21st Century Cures Act Update: Research Rigor and Reproducibility

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114th Meeting of the Advisory Committee to the Director (ACD)
National Institutes of Health
Porter Neuroscience Building, Building 35 A, Rooms 620/630, Bethesda, Maryland
June 8, 2017
Disclosures: None

Statute

Section 2039 requires the NIH Director to convene a workinggroup under the ACD to developand issue recommendations through the ACD for a formal policy,whichmay incorporate or be informed by relevant existing and ongoing activities,to enhance rigor and reproducibility of scientific research funded by NIH.

ACD Working Group

- ACD
  - Russ Altman (Chair)
  - Mary Sue Coleman
  - Lisa Cooper
  - Jose Florez
  - Linda Griffith
  - Peter MacLeish
- NIH
  - Michael Lauer
  - Pritty Joshi
  - Jennifer Plank-Bazinet
  - Patricia Valdez

Few Years Ago

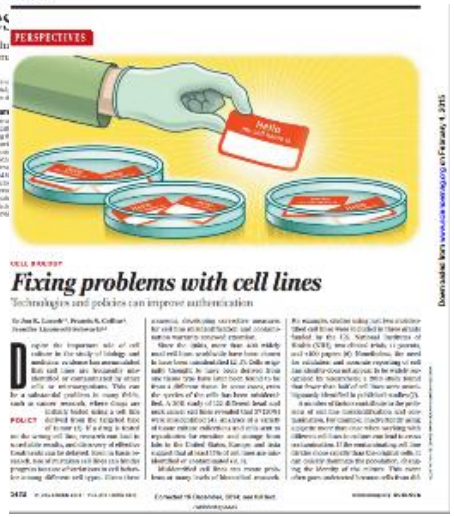

PERSPECTIVE

A call for transparent reporting to optimize the predictive value of preclinical research


