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

Problems!

BMJ

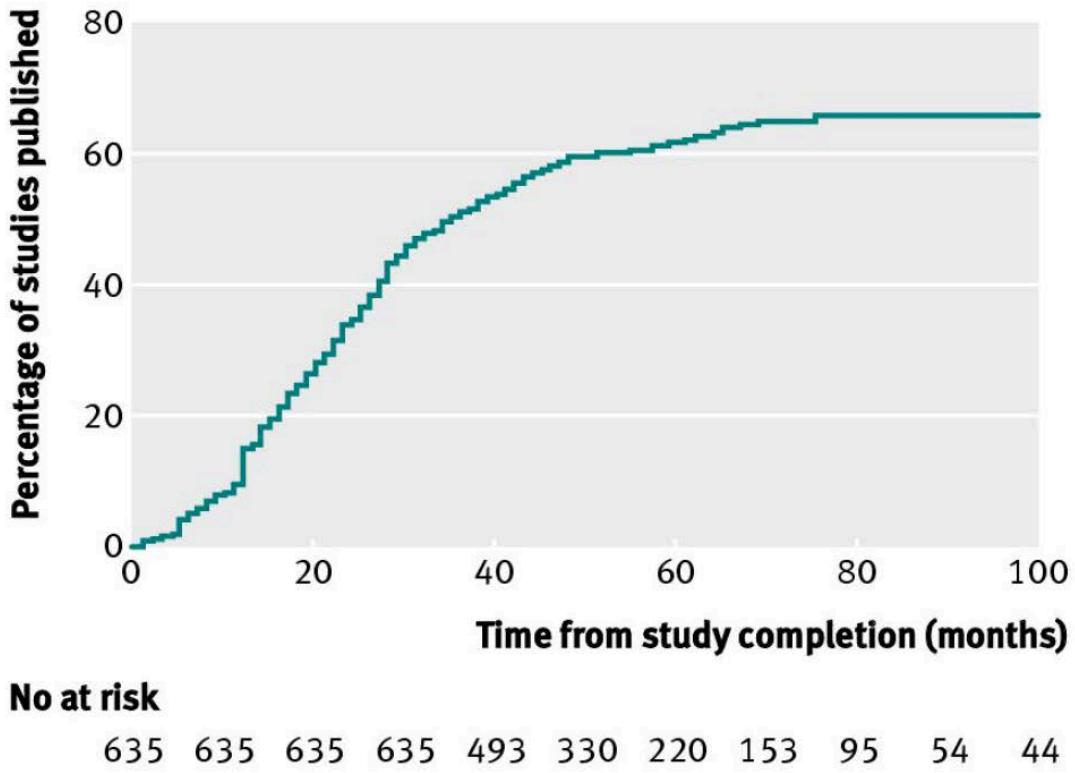
BMJ 2011;344:d7292 doi: 10.1136/bmj.d7292 (Published 3 January 2012)

RESEARCH

Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis

OPEN ACCESS

Joseph S Ross *assistant professor of medicine*[1 2], Tony Tse *program analyst at ClinicalTrials.gov*[3], Deborah A Zarin *director of ClinicalTrials.gov*[3], Hui Xu *postgraduate house staff trainee*[4], Lei Zhou *postgraduate house staff trainee*[4], Harlan M Krumholz *Harold H Hines Jr professor of medicine and professor of investigative medicine and of public health*[2 5 6]



"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"

BMJ 2011;344:d7292 doi: 10.1136/bmj.d7292 (Published 3 January 2012)

