ENHANCING REPRODUCIBILITY THROUGH RIGOR AND TRANSPARENCY

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Office of Extramural Programs

OVERVIEW

- Why the concern about reproducibility?
- The NIH response
- Training and Resources

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THE REPRODUCIBILITY CHALLENGE

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**.

- Noted by research c… ultiple publications
  - Across re…
  - Especially in preclinical

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

The Economist | World politics | Business & finance | Economics | Science & technology | Culture

Unreliable research

Trouble at the lab

Scientists like to think of science as self-correcting. To an alarming degree, it is not

Oct 19th 2013 | From the print edition

Like 11k Tweet 1,227

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.

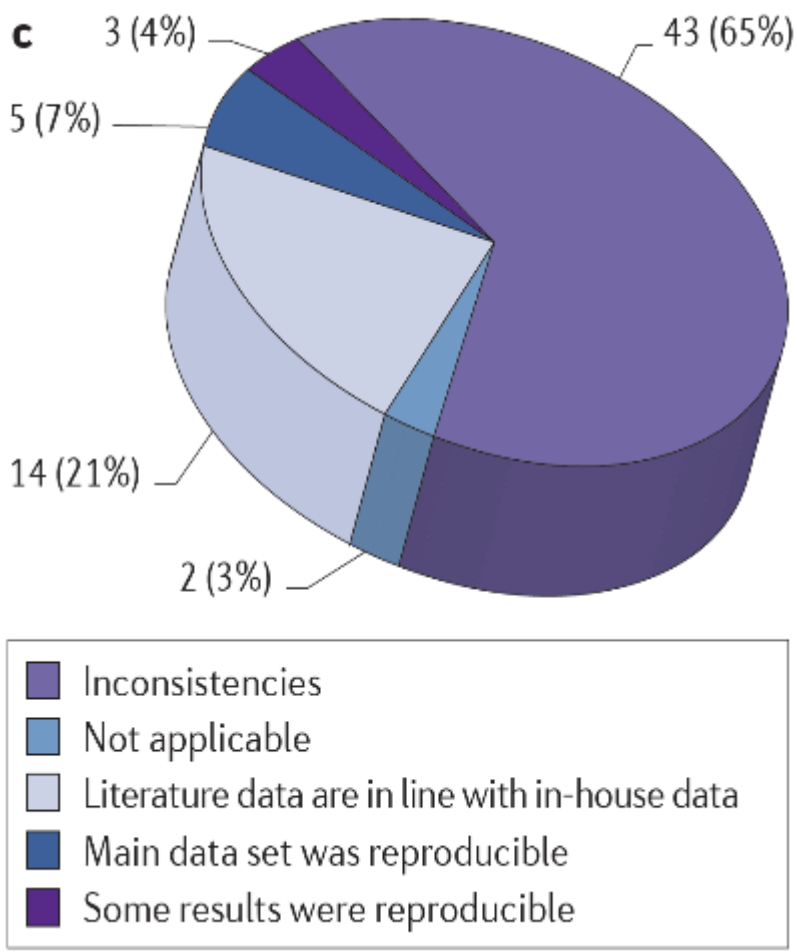
Reforming Science: Methodological and Cultural Reforms

NIH National Institu…

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

Prinz, Schlange and Asadullah
Bayer HealthCare

Nature Reviews Drug Discovery
2011; 10:712-713



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.

CHALLENGES TO RIGOR AND TRANSPARENCY IN REPORTING SCIENCE

- Science often viewed as self-correcting
  - Immune from reproducibility problems?
  - Principle remains true over the long-term
- Interrelated factors can short-circuit self-correction in the short- and medium-term,
  - Leads to reproducibility problem
  - Loss of time, money, careers, public confidence

FACTORS THAT "SHORT CIRCUIT" SELF-CORRECTION

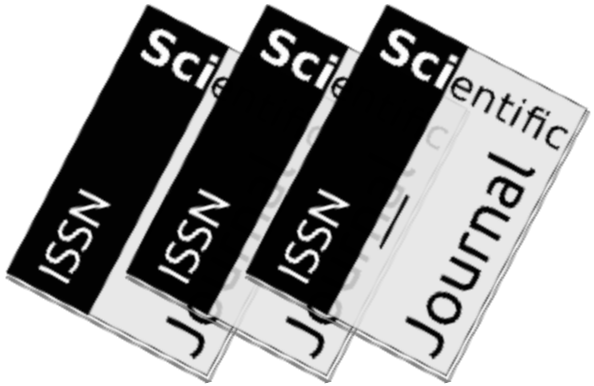
Current "hyper-competitive" environment fueled, in part, by:

