Facilitating Human Subject’s Research: NCI CIRB Initiative Open Forum

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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 Group 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
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
Stages of LOI/Concept Review & Protocol Development

Stage 1: LOI/concept approval
Target = 60 days (LOI), 90 days (concept)
- Submission of the Letter of Intent (LOI/concept) to the NCI
- NCI Review and conference call with investigators
- NCI approval and, if needed, pharmaceutical collaborator approval

Stage 2: Protocol submission
Target = 60 days (LOI), 90 days (concept)
- NCI approval, and if needed, pharmaceutical collaborator approval
- Protocol submission to the NCI for review

Stage 3: Protocol approval and activation
Target = 90 days (LOI), 120 days (concept)
- Protocol submission to the NCI for review
- NCI Review and conference call with investigators
- Approval of the protocol document by the NCI
- Site finalization: IRB approval, contract negotiations, FDA review, etc.
- Final approval and opening of the trial

Target for opening trial to enrollment is 210 (LOI)/300 (concept) days
Absolute deadline for opening trial to enrollment is 540 (LOI)/730 (concept) days
Comparison of Number of Protocol Revisions Prior to Activation

*Post OEWG Group Studies (All Phases) vs Historical Studies*

*As of December 2011*

- **Historical (n=137)**
- **Post OEWG (n=32)**
Breakdown of the study development stages

**Early Phase Studies**

- **LOI submission to LOI approval**: Pre-OEWG data = 110 days, Post-OEWG data = 78 days. Target = 60 days.
- **LOI approvals to protocol submission**: Pre-OEWG data = 60 days, Post-OEWG data = 60 days. Target = 60 days.
- **Protocol submission to trial activation**: Pre-OEWG data = 303 days, Post-OEWG data = 247 days. Target = 90 days.
Timeline Comparison of Study Activation - Early Phase Trials: Historical vs. Post-OEWG (Apr 2010 – Aug 2012)
Timeline Comparison of Study Activation for **Phase 3 Trials**:
Historical vs. Post-OEWG (Apr 2010 – Aug 2012)