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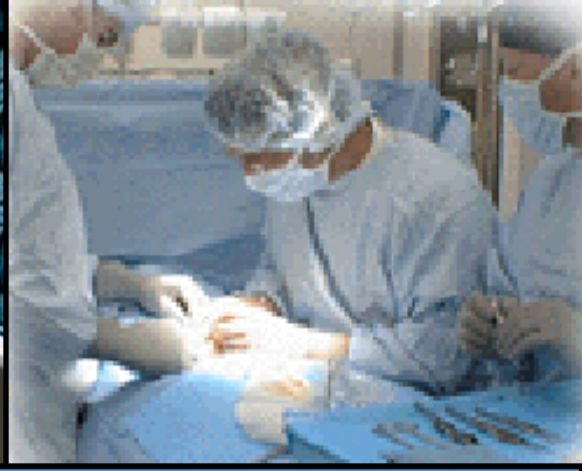

Impact of the Implementation of the Operational Efficiency Working Group (OEWG) Report on the Clinical Trials System

NCAB Meeting

February 8, 2013

Jeff Abrams, MD

Acting Director for Clinical Research

Division of Cancer Treatment and Diagnosis

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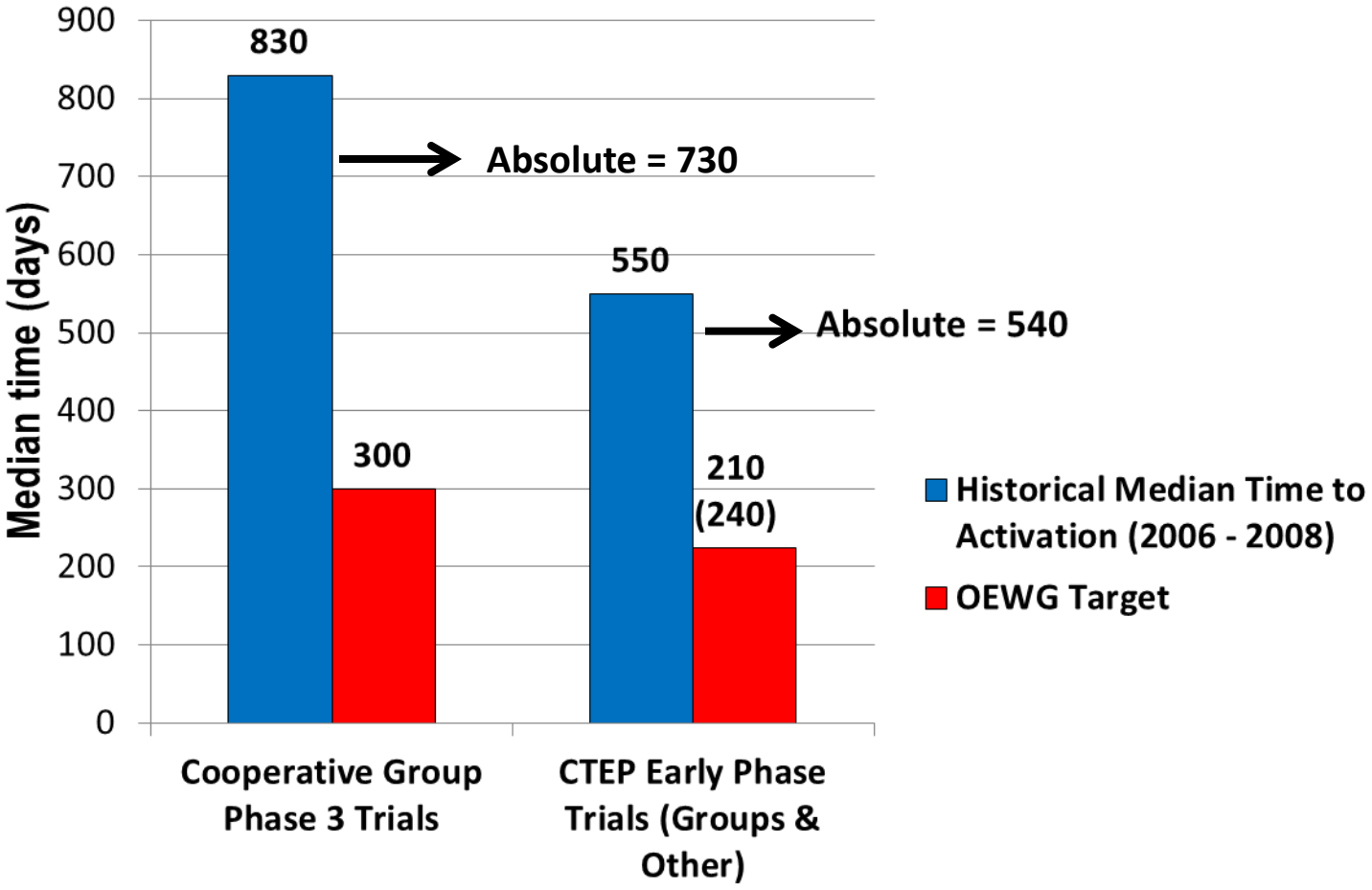
Operational Efficiency Working Group

