NIH Clinical Trial Stewardship to Enhance Quality, Rigor and Transparency

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Society of Behavioral Medicine March 31, 2016
Introspection
NIH Clinical Trials

NIH FY 2013 Budget ($29.15 billion)

$26.0 B

$3.15 B (12%)

Clinical Trials
2010 IOM Report

• 2012 NIH Surveyed IC to review of the applicability of the 12 recommendations.

• 2013 NIH convened Clinical Trial Working Group
### 2013 NIH CTWG Recommendations

**Table 2: National Institutes of Health (NIH) Clinical Trials Working Group Recommendations to Enhance NIH's Stewardship of Clinical Trials**

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<th>Clinical Trials Working Group recommendation</th>
<th>Description of recommendation</th>
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| 1. Improve application, acceptance, and award processes for clinical trials | • Institutes and Centers (IC) should establish and apply research priorities when reviewing and awarding clinical trial applications.  
• ICs could use alternative award mechanisms to manage trial cost and risk.  
• Applications should be submitted under trial-specific funding announcements which could enhance tracking and analysis across NIH.  
• Criteria for applications should be redesigned to more adequately assess the scientific merit and potential of applications. |
| 2. Improve peer review and Advisory Council review | • Peer review should be strengthened to include individuals such as biostatisticians.  
• Advisory Council recommendations should be more directly aligned with the Institute’s scientific priorities.  
• Inclusion of a DDLL review of NIH grant applications should be expanded. |
| 3. Incorporate trial-specific language into Notice of Award | • ICs should be strongly encouraged to include specific language in their Notice of Awards, such as data sharing and intellectual property.  
• The template Notice of Award should be revised to include more specific language related to the conduct of clinical trials. |
| 4. Improve monitoring systems, tools, and processes | • ICs need to develop monitoring systems that measure whether the conduct of the clinical trial adheres to the protocol.  
• Definitions of core elements should be consistent across ICs and reviewed on an annual basis.  
• Data collection should be conducted in a way that is consistent with the protocol. |
| 5. Train and empower program officers | • Program officers need appropriate training in order to properly evaluate clinical trial progress.  
• Program officers should also have enough administrative authority to implement and enforce warranted action. |
• Develop standard language for ICs to use when mandating the use of a single Institutional Review Board.  
• Create and post a toolbox with information on establishing agreements between research institutions. |
| 7. Disseminate clinical trial results | • Dissemination of results should be a requirement for successful completion of clinical trial funding.  
• Expand the range of NIH’s ClinicalTrials.gov website to include clinical trial results.  
• As a term of award, require publication by some specific deadline.  
• Withhold funding on applications from the grantee institution until sharing requirement is met. |
| 8. Good Clinical Practice training for investigators and staff | • All personnel involved in clinical trials should receive documented Good Clinical Practice training.  
• Refresher courses should be completed every three years. |
2014 Enhancing Reproducibility

Policy: NIH plans to enhance reproducibility

Francis S. Collins & Lawrence A. Tabak

27 January 2014

Francis S. Collins and Lawrence A. Tabak discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.

Journals unite for reproducibility

Consensus on reporting principles aims to improve quality control in biomedical research and encourage public trust in science.
NIH’s Ongoing Efforts to Enhance Clinical Trials
A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.
Public Benefits of Clinical Trial Data Sharing

• Inform future research and research funding decisions
• Mitigate bias (e.g., non publication of results, especially negative results)
• Prevent duplication of unsafe trials
• Meet ethical obligation to human subjects (i.e., that results inform science)
• Increase access to data about marketed products

All contribute to public trust in clinical research
Yet...Poor Publication Rates of Clinical Trial Results
Clinical Trial Information & Transparency
Multi-site IRB Review: Need for a Better Way
Streamlining IRB Review


Notice Number: NOT-OD-15-026

Key Dates
- Release Date: December 3, 2014
- Response Date: January 29, 2015
What We Heard

- 70% Supporting Comments
  - Researchers, Research Associations, Patient Advocates

- 30% Opposing Comments
  - IRBs/IRB members, Tribal Representatives, Research Organizations

What They Said

- Separate IRB reviews increase administrative burden and time it takes to get a study launched
- sIRB will encourage:
  - more consistent adherence to protocols;
  - use of standardized protocols, resulting in more rigorous/valid study results;
- Multiple IRB is review is duplicative
- Local IRBs focus on risk and liability (i.e., institutional interests) more than participant protections
- Changes required by local IRB changes are often trivial, they do not change nature or risk/benefit ratio of study, are often focused on the informed consent language
Streamlined IRB Review Implementation at NCATS

For Investigators

What is it?
The NCATS IRB-rely initiative aims to create a national cross-CTSA IRB reliance model for multi-center clinical trials in order to reduce duplication of effort and process inefficiency while maintaining strong human subjects protections in the initiation and oversight of human research.

