THE NIH PERSPECTIVE ON RIGOR AND REPRODUCIBILITY

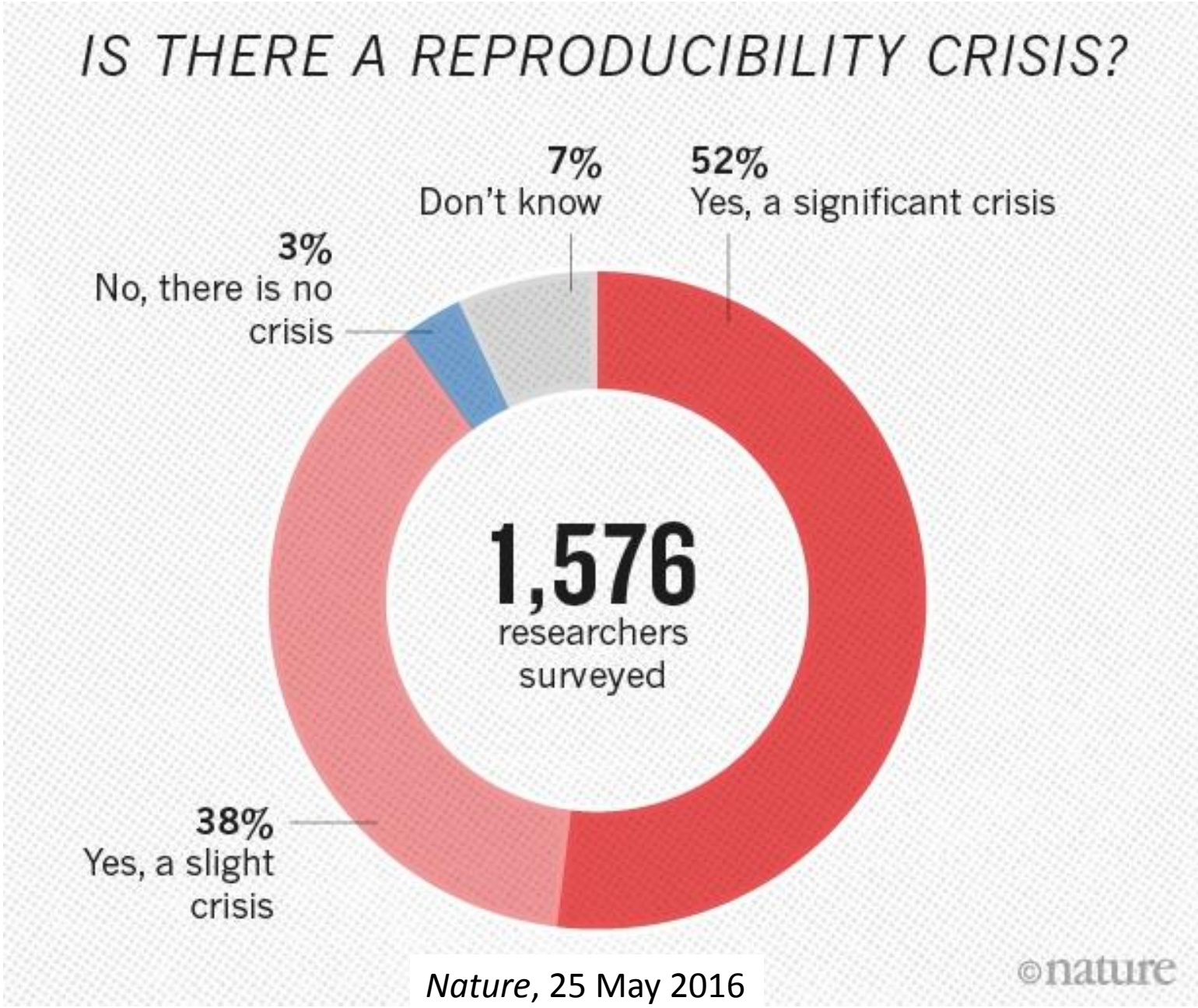
MAY 30, 2017

PATRICIA VALDEZ, PhD

NIH EXTRAMURAL RESEARCH INTEGRITY OFFICER

National Institutes of Health

Office of Extramural Programs



Nature, 25 May 2016

National Institutes of Health

The Reproducibili

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research

Why animal research needs to improve

Many of the studies that use animals to model human diseases are too small and too prone to bias to be trusted, says **Malcolm Macleod**.