We Did Not Believe It

The NEW ENGLAND JOURNAL of MEDICINE

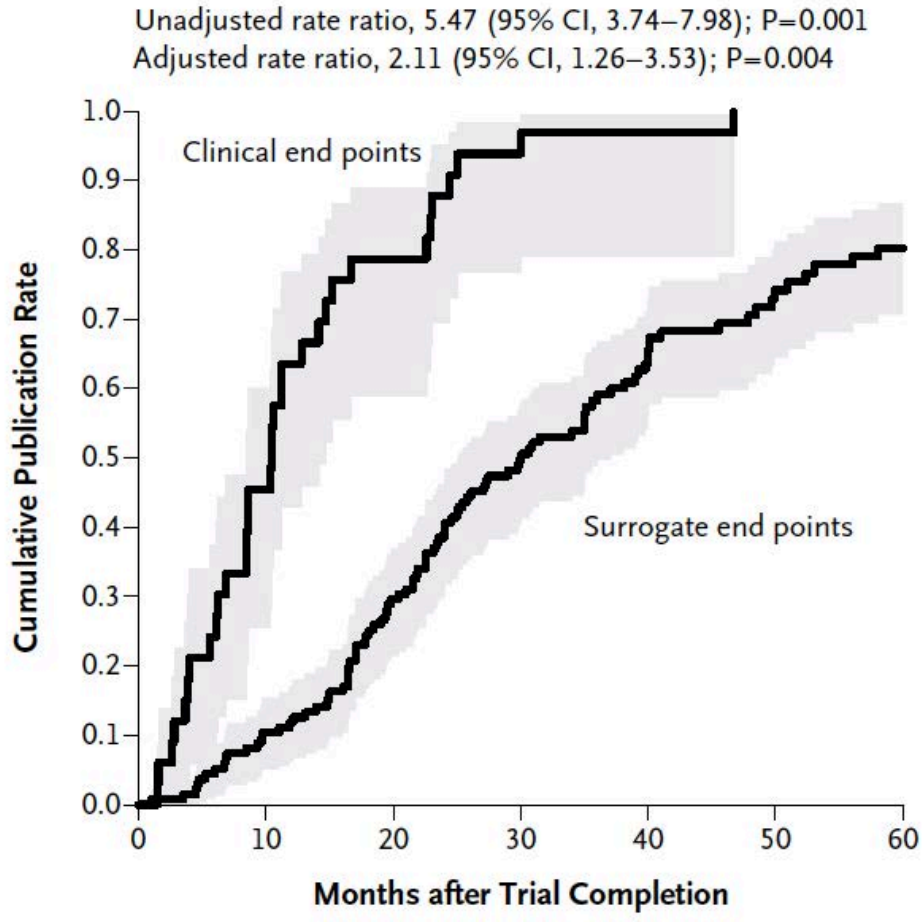
SPECIAL ARTICLE

Publication of Trials Funded by the National Heart, Lung, and Blood Institute

David Gordon, M.D., Ph.D., Wendy Taddei-Peters, Ph.D., Alice Mascette, M.D., Melissa Antman, Ph.D., Peter G. Kaufmann, Ph.D., and Michael S. Lauer, M.D.

ABSTRACT

"A number of parties share responsibility, **including funders**, investigators, academic medical centers, [universities], clinical research organizations, and ... journals."