- Historically low funding rates $$
- Grant review and promotion decisions depend too much on "high profile" publications

FACTORS THAT "SHORT CIRCUIT" SELF-CORRECTION

Publication practices:

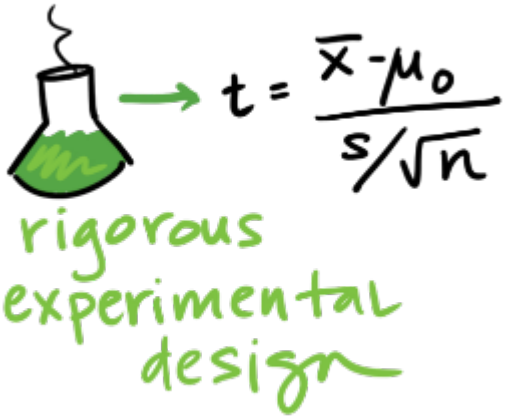
- Difficulty in publishing negative findings
- Overemphasis on the "exciting, big picture" finding sometimes results in publications leaving out necessary details of experiments



FACTORS THAT "SHORT CIRCUIT" SELF-CORRECTION

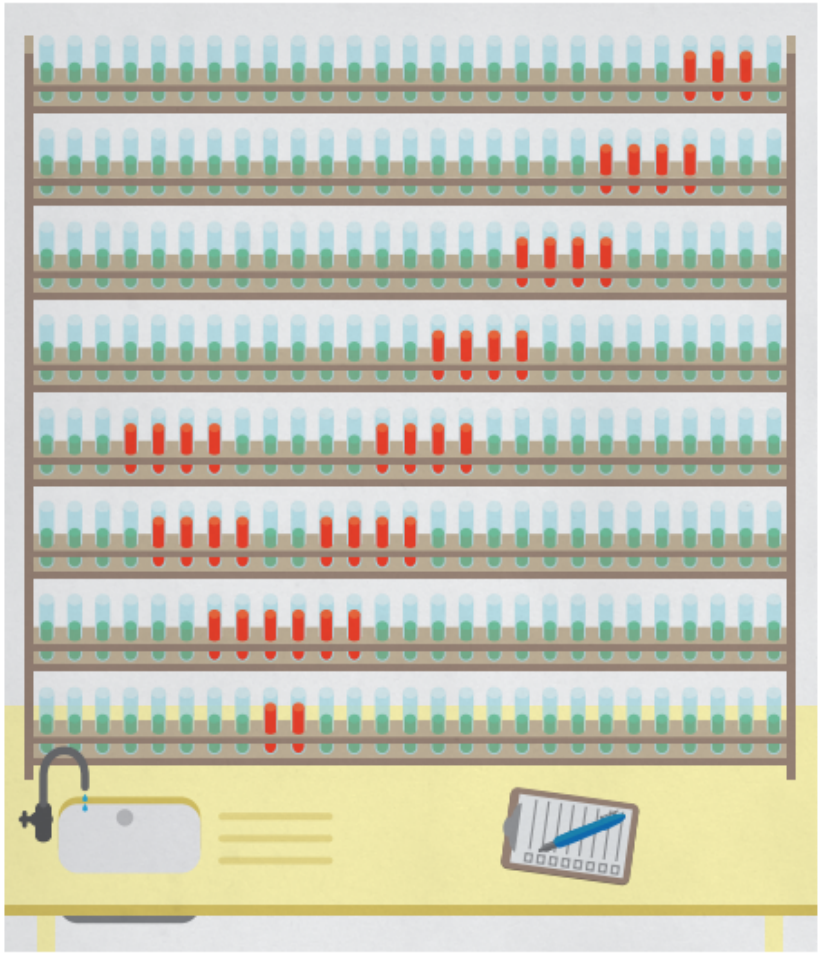
Poor training

- Inadequate experimental design
- Inappropriate use of statistics ("p-hacking")
- Incomplete reporting of resources used and/or unexpected variability in resources



OVERVIEW

- Why the concern about reproducibility?
- The NIH response
- Training and Resources



CHRIS RYAN/NATURE

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 scien
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viously 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.