Beware the creeping cracks of bias

Evidence is mounting that research is riddled with systematic errors. Left unchecked, this could erode public trust, warns **Daniel Sarewitz**.

Believe it or not: how much can we rely on published data on potential drug targets?

Florian Prinz, Thomas Schlange and Khusru Asadullah

False-Positive Psychology: Undisclosed Flexibility in Data Collection and Analysis Allows Presenting Anything as Significant

Raise standards for preclinical cancer research

C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

Drug targets slip-sliding away

The starting point for many drug discovery programs is a published report on a new drug target. Assessing the reliability of such papers requires a nuanced view of the process of scientific discovery and publication.

NIH National Institutes of

Reforming Science: Methodological and Cultural Reforms

THE NIH RESPONSE TO THE REPRODUCIBILITY ISSUE

The National Institutes of Health

One goal is to **“exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.”**

National Institutes of Health

PERSPECTIVE

doi:10.1038/nature11556

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

Story C. Landis[1], Susan G. Amara[2], Khusru Asadullah[3], Chris P. Austin[4], Robi Blumenstein[5], Eileen W. Bradley[6], Ronald G. Crystal[7], Robert B. Darnell[8], Robert J. Ferrante[9], Howard Fillit[10], Robert Finkelstein[1], Marc Fisher[11], Howard E. Gendelman[12], Robert M. Golub[13], John L. Goudreau[14], Robert A. Gross[15], Amelie K. Gubitz[1], Sharon E. Hesterlee[16], David W. Howells[17], John Huguenard[18], Katrina Kelner[19], Walter Koroshetz[1], Dimitri Krainc[20], Stanley E. Lazic[21], Michael S. Levine[22], Malcolm R. Macleod[23], John M. McCall[24], Richard T. Moxley III[25], Kalyani Narasimhan[26], Linda J. Noble[27], Steve Perrin[28], John D. Porter[1], Oswald Steward[29], Ellis Unger[30], Ursula Utz[1] & Shai D. Silberberg[1]

The US National Institute of Neurological Disorders and Stroke convened major stakeholders in June 2012 to discuss how to improve the methodological reporting of animal studies in grant applications and publications. The main workshop recommendation is that at a minimum studies should report on sample-size estimation, whether and how animals were randomized, whether investigators were blind to the treatment, and the handling of data. We recognize that achieving a meaningful improvement in the quality of reporting will require a concerted effort by investigators, reviewers, funding agencies and journal editors. Requiring better reporting of animal studies will raise awareness of the importance of rigorous study design to accelerate scientific progress.

NIH Publications on the Issue

PERSPECTIVES

CELL BIOLOGY

Fixing problems with cell lines

Technologies and policies can improve authentication

By Jon R. Lorsch[1*], Francis S. Collins[2], Jennifer Lippincott-Schwartz[2,3]

Despite the important role of cell culture in the study of biology and medicine, evidence has accumulated that cell lines are frequently misidentified or contaminated by other cells or microorganisms. This can be a substantial problem in many fields, such as cancer research, where drugs are initially tested using a cell line derived from the targeted type of tumor (*1*). If a drug is tested on the wrong cell line, research can lead to unreliable results, and discovery of effective treatments can be delayed. Even in basic research, use of mistaken cell lines can hinder progress because of variations in cell behavior among different cell types. Given these concerns, developing corrective measures for cell line misidentification and contamination warrants renewed attention.