How does it work?
For any IRB-rely Network multi-site human research study, the Overall PI will identify participating network sites and work with site Points of Contact (POCs) to establish the Reviewing IRB and Relying Sites.

Additional detail on these processes is available in the IRB-rely SOPs on “Establishing Reviewing IRBs and Relying Sites” and “Initial Review Submission and Review Process.” For a complete listing of all available IRB-rely SOPs, see the Resources page.
Moving from Compliance to Competency: A Harmonized Core Competency Framework for the Clinical Research Professional

PEER REVIEWED | Stephen A. Sonstein, PhD | Jonathan Seltzer, MD, MBA, MA, FACC | Rebecca Li, PhD | Honorio Silva, MD | Carolynn Thomas Jones, DNP, MSPH, RN | Esther Daemen, BSN, PG, PMP, MBA

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Clinical Trial Protocol Template

NIH and FDA Request for Public Comment on Draft Clinical Trial Protocol Template for Phase 2 and 3 IND/IDE Studies

Notice Number: NOT-OD-16-043

Key Dates
- Release Date: March 17, 2016
- Response Date: April 17, 2016

Clinical Research Policy

Clinical Trials

Clinical Trial Protocol Template Documents
- Guide Notice for Clinical Trial Protocol Template for Phase 2 and 3 IND/IDE Studies
- Comment Form for Clinical Trial Protocol Template
- Protocol Template: Instructional and Sample Text document (pdf)
- Protocol Template Shell (Headers only, no instructional and sample text) (doc)
- OSP "Under the Poliscope" Blog on Protocol Template
- "FDA Voice" Blog on Protocol Template
Other available templates tools

- NCI CTEP Template
- NCCIH Template
- NIAID Templates
- NIDCR Templates
Open Mike

Helping connect you with the NIH perspective, and helping connect us with yours

Posted on January 28, 2016 by Mike Lauer

Scientific Rigor in NIH Grant Applications

In part two of our series on rigor and transparency in research grant and career development award applications, we focus on scientific rigor, the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation, and reporting of results.

Dr. Michael Lauer is NIH’s Deputy Director for Extramural Research, serving as the principal
Consolidated List of Reviewer Documents – In Alphabetical Order

Review Criteria Information

- Additional Comments to Applicant Box PDF - 161 KB (12/18/2015)
- Applications Proposing Use of Human Embryonic Stem Cells PDF - 123 KB (03/21/2016) NEW
- Budget and Period of Support Information PDF - 284 KB (03/05/2012)
- Frequently Asked Questions for Reviewers on NIH Application Submission PDF - 32 KB (03/18/2015)
- Guidelines for the Review of the Human Subjects Section PDF - 182 KB (03/21/2016) NEW
- Guidelines for the Review of Inclusion PDF - 153 KB (03/21/2016) NEW
- Overall Impact vs Significance PDF - 138 KB (03/21/2016) NEW
- Resource Sharing Plans PDF - 73 KB (03/18/2015)
- Review Criteria at a Glance – Master PDF - 110 KB (03/21/2016) NEW
- Review Criteria at a Glance – Research PDF - 67 KB (03/21/2016) NEW

https://grants.nih.gov/grants/peer/reviewer_guidelines.htm
Guidelines for the Review of the Human Subjects Section

Requirements and Responsibilities

As required by federal regulations (45 C.F.R. 46) and NIH policy, applications that propose to involve human subjects must address:

1. the risk to subjects
2. the adequacy of protections against risk
3. potential benefits of the research to subjects and others
4. the importance of the knowledge to be gained
5. For clinical trials, data and safety monitoring plan and a data and safety monitoring board for Phase III trials.

Applicant Responsibilities: Applications must designate if human subjects are involved, and if so, whether the proposed activities meet the criteria for exemption. Applications that involve human subjects must include a Protection of Human Subjects Section that addresses the points noted above. Applications that are not proposing human subjects research but will use human data or biological specimens, must provide a justification for the claim of no involvement of human subjects.

Scientific Review Group (SRG) Responsibilities: NIH Peer Review regulations (42 C.F.R. 52h) specify that reviewers will take into account the adequacy of the proposed protections for humans in determining overall impact that the research in the application could have on the research field involved. Therefore, the SRGs must factor their evaluation of the proposed plans to protect human subjects from research risks, into their overall evaluation of an application’s scientific and technical merit and overall impact score.
Questions?

Thank you