No. at Risk

Surrogate end points	199	158	110	67	40	24	16
Clinical end points	45	22	7	2	1	0	0

N Engl J Med 2013;369:1926-34

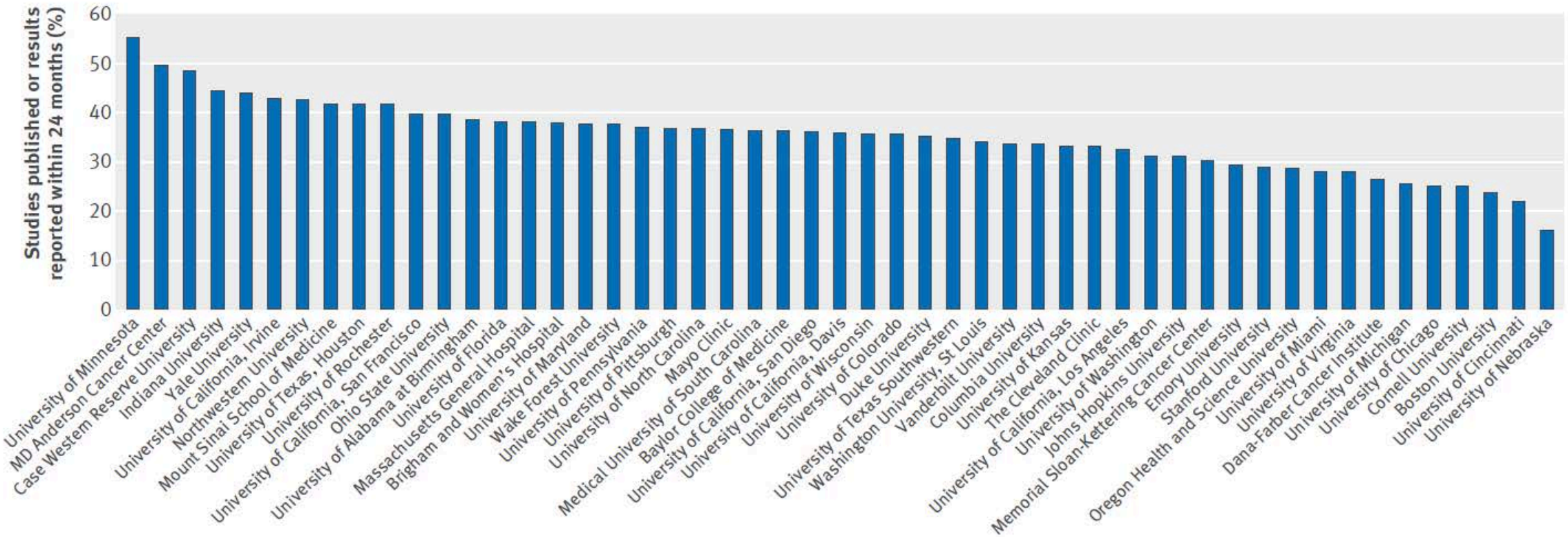
At *Your* Institution

RESEARCH

OPEN ACCESS

Publication and reporting of clinical trial results: cross sectional analysis across academic medical centers

Ruijun Chen,[1] Nihar R Desai,[2,3] Joseph S Ross,[3,4,5,6] Weiwei Zhang,[3] Katherine H Chau,[1] Brian



"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

Just How Serious This Is…

OPINION POLICY-ISH

Academic Medical Centers Get An F In Sharing Research Results

February 23, 2016 · 1:59 PM ET

HARLAN KRUMHOLZ

Who will check the study results if they aren't made public?

Simone Golob/Corbis

"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

Continued… “Sharing Results Should Not Be Optional”

OPINION POLICY-ISH

Academic Medical Centers Get An F In Sharing Research Results

February 23, 2016 · 1:59 PM ET

HARLAN KRUMHOLZ

Who will check the study results if they aren't made public?

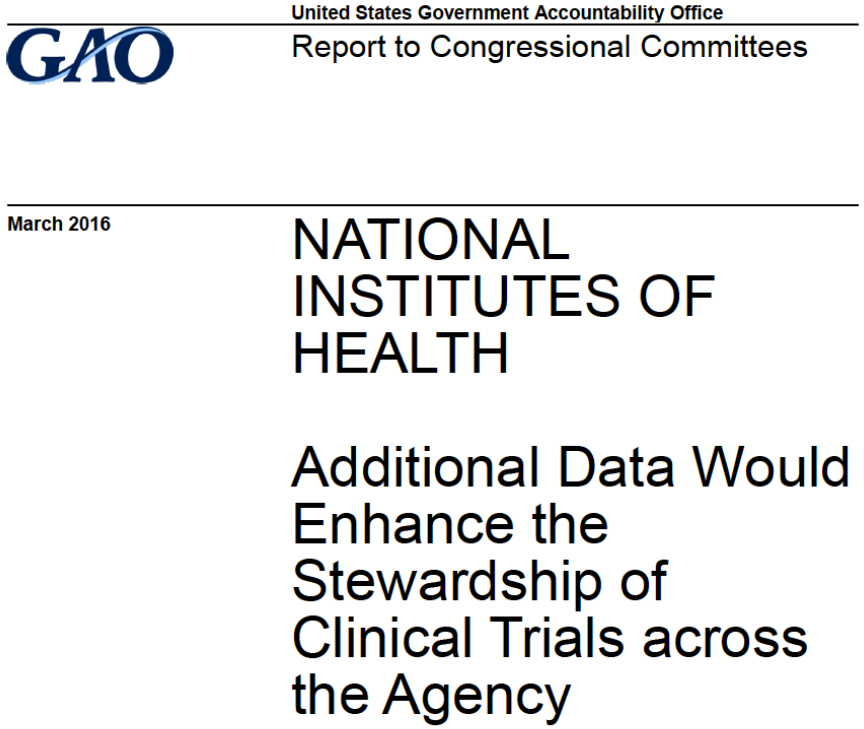
Simone Golob/Corbis

“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

More Problems



"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."