POLICY

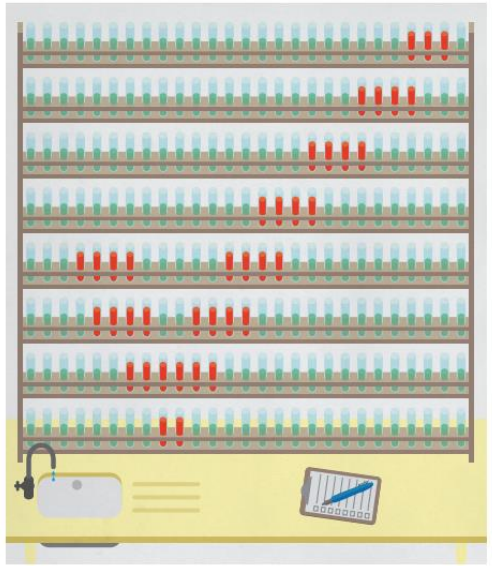
Since the 1960s, more than 400 widely used cell lines worldwide have been shown to have been misidentified (*2*, *3*). Cells originally thought to have been derived from one tissue type have later been found to be from a different tissue. In some cases, even the species of the cells has been misidentified. A 2011 study of 122 different head and neck cancer cell lines revealed that 37 (30%) were misidentified (*4*). Analyses of a variety of tissue culture collections and cells sent to repositories for curation and storage from labs in the United States, Europe, and Asia suggest that at least 15% of cell lines are misidentified or contaminated (*4*, *5*).

Misidentified cell lines can create problems at many levels of biomedical research. For example, studies using just two misidentified cell lines were included in three grants funded by the U.S. National Institutes of Health (NIH), two clinical trials, 11 patents, and >100 papers (*6*). Nonetheless, the need for validation and accurate reporting of cell line identity does not appear to be widely recognized by researchers; a 2013 study found that fewer than half of cell lines were unambiguously identified in published studies (*7*).

A number of factors contribute to the problems of cell line misidentification and contamination. For example, inadvertently using a pipette more than once when working with different cell lines in culture can lead to cross contamination. If the contaminating cell line divides more rapidly than the original cells, it can quickly dominate the population, changing the identity of the culture. This event often goes undetected because cells from dif-

Corrected 19 December, 2014; see full text.

Published by AAAS



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.

A growing chorus of concern, from scientists and laypeople, contends that the complex system for ensuring shorter term, however, the checks and balances that once ensured scientific fidelity have been hobbled. This has compromised

outnumbered by the hundreds of thousands published each year in good faith.

Instead, a complex array of other factors seems to have contributed to the lack of reproducibility. Factors include poor training of researchers in experimental design; increased emphasis on making provocative statements rather than presenting technical details; and publications that do not report basic elements of experimental design[4]. Crucial experimental design elements that are all too frequently ignored include blinding, randomization, replication, sample-size calculation and the effect of sex differences. And some scientists reputedly use a 'secret sauce' to make their experiments work — and withhold details from publication or describe them only vaguely to retain a competitive edge[5]. What hope is there that other scientists will be able to build on such work to further biomedical progress?

Exacerbating this situation are the policies and attitudes of funding agencies, academic centres and scientific publishers. Funding agencies often uncritically encourage the overvaluation of research published in high-profile journals. Some academic centres also provide incentives for publications in such journals, including promotion and tenure, and in extreme circumstances, cash rewards[6].

Then there is the problem of what is not published. There are few venues for researchers to publish negative data or papers that point out scientific flaws in previously published work. Further compounding the problem is the difficulty of accessing unpublished data — and the failure of funding agencies to establish or enforce policies that insist on data access.

PRECLINICAL PROBLEMS

Reproducibility is potentially a problem in all scientific disciplines. However, human clinical trials seem to be less at risk because they are already governed by various regulations that stipulate rigorous design and independent oversight — including randomization, blinding, power estimates, pre-registration of outcome measures in standardized, public databases such as ClinicalTrials.gov and oversight by institutional review boards and data safety monitoring boards. Furthermore, the clinical trials community has taken important steps towards adopting standard reporting elements[7].

