NIH Clinical Trials Policy and Implementation

Michael S Lauer, MD
Deputy Director for Extramural Research
National Institutes of Health

165th Meeting of the National Advisory Child Health and Human Development Council
September 14, 2017
Building 31, C-Wing, Conference Room 6, NIH Campus, Bethesda, MD
Disclosures: None
“There are many [NIH-funded] trials not covered by [FDAAA], such as trials of behavioral interventions and surgical procedures. No policies exist to make sure that the public has access to results from NIH funded research that is not published”
We Did Not Believe It

“A number of parties share responsibility, including funders, investigators, academic medical centers, [universities], clinical research organizations, and ... journals.”
“Despite the ethical mandate and expressed values of academic institutions, there is poor performance and noticeable variation in the dissemination of clinical trial results across leading academic medical centers.”

BMJ 2016;352:i637
"We have a bottleneck at our nation's bastions of research excellence. Too many times, study results are neither reported on the government website, clinicaltrials.gov, nor published in a journal. The failure to share results is so pervasive that it seems inappropriate to blame individuals. Instead, it is a systemic problem."

http://www.npr.org/sections/health-shots/2016/02/23/467712481/academic-medical-centers-get-an-f-in-sharing-research-results
“Not reporting results violates the basic principle of the scientific method. It hurts patients, society and science. It dishonors the people who gave their consent and bore the risk of participating...

The holding back of the results impedes progress toward scientific breakthroughs, corrupts the medical literature and wastes research funding.”

http://www.npr.org/sections/health-shots/2016/02/23/467712481/academic-medical-centers-get-an-f-in-sharing-research-results
NIH’s OD reviews some data on clinical trial activity across NIH but has not finalized what additional data it needs or established a process for using these data to enhance its stewardship.

NIH is limited in its ability to make data-driven decisions regarding the use of its roughly $3 billion annual investment in clinical trials.”
A Proposed HHS Regulation and NIH Policy to Further the Impact of Clinical Trials Research

Sharing and Reporting the Results of Clinical Trials

The principle of data sharing dates to the dawn of scientific discovery—it is how researchers from different disciplines and countries form collaborations, learn from others, identify new scientific opportunities, and work to turn newly discovered information into shared knowledge and practical advances. When research involves human volunteers who agree to participate to test new drugs, devices, or other interventions, the principle of data sharing properly assumes an ethical mandate. These participants:

Compendium of Public Comments on the Draft NIH Policy on Dissemination of NIH-Funded Clinical Trial Information
November 19, 2014 – March 29, 2015
Now the Policy Exists…

“A fundamental premise of all NIH-funded research is that the results must be disseminated …

In research involving human beings, scientists have an ethical obligation to ensure that the burden and risk that volunteers assume comes to something, at the very least by ensuring that others are aware of the study and that its findings contribute…”
Toward a New Era of Trust and Transparency in Clinical Trials

Clinical trials are the most publicly visible component of the biomedical research enterprise, from the potential human application of novel laboratory findings to the generation of robust evidence about treatments or preventive interventions in routine clinical care. These trials are also the point at which biomedical research most directly engages human participants—dedicated volunteers who trust investigators to uphold the highest standards of scientific rigor and ethical oversight. While clinical trials have evolved and improved over time—producing impressive advances in diagnosis, treatment, and prevention—there are still major challenges. Therefore, fundamental changes are needed to reflect science and society’s movement to increase efficiency, accountability, and transparency in clinical research.

As the largest public funder of clinical trials in the United States, currently investing more than $3 billion annually, the National Institutes of Health (NIH) is uniquely positioned to help ensure that all involved in the clinical trial enterprise have the appropriate knowledge about the design, conduct, monitoring, recording, analysis, and reporting of clinical trials. While GCP training on its own may not be sufficient, it provides a consistent and high-quality standard.

Another important change at the beginning of the clinical trial lifecycle is a new NIH policy that will require all applications for clinical trials to be submitted in response to clinical trial-specific Funding Opportunity Announcements (FOAs). This will mean that applications including one or more clinical trials will no longer be accepted in response to parent funding announcements, which are broad FOAs that allow researchers to submit investigator-initiated applications without specific elements appropriate to describe and evaluate a trial. Under this policy, NIH trial applications will need to consider key elements of research design and conduct that are specific to clinical trials.

NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information

Notice Number: NOT-OD-16-149
Laudable Goal … But …

“We disagree with commenters who suggested that there is no need for coverage of certain types of trials. The benefits of transparency and the need to fulfill the ethical obligation to participants is as relevant to these types of trials as to any other type.

We believe that 12 months represents an appropriate balance between investigators’ interests and the interests of the public in having access to the results of a publicly funded trial.”

Francis S. Collins, M.D., Ph.D.
Director
National Institutes of Health

Enabling Systems (Culture) Change

Clinical Trial Processes

- Idea
- Application
- Application Review
- Funding
- IRB Review
- FDA Review
- Enrollment and Data Collection
- Results

New NIH Reforms & their start dates

- Good Clinical Practice training
  - Jan. 1, 2017
- Clinical trial-specific funding opportunity announcements
- Grant application form changes
  - Due dates on or after Jan. 25, 2018

Single IRB policy
- Jan. 25, 2018

Protocol template
- Available May 2, 2017

Expanded Clinicaltrials.gov registration & results submission policy
- Jan. 18, 2017

Sharing and Reporting the Results of Clinical Trials

Data for Stewardship

Report Results

Register

Additional Data Would Enhance the Stewardship of Clinical Trials across the Agency

NATIONAL INSTITUTES OF HEALTH

United States Government Accountability Office
Report to Congressional Committees

National Institutes of Health
Office of Extramural Research
Clinical Trial Requirements for Grants and Contracts

NIH is launching a series of initiatives that are rolling out in 2017-2018 to enhance the accountability and transparency of clinical research. These initiatives target key points along the whole clinical trial lifecycle from concept to results reporting. Learn more about these changes and how they will affect your research.

NIH Definition of a Clinical Trial

A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other controls) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. Learn more
Requirements for Registering & Reporting NIH-funded Clinical Trials in ClinicalTrials.gov

All NIH-funded clinical trials are expected to register and submit results information to ClinicalTrials.gov, as per the "NIH Policy on Dissemination of NIH-Funded Clinical Trial Information" for competing applications submitted on or after 1/18/2017. This website provides resources for understanding and complying with this NIH policy and the federal regulations in Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) as implemented by 42 CFR Part 11 (Final Rule).

Steps for NIH Applicants & Grantees

This decision tree guides you through specific actions and checkpoints related to the NIH policy and federal regulations on registering and submitting results information to ClinicalTrials.gov.

Policy and Regulations on ClinicalTrials.gov Registration and Reporting

“To realize the benefits of a clinical trial, the data must be broadly shared quickly. The DHHS has released a regulation for registration and summary results reporting. The NIH will withhold clinical trial funding if the agency is unable to verify adequate registration and results reporting…”

JAMA 2016 (online September 16, 2016)
A surprising amount of medical research isn’t made public. That’s dangerous.

When the results of clinical trials aren’t made public, the consequences can be dangerous — and potentially deadly.

UPDATE: The deadline for comments on the Notice of Proposed Rule Making (NPRM) and the NIH policy for clinical trials reporting has been extended to 5:00 p.m. ET on Monday, March 23. For more information, please see the latest Federal Register Notices for the NPRM and for the proposed NIH Policy, which posted on February 19, 2015.
