/or expansion of academic incentives to participate in the development and conduct of multi-site trials?
- Will the changes result in improved accrual?