Overview of Recommendations & Implementation

- New process to develop trials in interactive & collaborative fashion
- Timelines for target and absolute timelines for trial development (review of proposal to activation)
- Developed implementation plans to achieve targets
  - **As of Apr 2010:** All treatment trials monitored per new timelines
  - **As of Jan 2011:** All trials that do not achieve "absolute" deadlines do not go forward

Historical *vs* OEWG
Target & Absolute Timelines



Protocol terminated if absolute timelines not achieved

Revision of Timelines in April 2012

- **New Absolute Deadlines Based on Initial Assessment of Improvement in Timelines**
  - Decrease for Early Phase Studies (including larger Phase 2 Concepts) from 540 to 450 days
  - Decrease for Phase 3 Studies from 730 to 540 days
  - Implementation in April 2012

- **Institution of 6 Month Deadline for CTEP Cooperative Research & Development (CRADA) Agreements**

Update on Implementation

- **In March 2010, the OEWG provided recommendations to the NCI on strategies to decrease the time required to activate NCI-sponsored clinical trials**

- **A major component of the recommendations was the creation of target timelines and absolute deadlines for studies to go from Concept/LOI submission to activation (activation defined as study open to patient enrollment) with revision of absolute deadlines in April 2012**

  - **Phase 1 and 2 Studies:**
    - **Target Timeline – 210 days (7 months)**
    - **Absolute Deadline – ~~540 days~~ Now 450 days (15 months)**

  - **Phase 3 Studies:**
    - **Target Timeline – 300 days (10 months)**
    - **Absolute Deadline – ~~730 days~~ Now 540 days (18 months)**

NCI/DCTD/CTEP Response

- Project Managers were hired to closely track study timelines
- Secure website developed to allow investigators, operations staff, and NCI staff to monitor timelines
- Routine conference calls between NCI reviewers and external investigators instituted at key points in the review process to quickly resolve issues and decrease the need for multiple document revisions
- Medical Editors were hired with responsibilities including compiling and editing Consensus Reviews and inserting applicable revisions directly into an unofficial copy of the Protocol using Track Changes®, thus saving investigators valuable time

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OEWG Conference Call Process

- **Calls between study team & NCI to clarify/discuss Consensus Review to prevent review iterations that may slow the approval process**
- **Conference calls occur at several key points:**
  - **LOI's: on-hold, approved pending drug company review, or approved**
  - **Concepts: pending response to Steering Cmte evaluation or approved**
  - **Protocols: pending response to Consensus Review**
  - **Ad Hoc: as special issues arise during study development**
- **Approximately 686 conference calls between April 2010 – Sept 2012:**
  - **247 calls for LOI's**
  - **156 calls for Concepts**
  - **262 calls for Protocols**