COMMENT

NIH to balance sex in cell and animal studies

Janine A. Clayton and **Francis S. Collins** unveil policies to ensure that preclinical research funded by the US National Institutes of Health considers females and males.

More than two decades ago, the US National Institutes of Health (NIH) established the Office of Research on Women's Health (ORWH). At that time, the Congressional Caucus for Women's Issues, women's health advocacy groups and NIH scientists and leaders agreed that excluding women from clinical research was bad for women and bad for science. In 1993, the NIH Revitalization Act required the inclusion of women in NIH-funded clinical research.

Today, just over half of NIH-funded clinical-research participants are women. We know much more about the role of sex and gender in medicine, such as that low-dose aspirin has different preventive effects in women and men, and that drugs such as calls to action[1]. Publications often continue to neglect sex-based considerations and analyses in preclinical studies[2,3]. Reviewers, for the most part, are not attuned to this failure. The over-reliance on male animals and cells in preclinical research obscures key sex differences that could guide clinical studies. And it might be harmful: women experience higher rates of adverse drug reactions than men do[4]. Furthermore, inadequate inclusion of female cells and animals in experiments and inadequate analysis of data by sex may well contribute to the troubling rise of irreproducibility in preclinical biomedical research, which the NIH is now actively working to address[5,6].

The NIH plans to address the issue of sex and gender inclusion across biomedical research multi-dimen-

stakeholders including publishers. This move is essential, potentially very powerful and need not be difficult or costly.

BETTER WITH BOTH

Certain rigorous studies evaluating the effects of sex differences have been effective in bridging the divide between animal and human work. One example concerns multiple sclerosis (MS). Women are more susceptible to MS than men are, but develop less-severe forms of the disease. The most widely accepted MS animal model — rodent experimental autoimmune encephalomyelitis (EAE) — has revealed[7] that sex differences in MS are related to both reproductive and non-reproductive factors. Findings[8] that oestrogen therapy provided benefits in rodent EAE

New Journal Policies to Enhance Reproducibility

Science

EDITORIAL

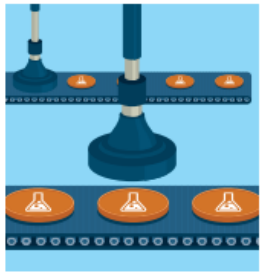
Journals unite for reproducibility

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.aaa1724

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.8

BREAKOUT 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. ■

NIH National Institutes of Health

Principles and Guidelines for Reporting Preclinical Research

- Rigorous statistical analysis
- Transparency in reporting
  - Standards
  - Replicates
  - Statistics
  - Randomization
  - Blinding
  - Sample size estimation
  - Inclusion/exclusion criteria
- Data and material sharing
- Consideration of refutations
- Consider establishing best practice guidelines for:
  - Antibodies
  - Cell lines
  - Animals

http://www.nih.gov/about/reporting-preclinical-research.htm

APPLICATION, REVIEW, AND PROGRESS REPORT UPDATES

Enhancing Reproducibility through Rigor and Transparency

Rigor + Transparency → Reproducibility

Easy to measure

Difficult to measure

Short-term focus to achieve long-term goal

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

Research Performance Progress Reports (RPPR)

Reporting on rigor and transparency:

- Evaluate rigor for past year and upcoming year,
- Prepare non-competing renewals for the next competitive renewal, and
- Help NIH implement and evaluate the policy for both current and new awards.