> *"Efforts by the NIH alone will not be sufficient to effect real change in this unhealthy environment."*

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

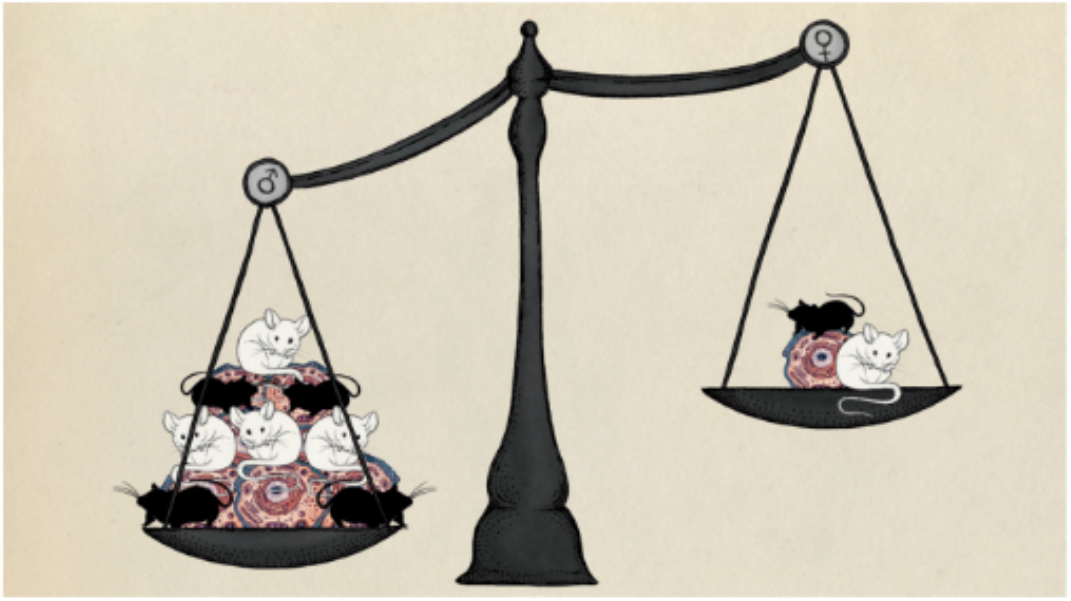

ILLUSTRATION BY KARIE SCOTT

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

"Over the course of FY 2015, NIH plans to roll out policies that will require applicants to address inclusion of both sexes in biomedical research."

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[3,4]

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-

ILLUSTRATION: PETER AND MARIA HOEY/WWW.PETERHOEY.COM

Corrected 19 December, 2014; see full text.

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A 2011 study of 122 different head and neck cancer cell lines revealed that 37 (30%) were misidentified

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NEW JOURNAL POLICIES TO ENHANCE REPRODUCIBILITY

Science

EDITORIAL

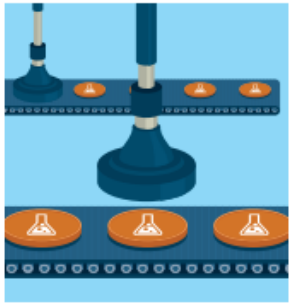
Journals unite for reproducibility

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 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.aa>"

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.

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PRINCIPLES AND GUIDELINES FOR REPORTING PRECLINICAL RESEARCH

- Rigorous statistical analysis
- Transparency in reporting
- Data and material sharing
- Consideration of refutations
- Consider establishing best practice guidelines for:
  - Antibodies
  - Cell lines
  - Animals

- Standards
- Replicates
- Statistics
- Randomization
- Blinding
- Sample size estimation
- Inclusion/exclusion criteria