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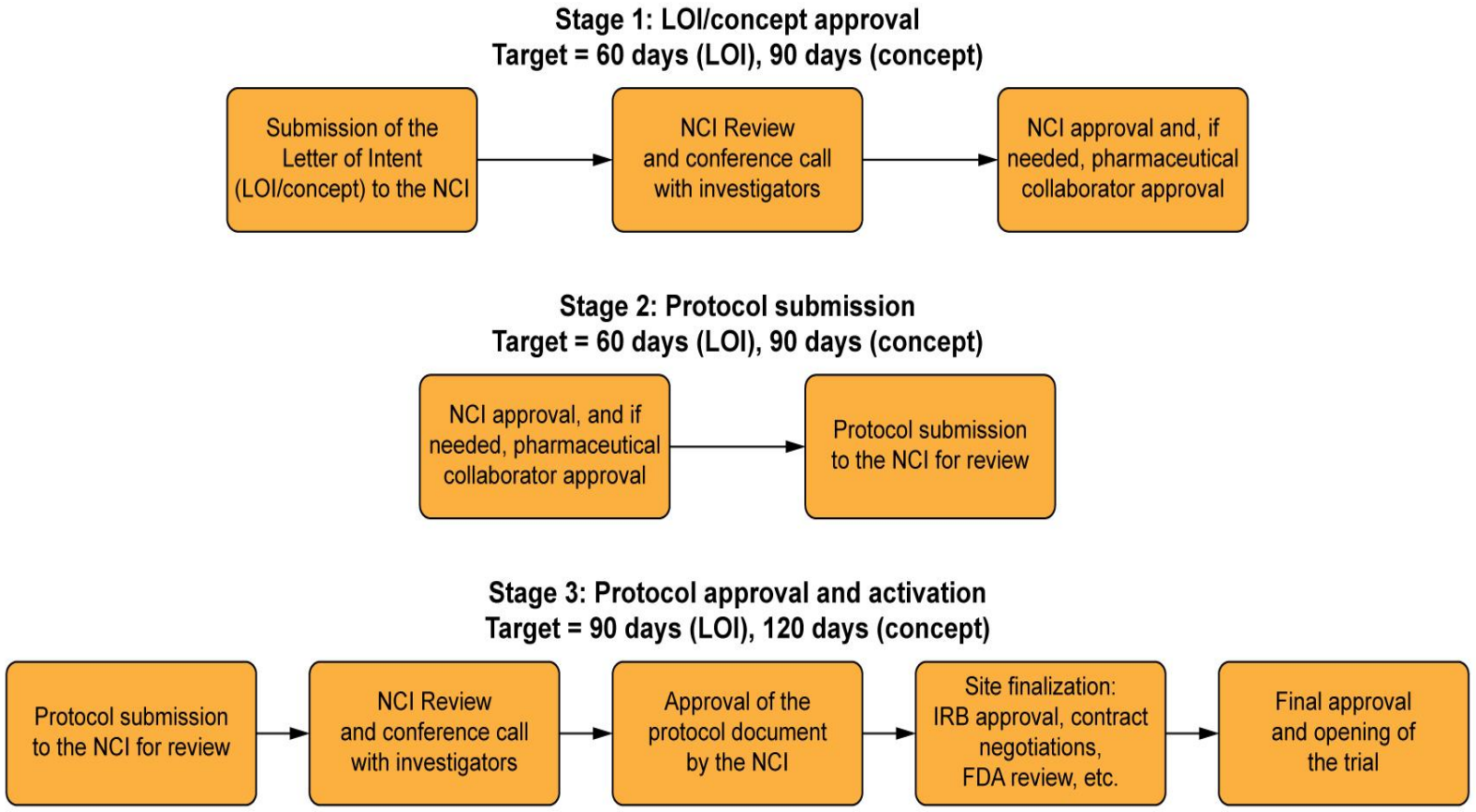
Stages of LOI/Concept Review & Protocol Development



Target for opening trial to entrollment is 210 (LOI)/300 (concept) days

Absolute deadline for opening trial to enrollment is 540 (LOI)/730 (concept) days