NIH to balance sex in cell and animal studies

NIH plans to enhance reproducibility

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


PERSPECTIVES

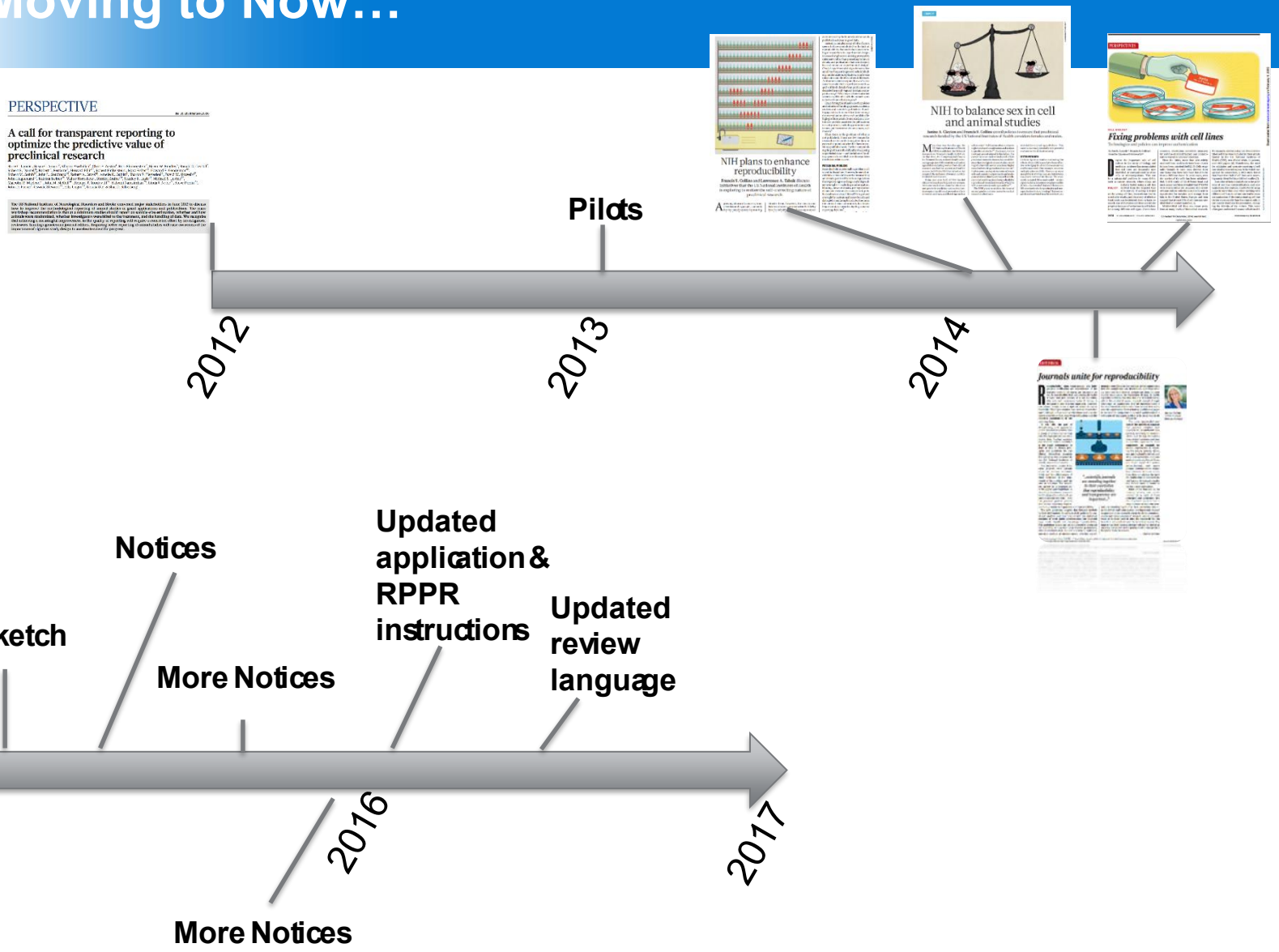
Fixing problems with cell lines

Technologies and policies can improve authentication

Pilots

2012 2013 2014

Moving to Now…



(See handout for links to notices)

Multi-Stakeholder Approach

EDITORIAL

Science

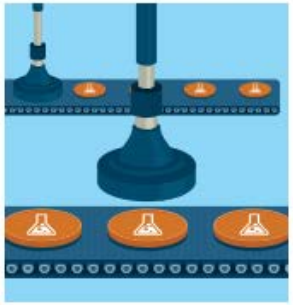
Journals unite for reproducibility

Reproducibility, rigor, transparency, and independent verification are cornerstones of the scientific method. Of course, just because a result is reproducible does not necessarily make it right, and just because it is not reproducible does not necessarily make it wrong. A transparent and rigorous approach, however, can almost always shine a light on issues of reproducibility. This light ensures that science moves forward, through independent verifications as well as the course corrections that come from refutations and the objective examination of the resulting data.

It was with the goal of strengthening such approaches in the biomedical sciences that a group of editors representing over 30 major journals, representatives from funding agencies, and scientific leaders assembled at the AAAS headquarters in June of 2014 to discuss principles and guidelines for preclinical biomedical research. The gathering was convened by the U.S. National Institutes of Health, *Nature*,* and *Science*.

The discussion ranged from what journals were already doing to address reproducibility and the effectiveness of those measures, to the magnitude of the problem and the cost of solutions. The attendees agreed on a common set of Principles and Guidelines in Reporting Preclinical Research (www.nih.gov/about/reporting-preclinical-research.htm) that list proposed journal policies and author reporting requirements to promote transparency and reproducibility.

The new guidelines suggest that journals include in their information for authors their policies for statistical analysis and how they review the statistical accuracy of work under consideration. Any imposed page limits should not discourage reproducibility. The guidelines encourage using a checklist to ensure the reporting of important experimental parameters, such as standards used, number and type of replicates, statistics, method of randomization, whether experimenters were blind to the conduct of the experiment, how the sample size was determined, and what criteria were used to include or exclude any data. Journals should recommend the deposition of data in public repositories where available and link data bidirectionally to the published paper. Journals should strongly encourage, as appropriate, that all materials used in the experiment be shared with those who wish to replicate the experiment. Once a journal publishes a paper, it assumes the obligation to consider publication of a refutation of that paper, subject to its usual standards of quality.



"...scientific journals are standing together in their conviction that reproducibility and transparency are important..."

The more open-ended portion of the guidelines suggests that journals establish best practices for image-based data (such as screening for manipulation and storing full-resolution archival versions) and how to describe experiments more completely. An example for animal experiments is reporting the source, species, strain, sex, age, husbandry, inbred and strain characteristics, or transgenic animals, etc. For cell lines, one might report the source, authentication, and mycoplasma contamination status. The existence of these guidelines does not obviate the need for replication or independent verification of research results, but should make it easier to perform such replication.

Some of the journals at the meeting already had implemented all or most of these principles and guidelines. But the important point is that a large number of scientific journals are standing together in their conviction that reproducibility and transparency are important issues.† As partners to the research enterprise in the communication and dissemination of research results, journals want to do their part to raise the standards for the benefit of all scientists and the benefit of society. The hope is that that these guidelines will not be viewed as onerous, but as part of the quality control that justifies the public trust in science.

– Marcia McNutt

Marcia McNutt
Editor-in-Chief
Science *Journals*

*See www.nature.com/news/1.16259. † A list of all journals and publishers signatory to the principles and guidelines www.nih.gov/about/reporting-preclinical-research.htm.