TRAINING TO ENHANCE REPRODUCIBILITY

Training

- NIH will require a description of instruction in the design and conduct of rigorous experiments.
  - Institutional training
  - Institutional career development
  - Individual fellowships
- See NOT-OD-16-034

Clearinghouse for Trainir ×

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

NIH National Institute of General Medical Sciences

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NIGMS Home > Training, Workforce Development, & Diversity > Clearinghouse for Training Modules to Enhance Data Reproducibility

Clearinghouse for Training Modules to Enhance Data Reproducibility

In January 2014, NIH launched a series of initiatives to enhance rigor and reproducibility in research. As a part of this initiative, NIGMS, along with nine other NIH institutes and centers, issued the funding opportunity announcement RFA-GM-15-006 to develop, pilot and disseminate training modules to enhance data reproducibility. Graduate students, postdoctoral fellows and early stage investigators are the primary audiences for these training modules.

For the benefit of the scientific community, we will be posting the products of these grants on this Web site as they become available in the future.

In addition, we are sharing here a series of four training modules developed by NIH. These modules focus on integral aspects of rigor and reproducibility in the research endeavor, such as bias, blinding and exclusion criteria. The modules are not meant to be comprehensive, but rather are intended as a foundation to build on and a way to stimulate conversations, which may be facilitated by the use of the accompanying discussion materials. Currently, the modules are being integrated into NIH intramural training activities.

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 experimental methods, rationale and other pertinent information must be accessible and understandable. This module highlights the need to include all relevant details in publications to ensure that other studies are able to build upon the 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 selection and other biases as well as

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Related Information

Administrative Supplements to NIGMS Predoctoral Training Grants

NIH Web Portal on Rigor and Reproducibility

NIH Grants & Funding Web Site on Rigor and Reproducibility in Grant Applications

NIH Reproducibility Workshops

- Cell Biology
- Structural Biology
- Genome Technology
- Cell Culture Studies
  - Videocast [Day 1 | Day 2]

Administrative Supplements for Predoctoral Training in Rigor

*"Graduate schools 'mostly teach **facts** the first year,' said Jon Lorsch, director of the National Institute of General Medical Sciences at the NIH. 'They should teach **methods**.'"*

-Harris, Richard. (2017). *Rigor Mortis: How Sloppy Science Creates Worthless Cures, Crushes Hope, and Wastes Billions.* New York: Basic Books.

https://www.nigms.nih.gov/training/instpredoc/Pages/projects-16-060.aspx

National Institute of General Medical Sciences

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NIGMS Home > Training, Workforce Development, & Diversity > Institutional Predoctoral Training Grants > Projects Funded Under PA-16-060

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Projects Funded Under PA-16-060