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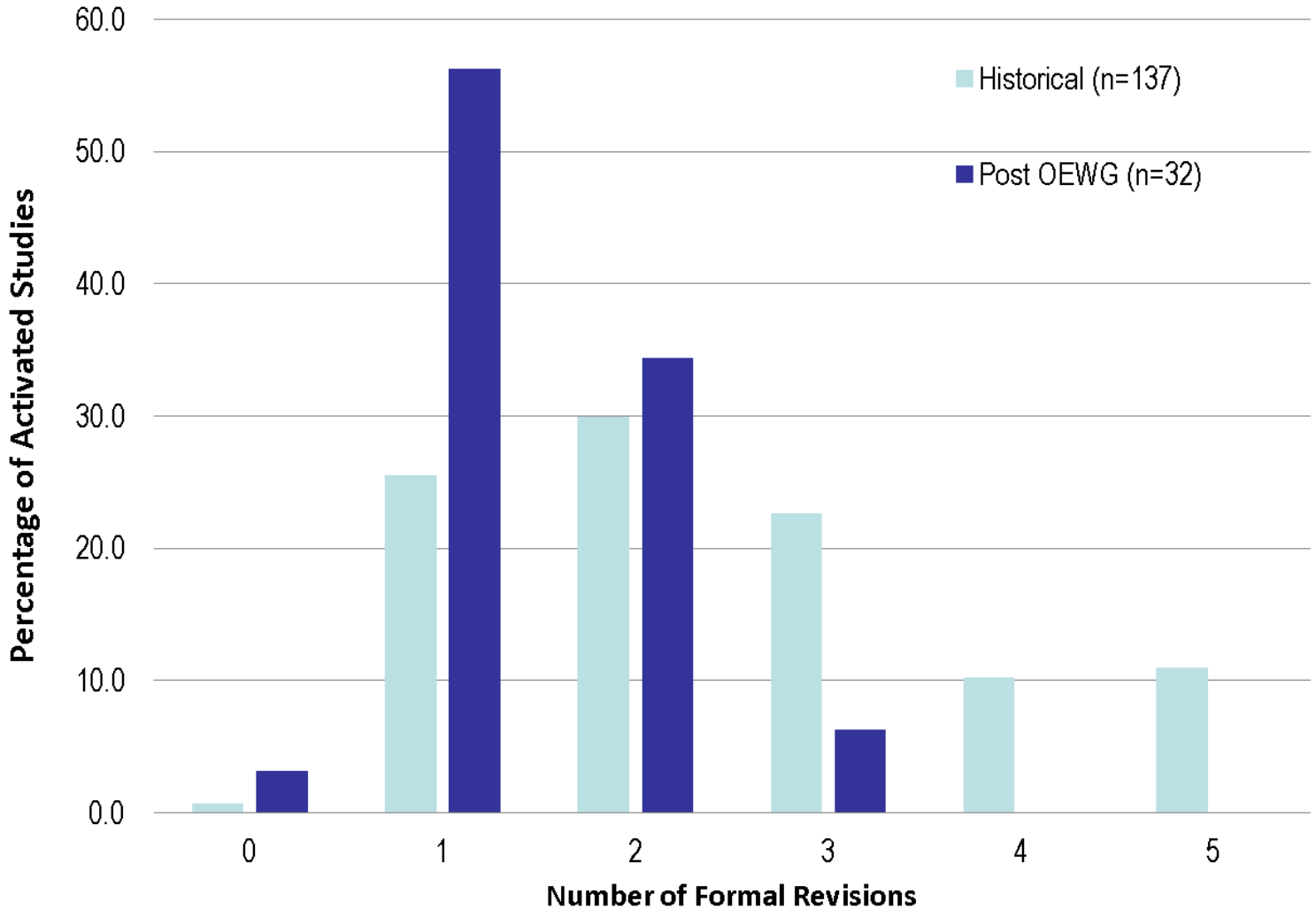