10.1126/science.aaa

nature

EDITORIALS

CONSERVATION Saving species is far from a walk in the park p.8

WORLD VIEW Psychology gears up to check its workings p.9

BREAKFAST Chimps plan days to ensure they nab tastiest figs p.11

Journals unite for reproducibility

Consensus on reporting principles aims to improve quality control in biomedical research and encourage public trust in science.

Reproducibility, rigour, transparency and independent verification are cornerstones of the scientific method. Of course, just because a result is reproducible does not make it right, and just because it is not reproducible does not make it wrong. A transparent and rigorous approach, however, will almost always shine a light on issues of reproducibility. This light ensures that science moves forward, through independent verifications as well as the course corrections that come from refutations and the objective examination of the resulting data.

It was with the goal of strengthening such approaches in the biomedical sciences that a group of editors representing more than 30 major journals, representatives from funding agencies, and scientific leaders assembled at the American Association for the Advancement of Science's headquarters in June 2014 to discuss principles and guidelines for preclinical biomedical research. The gathering was convened by the US National Institutes of Health, *Nature* and *Science* (see *Science* 346, 679; 2014).

The discussion ranged from what journals were already doing to address reproducibility — and the effectiveness of those measures — to the magnitude of the problem and the cost of solutions. The attendees agreed on a common set of Principles and Guidelines in Reporting Preclinical Research (see go.nature.com/ezjl1p) that list proposed journal policies and author reporting requirements in order to promote transparency and reproducibility.

The guidelines recommend that journals include in their information for authors their policies for statistical analysis and how they review the statistical accuracy of work under consideration. Any imposed page limits should not discourage reproducibility. The guidelines encourage using a checklist to ensure reporting of important experimental parameters, such as standards used, number and type of replicates, statistics, method of randomization, whether experiments were blinded, how the sample size was determined and what criteria were used to include or exclude any data. Journals should recommend deposition of data in public repositories, where available, and link data bidirectionally when the paper is published. Journals should strongly encourage, as appropriate, that all materials used in the experiment be shared with those who wish to replicate the experiment. Once a journal publishes a paper, it assumes the obligation to consider publication of a refutation of that paper, subject to its usual standards of quality.

"The guidelines encourage using a checklist to ensure reporting of important experimental parameters."

The more open-ended portion of the guidelines suggests that journals establish best practices for dealing with image-based data (for example, screening for manipulation, storing full-resolution archival versions) and for describing experiments in full. An example for animal experiments is to report the source, species, strain, sex, age, husbandry and inbred and strain characteristics for transgenic animals. For cell lines, one might report the source, authentication and mycoplasma contamination status. The existence of these guidelines does not obviate the need for replication or independent verification of research results, but should make it easier to perform such replication.

Some of the journals at the meeting had already had all or most of these principles and guidelines in place. But the point is that a large number of scientific journals are standing together in their conviction that reproducibility and transparency are important issues. As partners to the research enterprise in the communication and dissemination of research results, we want to do our part to raise the standards for the benefit of scientists and of society. The hope is that these guidelines will be viewed not as onerous, but as part of the quality control that justifies the public trust in science. ■

Multi-Stakeholder Approach

Co-Sponsored NIH Guidelines for Preclinical Reporting

AAAS

Signed on to NIH Guidelines for Preclinical Reporting

SfN
AACR

Webpages for R&R Resources

SfN
APS

Published Reports with Recs for Enhancing Rigor

FASEB
ASM
ASCB

Hosted Symposia/Sessions on R&R

FASEB
APS
AAAS

Responded to NIH RFI Inviting Comment on Reagent-Related Barriers

AAI
The Endocrine Society

Conducted a Member Survey on Reproducibility

ASCB

RPG Application and Review

Element of Rigor	Section of Application	Criterion Score	Additional Review Consideration	Contribute to Overall Impact?
Scientific Premise	Research Strategy	Significance	NA	Yes
Scientific Rigor		Approach	NA	Yes
Consideration of Relevant Biological Variables Such as Sex		Approach	NA	Yes
Authentication of Key Biological and/or Chemical Resources	New Attachment	NA	Adequate or Inadequate	No

Resources

NIH National Institutes of Health
Office of Extramural Research

Grants & Funding
NIH's Central Resource for Grants and Funding Information

HOME | ABOUT GRANTS | FUNDING | POLICY & COMPLIANCE

Home » Policy & Compliance » Rigor and Reproducibility

About OER
- NIH Grants Policy Statement
- Notices of Policy Changes
- Compliance & Oversight
- Select Policy Topics +

Rigor and Reproducibility

Scientific rig
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to assist the
progress re

On This
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- Guidar
- Resou
- News
- Refere