GAO-16-304

Notice of Revised NIH Definition of "Clinical Trial"

A Long Road

Notice Number:

NOT-OD-15-015

Key Dates

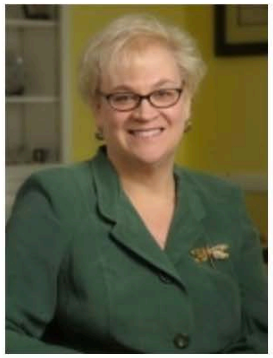
Release Date: October 23, 2014

Rock Talk

Helping connect you with the NIH perspective

Posted on **November 19, 2014** by **Sally Rockey**

A Proposed HHS Regulation and NIH Policy to Further the Impact of Clinical Trials Research



Dr. Sally Rockey

VIEWPOINT

Sharing and Reporting the Results of Clinical Trials

Kathy L. Hudson, PhD
National Institutes of Health, Bethesda, Maryland.

Francis S. Collins, MD, PhD
National Institutes of Health, Bethesda, Maryland.

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 i
to test new drugs, devices, or other inter
principle of data sharing properly assumes
ethical mandate. These participants

be blamed entirely. A recent analysis of 400 clinical studies revealed that 30% had not shared results through publication or through results reporting in ClinicalTrials.gov within 4 years of completion.[4] This is a serious issue and the proposed rule underscores the intent of NIH to take strong action to promote timely

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…

42 CFR Part 11

[Docket Number NIH-2011-0003]

RIN: 0925-AA55

Clinical Trials Registration and Results Information Submission

Effective Date

This policy is effective January 18, 2017.

Date: September 12, 2016

Francis S. Collins, M.D., Ph.D.

Director

National Institutes of Health

"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…"

https://www.federalregister.gov/documents/2016/09/21/2016-22379/nih-policy-on-the-dissemination-of-nih-funded-clinical-trial-information

Publicity

JAMA Published online September 16, 2016

Opinion

VIEWPOINT

Toward a New Era of Trust and Transparency in Clinical Trials

Kathy L. Hudson, PhD
National Institutes of Health, Bethesda, Maryland.

Michael S. Lauer, MD
National Institutes of Health, Bethesda, Maryland.

Francis S. Collins, MD, PhD
National Institutes of Health, Bethesda, Maryland.

Supplemental content

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

The aim is 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 con-

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Open Mike

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

Posted on **September 16, 2016** by **Mike Lauer and Carrie Wolinetz**

Building Better Clinical Trials through Stewardship and Transparency

— *Dr. Carrie Wolinetz is NIH's Associate Director for Science Policy, and writes*

NIH is the largest public funder of clinical trials in the United States. As stewards of this research enterprise, we have been actively listening and discussing how to overcome hurdles and shortcomings that we, and others in the research community, have identified. If you've been following the conversation, you'll know that NIH already has implemented some key reforms to enhance clinical trial stewardship. Today, in a Viewpoint Essay published in the Journal of the American Medical Association (JAMA), we provide an overview of how these reforms, and new initiatives, fit in to the broader picture of building a better clinical trial enterprise through better stewardship, accountability, and transparency.

Dr. Michael Lauer is NIH's Deputy Director for Extramural Research, serving as the principal scientific leader and advisor to the NIH Director on the NIH extramural research program.

Search

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

Notice Number: NOT-OD-16-149

NIH National Institutes of Health
Office of Extramural Research

Laudable Goal … But ...

42 CFR Part 11

[Docket Number NIH-2011-0003]

RIN: 0925-AA55

Clinical Trials Registration and Results Information Submission

Effective Date

This policy is effective January 18, 2017.

Date: September 12, 2016

Francis S. Collins, M.D., Ph.D.