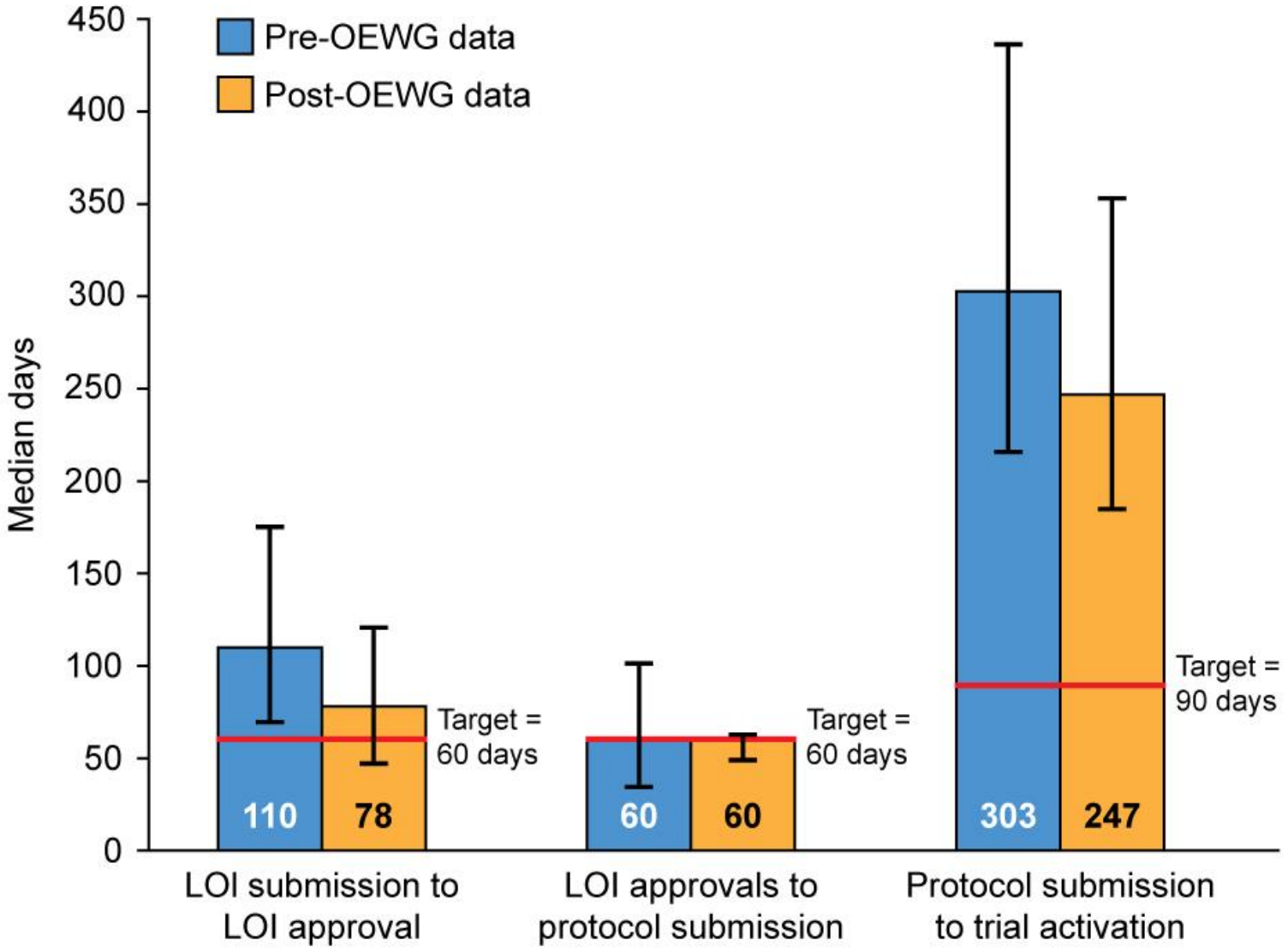
Comparison of Number of Protocol Revisions Prior to Activation