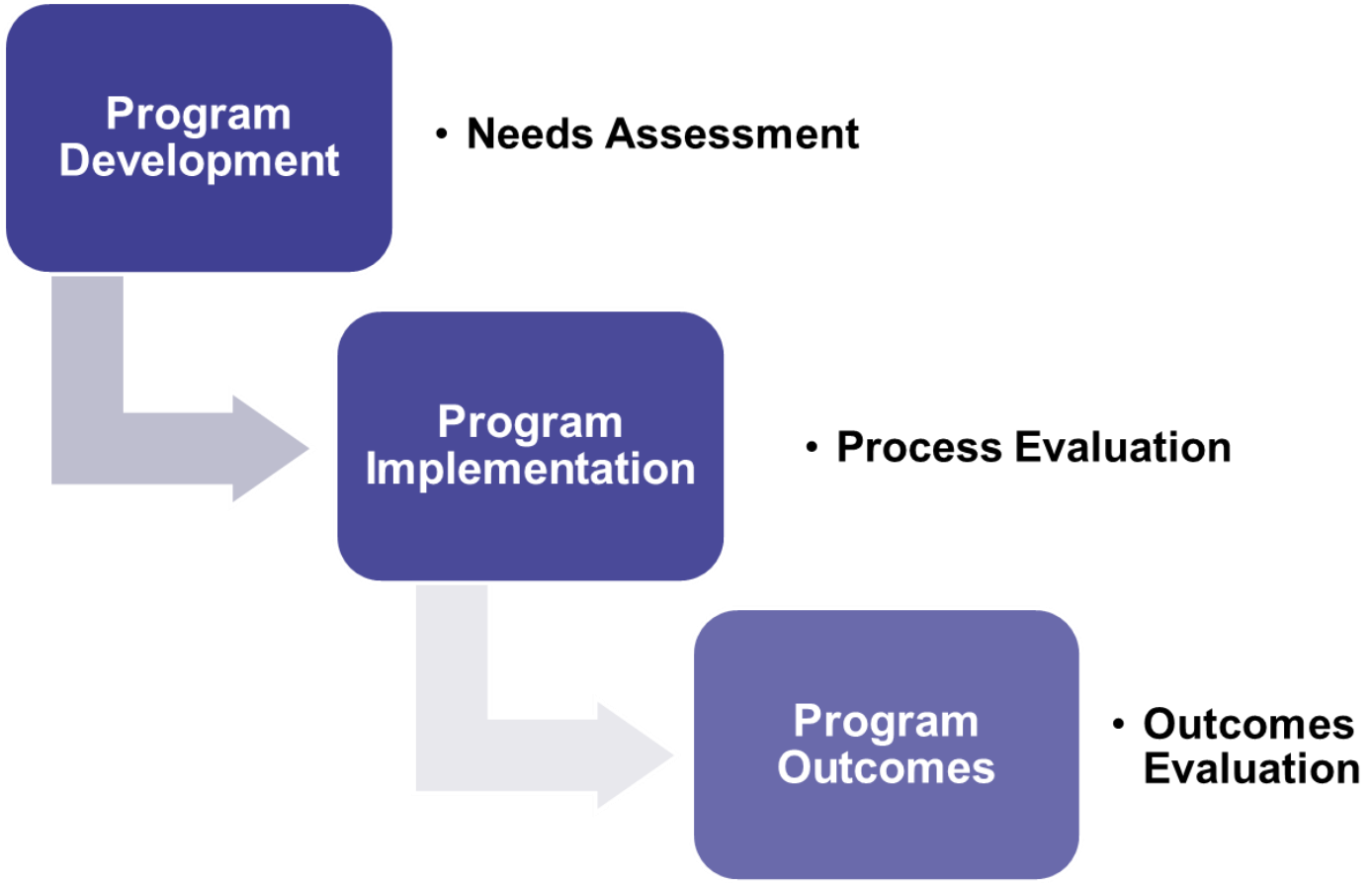
Listed below are the details of the projects funded under PA-16-060.

- Training in Experimental Rigor and Reproducibility
- Open Source Training in Computational Competence and Hands-on Data Analysis
- Experimental Design, Biostatistics and Quantitative Analysis
- Fundamental Concepts of Study Design, Statistics and Informatics
- Ensuring Rigor and Reproducibility: A Team Based Approach
- Promotion of Strong Foundations in Research Design and Methods Towards Reproducible and Rigorous Research
- Development of an Online Course on Statistical and Computational Tools for Reproducible Science
- Improved Reagent Verification as a Means for Enhanced Research Reproducibility
- Experimental Design, Biostatistics and Biological Variable Consideration
- Rigor and Reproducibility Training for Cellular and Molecular Medicine Research
- Integrating Concepts of Rigor, Repeatability and Reproducibility in Molecular Biology
- Training in Design of Research Methods for Reproducibility and Rigor
- Adoption of Good Research Practices
- Integrated Introduction to Biostatistics and Computation

Training in Experimental Rigor and Reproducibility
Principal Investigator: Christopher J. Chang, Ph.D., University of California, Berkeley