Director

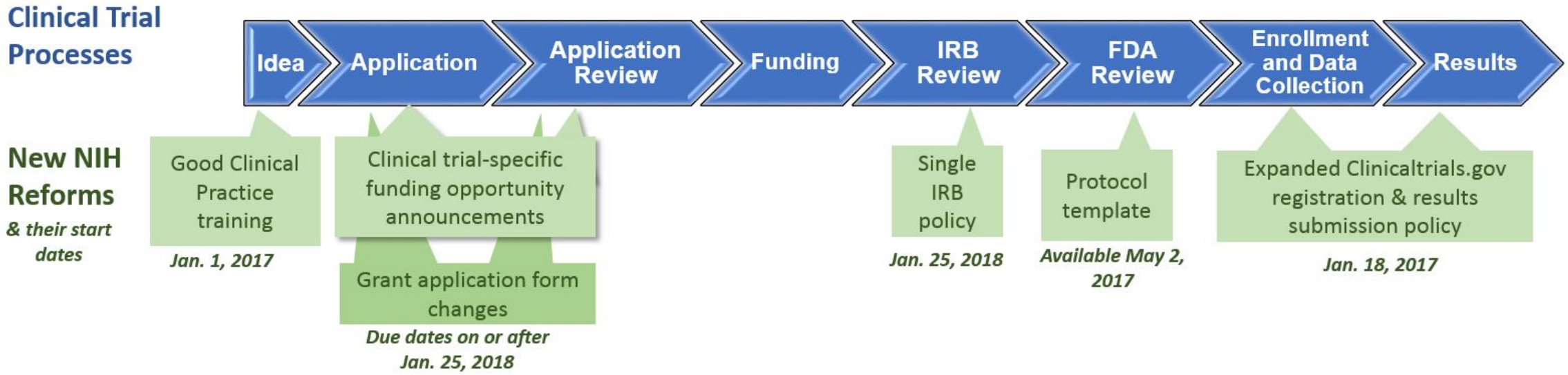
National Institutes of Health

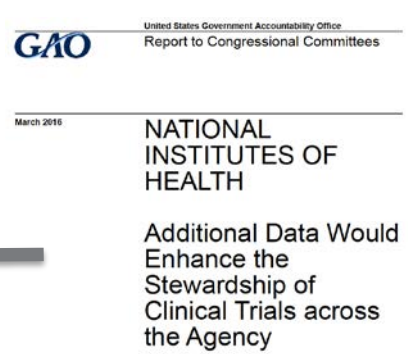
"We disagree with commenters who suggested that there is no need for coverage of certain types of trials. The benefits of transparency and the need to fulfill **the ethical obligation to participants** is as relevant to these types of trials as to any other type.

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.**"

https://www.federalregister.gov/documents/2016/09/21/2016-22379/nih-policy-on-the-dissemination-of-nih-funded-clinical-trial-information

Enabling Systems (Culture) Change





Data for Stewardship ← Additional Data Would Enhance the Stewardship of Clinical Trials across the Agency ← Register ← Report Results

Policy & Compliance

NIH Grants Policy Statement

Notices of Policy Changes

Compliance & Oversight

Select Policy Topics

Animal Welfare

Application Submission Policies

Clinical Trial Requirements

- Clinical Trial Definition
- Why the Changes
- Good Clinical Practice
- Specific Funding Opportunities
- New Form
- Single IRB Policy
- Protocol Template
- Registration and Reporting

Clinical Trial Requirements for Grants and Contracts

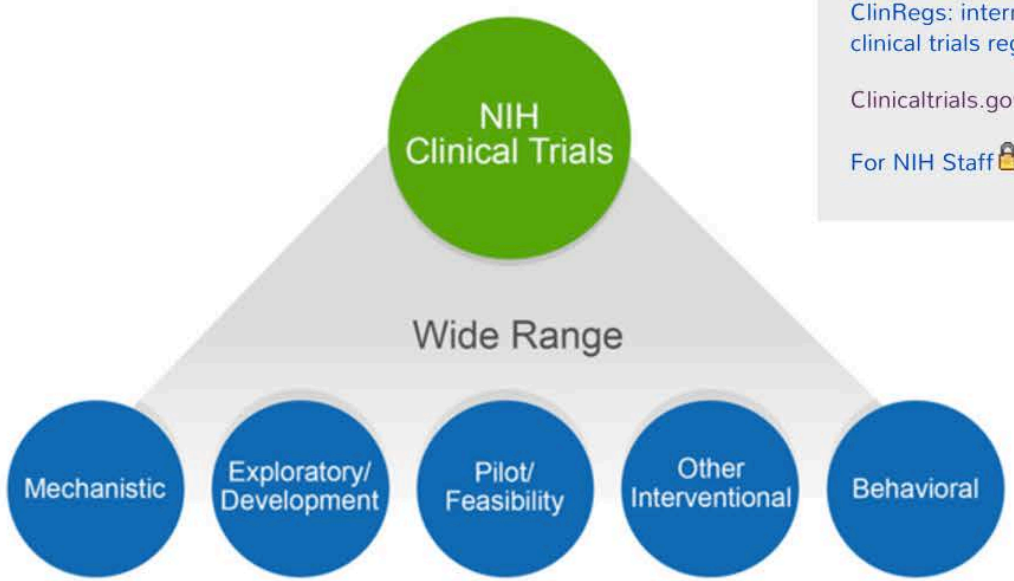
NIH is launching a series of initiatives that are rolling out in 2017-2018 to enhance the accountability and transparency of clinical research. These initiatives target key points along the whole clinical trial lifecycle from concept to results reporting. Learn more about these changes and how they will 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 control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. Learn more