Post OEWG Group Studies (All Phases) vs Historical Studies
As of December 2011



Breakdown of the study development stages

Early Phase Studies



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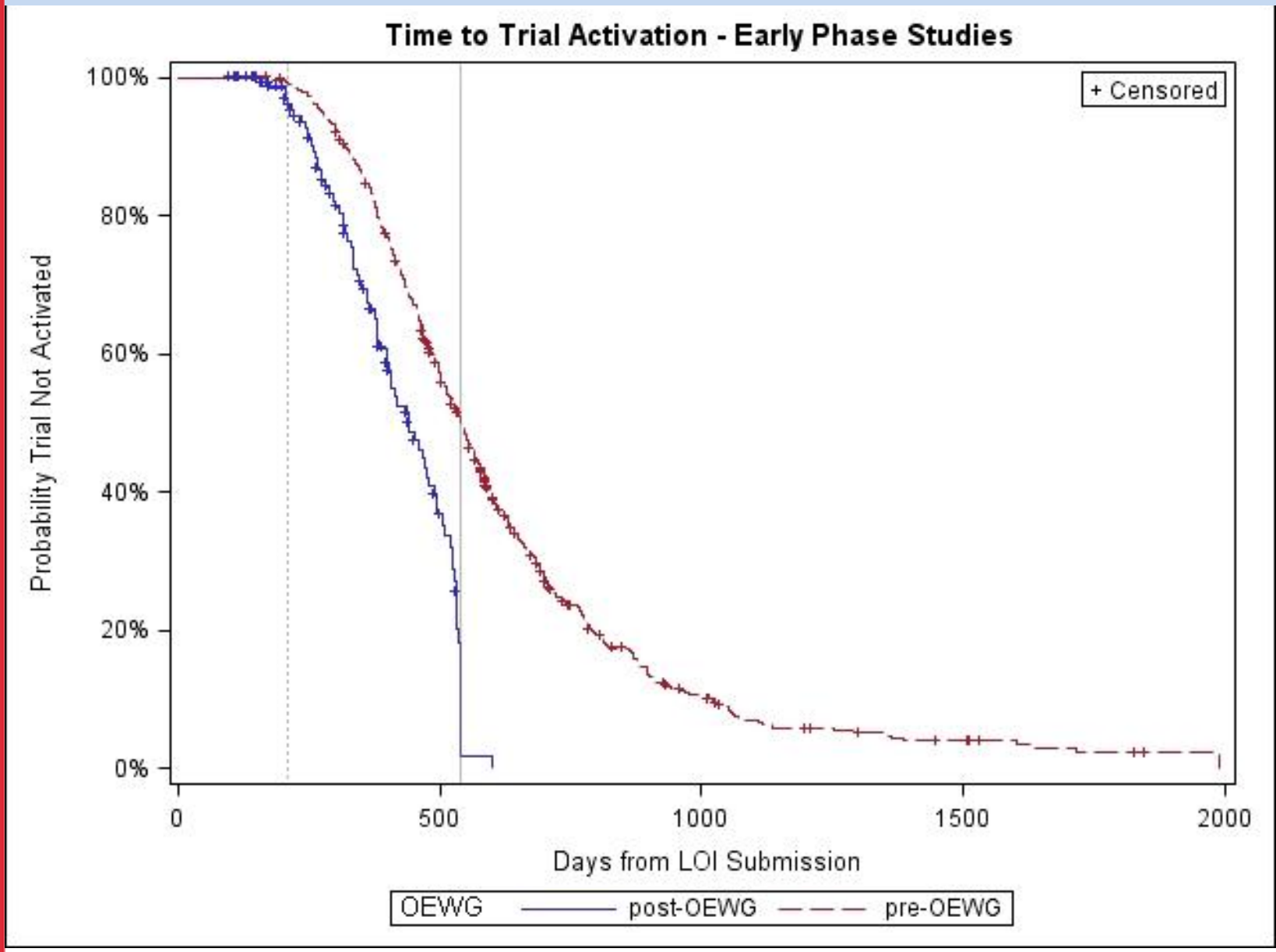
Timeline Comparison of Study Activation-Early Phase Trials: Historical vs. Post-OEWG (Apr 2010 – Aug 2012)