Rigor and Reproducibility
https://grants.nih.gov/reproducibility/
National Institutes of Health
Office of Extramural Research
Grants & Funding
NIH's Central Resource for Grants and Funding Information
Entire Site
Search this Site
eRA | Glossary & Acronyms | FAQs | Help
HOME
ABOUT GRANTS
FUNDING
POLICY & COMPLIANCE
NEWS & EVENTS
ABOUT OER
Home » Policy & Compliance » Rigor and Reproducibility
NIH Grants Policy Statement
Notices of Policy Changes
Compliance & Oversight
Select Policy Topics
Rigor and Reproducibility
Scientific rigor and transparency in conducting biomedical research is key to the successful application of knowledge toward improving health outcomes. The information provided on this website is designed to assist the extramural community in addressing rigor and transparency in NIH grant applications and progress reports.
On This Page:
Goals
Guidance: Rigor and Reproducibility in Grant Applications
Resources
News
References
Goals
The NIH strives to exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science. Updates to grant applications instructions and review language are intended to:
clarify long-standing expectations to ensure that NIH is funding the best and most rigorous science,
highlight the need for applicants to describe details that may have been previously overlooked,
highlight the need for reviewers to consider such details in their reviews through updated review language, and
minimize additional burden.
Related Resources
FAQs
ORWH Studying Sex to Strengthen Science (S4)
NIH Rigor and Reproducibility
NIGMS Training Modules
Intranet Resources on Rigor and Transparency (NIH Staff Only)
Contact: reproducibility@nih.gov

Ongoing Evaluation



Instruction in the Responsible Conduct of Research

Requirements:

- At least 8 contact hours
- Minimum of once every four years
- Training at each career stage

Thank You!

reproducibility@nih.gov

Appendix Slides

Scientific Premise

RESEARCH STRATEGY: SIGNIFICANCE

Describe the scientific premise for the proposed project, including consideration of the strengths and weaknesses of published research or preliminary data crucial to the support of your application.

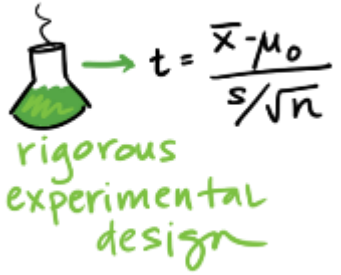
SIGNIFICANCE – REVIEW QUESTION

Is there a strong scientific premise for the project?

GUIDANCE

- [FAQs on Scientific Premise]
  - Excerpt: “Scientific premise concerns the quality and strength of the research used to form the basis for the proposed research question. NIH expects applicants to describe the general strengths and weaknesses of the prior research being cited by the applicant as crucial to support the application.”
- [Reviewer Guidance on Scientific Premise]
  - Excerpt: “A weak scientific premise, or the failure to address scientific premise adequately, may affect criterion and overall impact scores.”
- [Blog Post on Scientific Premise]

Scientific Rigor



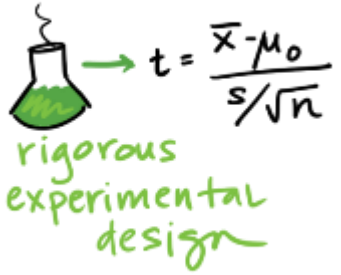
RESEARCH STRATEGY: APPROACH

Describe the experimental design and methods proposed and how they will achieve robust and unbiased results.

APPROACH – REVIEW QUESTIONS

Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed?

GUIDANCE



- FAQs on Scientific Rigor
  - Excerpt: “Scientific rigor is the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation and reporting of results. This includes full transparency in reporting experimental details so that others may reproduce and extend the findings.”
- Reviewer Guidance on Scientific Rigor
  - Excerpt: “The applicant should describe experimental controls, plans to reduce bias (blinding, randomization, subject inclusions and exclusion criteria, etc.), power analyses, and statistical methods, as appropriate.”
- Blog Post on Scientific Rigor

Relevant Biological Variables

RESEARCH STRATEGY: APPROACH

Explain how relevant biological variables, such as sex, are factored into research designs and analyses for studies in vertebrate animals and humans. For example, strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex.