Your human subjects study may meet the NIH definition of a clinical trial.

FIND OUT HERE



Related Resources

FAQs

Training Resources

Research Involving Human Subjects

ClinRegs: international clinical trials regulations

Clinicaltrials.gov

For NIH Staff

https://grants.nih.gov/policy/clinical-trials.htm

Policy & Compliance

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Protocol Template

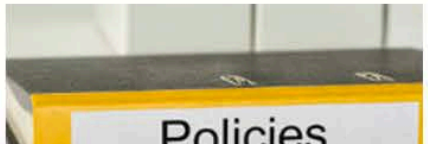
Registration and

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

Related Resources

FAQs

Training Resources

Research Involving Human Subjects

ClinRegs: international clinical trials regulations

Clinicaltrials.gov

For NIH Staff

Related Resources

Frequently Asked Questions

https://grants.nih.gov/policy/clinical-trials/reporting/index.htm

Accountability, Ethical Mandate, Transparency

VIEWPOINT

Toward a New Era of Trust and Transparency in Clinical Trials

Kathy L. Hudson, PhD
National Institutes of Health, Bethesda, Maryland.

Michael S. Lauer, MD
National Institutes of Health, Bethesda, Maryland.

Francis S. Collins, MD, PhD
National Institutes of Health, Bethesda, Maryland.

"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)

Accountability, Ethical Mandate, Transparency - About Time

Vox EXPLAINERS POLITICS & POLICY WORLD CULTURE SCIENCE & HEALTH IDENTITIES MORE

30 FOR 30 Stories you need to hear to believe. Listen on Apple Podcasts

A surprising amount of medical research isn't made public. That's dangerous.

Updated by Stephanie Wykstra | Aug 1, 2017, 8:40am EDT

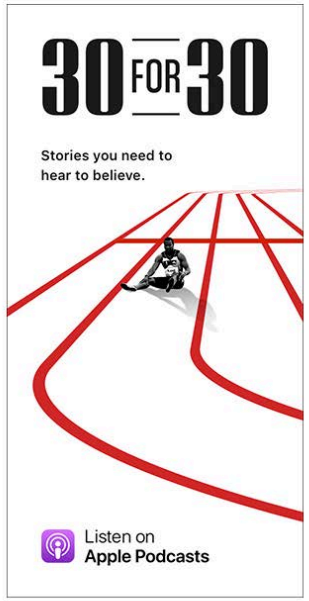
TWEET SHARE

Dan Kitwood / Staff

THE BIG IDEA

Outside contributors' opinions and analysis of the most important issues in politics, science, and culture.

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



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NEWS RELEASES

Wednesday, November 19, 2014

HHS and NIH take steps to enhance transparency of clinical trial results

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 13, 2015.

Institute/Center

NIH Office of the Director (OD)

Contact

NIH News Media Branch

301-496-5787

Related Links

NPRM Federal Register Notice pdf

NIH Guide to Proposed NIH Policy

Summary of Proposed Changes

https://www.vox.com/the-big-idea/2017/8/1/16012946/clinical-trial-research-public-transparency
https://www.nih.gov/news-events/news-releases/hhs-nih-take-steps-enhance-transparency-clinical-trial-results