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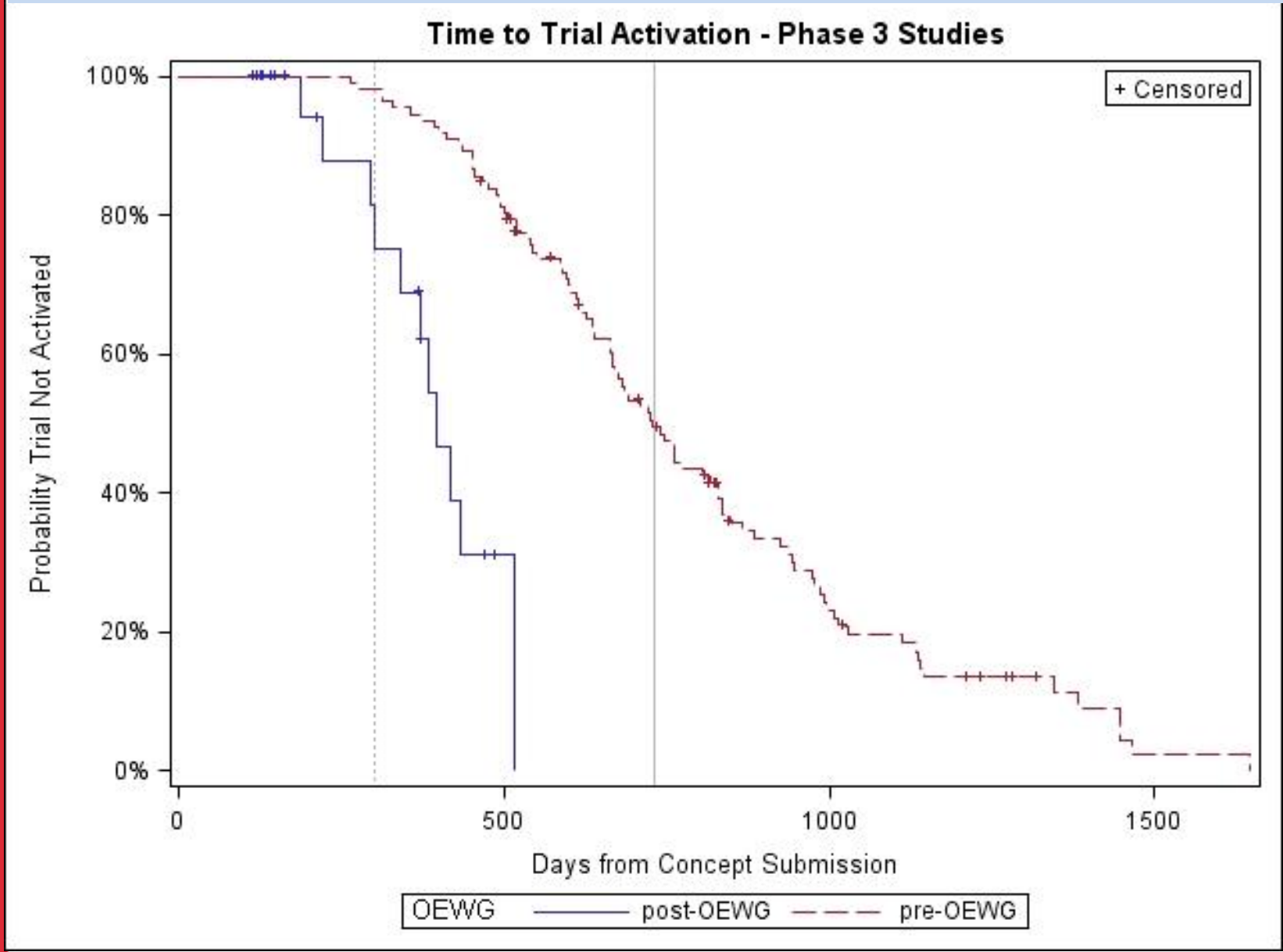
Timeline Comparison of Study Activation for Phase 3 Trials: Historical vs. Post-OEWG (Apr 2010 – Aug 2012)



Comprehensive Changes Undertaken to Improve Trial Initiation Timelines

	Change	Implementation
Target Timeline	**An ideal goal, achievable if all partners function optimally**	**7 months for phase 1-2 trials and 10 months for phase 3 trials**
Absolute Deadline	**An immoveable date by which the trial must be open to patient enrollment**	**18 months for phase 1-2 trials and 24 months for phase 3 trials***
Staffing Additions	**New positions created to manage protocol timelines and to assist physicians with protocol authorship, revisions, and editing**	
Process Improvement	**Implementation of uniform templates for protocol development and for reviewers' comments**	**Requirement for prompt teleconferences to resolve scientific and regulatory review issues at each step of review**
Information Technology	**Creation of a website to track all phases of protocol's life cycle**	

*The absolute timelines were revised in April 2012 to be more stringent – 15 months for phase 1-2 trials and 18 months for phase 3