APPROACH – REVIEW QUESTION

Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

GUIDANCE

- FAQs on Biological Variables
  - Excerpt: “Addressing the influence of sex in biomedical research with animals does not necessarily imply an increase in costs. Rather, well-designed research either tests or controls for variables that might influence outcomes, and sex is one such variable among many that must be considered to obtain valid results.”
- Reviewer Guidance on Biological Variables
  - Excerpt: “A justification is expected if the application proposes to study one sex, for example in the case of a sex-specific condition or phenomenon (e.g., ovarian or prostate cancer), acutely scare resources, or sex-specific hypotheses when there are known differences between males and females.”
- SABV Flowchart
- Blog Post on Biological Variables, and here, and here.

Authentication of Key Resources

Other Research Plan Sections - Instructions

If applicable to the proposed science, briefly describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies. No more than one page is suggested.

Key biological and/or chemical resources are characterized as follows.

- Key biological and/or chemical resources may or may not be generated with NIH funds and: 1) may differ from laboratory to laboratory or over time; 2) may have qualities and/or qualifications that could influence the research data; and 3) are integral to the proposed research. These include, but are not limited to, cell lines, specialty chemicals, antibodies, and other biologics.
- Standard laboratory reagents that are not expected to vary do not need to be included in the plan. Examples are buffers and other common biologicals or chemicals.
- See NIH's page on Rigor and Reproducibility for more information.

Authentication of Key Resources

Other Research Plan Sections - Review

For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.

GUIDANCE

- FAQs on Authentication
  - Excerpt: “The new application instructions and review language on authentication of key biological and/or chemical resources are intended for applications proposing use of *established* research resources that should be authenticated prior to and during use.”
- Reviewer Guidance on Authentication
  - Excerpt: “Reviewers will discuss the authentication plan after scoring; comments on key resource authentication should not affect scores.”
- Blog Post on Authentication, and here, and here.

Department of Health and Human Services
Part 1. Overview Information

Participating Organization(s)

National Institutes of Health (NIH)

Components of Participating Organizations

National Institute of General Medical Sciences (NIGMS)
National Cancer Institute (NCI)
National Institute on Aging (NIA)
National Institute of Allergy and Infectious Diseases (NIAID)
National Institute of Biomedical Imaging and Bioengineering (NIBIB)
National Institute of Dental and Craniofacial Research (NIDCR)
National Institute on Drug Abuse (NIDA)
National Institute of Neurological Disorders and Stroke (NINDS)
National Center for Advancing Translational Sciences (NCATS)
Division of Program Coordination, Planning and Strategic Initiatives, Office of Research Infrastructure Programs (ORIP)
Office of Research on Women's Health (ORWH)

Funding Opportunity Title

Tools for Cell Line Identification (SBIR [R43/R44])

Activity Code

R43/R44 Small Business Innovation Research (SBIR) Grant - Phase I, Phase II, and Fast-Track

Announcement Type

New

Related Notices

None

Funding Opportunity Announcement (FOA) Number

PA-16-186

RPPR

B.2 What was accomplished under these goals?

Goals are equivalent to specific aims. In the response, emphasize the *approaches taken to ensure robust and unbiased results. Include the* significance of the findings to the scientific field.

B.6 What do you plan to do for the next reporting period to accomplish the goals?

Include any important modifications to the original plans, *including efforts to ensure that the approach is scientifically rigorous and results are robust and unbiased*. Provide a scientific justification for any changes involving research with human subjects or vertebrate animals. A detailed description of such changes must be provided under Section F. Changes.

GUIDANCE

- FAQs on Progress Reports
  - Excerpt: “Investigators will be directed to emphasize the approaches taken to ensure robust and unbiased results, including any developments affecting the proposed experimental design, methodology, analysis and interpretation in the NIH Research Performance Progress Report (RPPR). If sufficient information is not provided in the progress report, program officials may request the additional information needed to assess progress.”
- Training module for Program Officers (NIH-only)
  - Excerpt: “During their review of scientific progress reports, program staff should ensure that the research was conducted in accordance with the updated policy on rigor and transparency.”