NIH Rigor and Reproducibility Training Modules

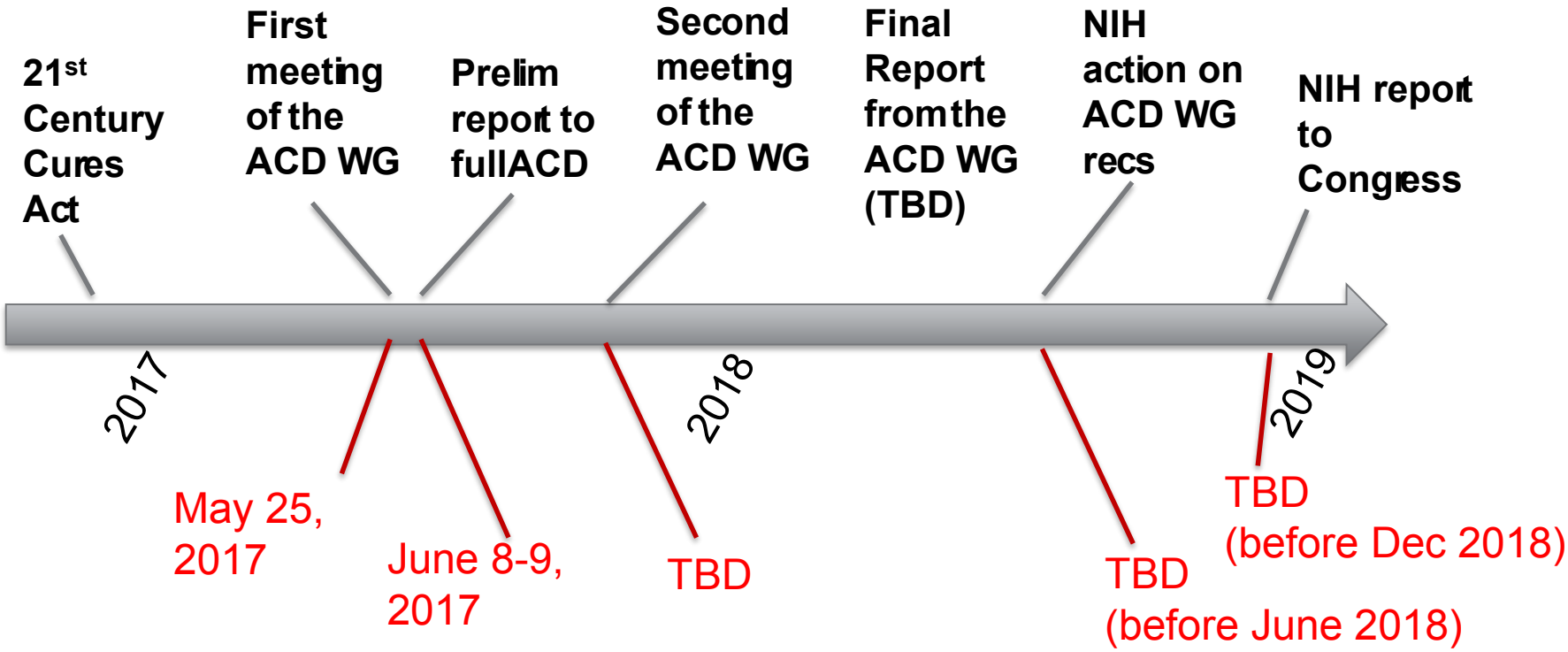
Introduction to the Modules [PDF, 110KB]

Module 1: Lack of Transparency
In order to reproduce someone else's findings adequately, the ex
other pertinent information must be accessible and understandal
to include all relevant details in publications to ensure that other
research appropriately and accurately.
Lack of Transparency Discussion Material [PDF, 97.2KB]

Module 2: Blinding and Randomization
Sample blinding and randomization are key elements in reducing
as in permitting reliable statistical testing. This module presents
randomization, as well as the impact of issues that may introduc
Blinding and Randomization Discussion Material [PDF, 104KB]

https://grants.nih.gov/reproducibility/index.htm
https://www.nigms.nih.gov/training/pages/clearinghouse-for-training-modules-to-enhance-data-reproducibility.aspx

Timeline for ACD WG



Interim Recommendations

- Application
  - Highlight what's important
  - Section(s) for rigor
  - Not just authentication
  - "CONSORT-like" checklist
  - Clarifies review priorities
- Resources
  - Validated, vetted materials

Trial design	3a
	3b
Participants	4a
	4b
Interventions	5
Outcomes	6a
	6b
Sample size	7a
	7b
Randomisation:	
Sequence	8a
generation	8b
Allocation	9
concealment mechanism	
Implementation	10
Blinding	11a

http://www.consort-statement.org/

Interim Recommendations

- Training
  - Ongoing funded projects (PA-16-060)
  - Incorporate into spectrum of ethics training
  - NAS: “detrimental research practices”

https://www.nap.edu/catalog/21896/fostering-integrity-in-research