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

OUR GUIDING PRINCIPLES FOR RIGOR & TRANSPARENCY

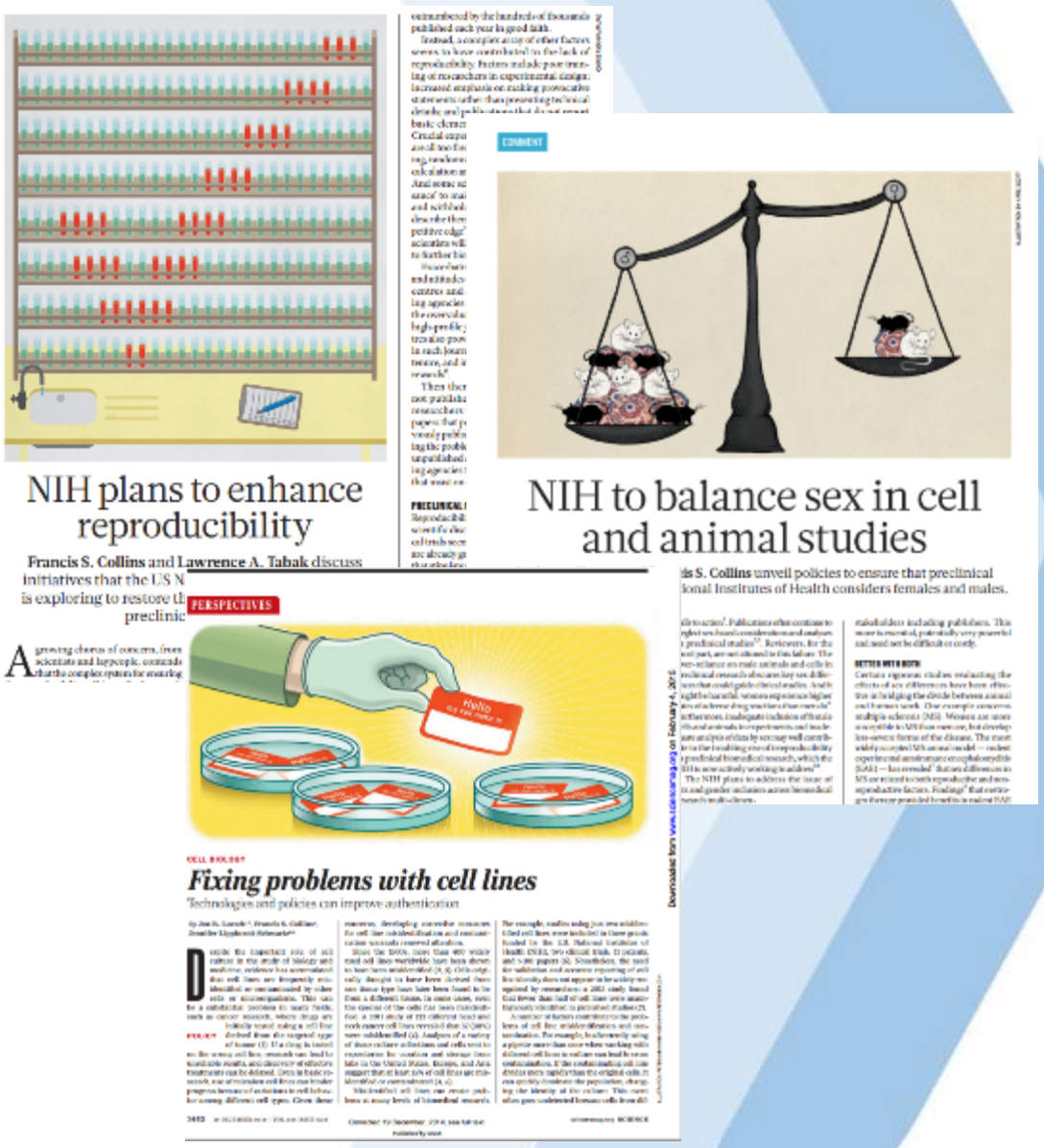
- C*larify* NIH's long-standing expectations regarding rigor and transparency in applications
- Raise awareness and begin culture shifts in the scientific community
- Prompt applicants to consider issues that they may have previously down-played or ignored

OUR GUIDING PRINCIPLES FOR RIGOR & TRANSPARENCY

- Improve the way that applicants describe their work; provide sufficient information for reviewers
- Demonstrate to our public stakeholders that NIH is seriously considering their concerns
- As always, ensure that NIH is investing in the best science and minimizing unnecessary burden

FOUR AREAS OF CLARIFICATION

- Scientific premise
- Scientific rigor
- Relevant Biological Variables, Such as Sex
- Authentication of Key Biological and/or Chemical Resources



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CELL BIOLOGY

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Technologies and policies can improve authentication

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

SCIENTIFIC PREMISE

The research used to form the basis for the proposed research question

- observations,
- preliminary data, or
- published literature

Consideration may include

- attention to the rigor of the previous experimental designs
- incorporation of relevant biological variables and authentication of key resources

SCIENTIFIC PREMISE
RESEARCH STRATEGY: SIGNIFICANCE

- Explain the importance of the problem or critical barrier to progress in the field that the proposed project addresses.
- 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.
- Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
- Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

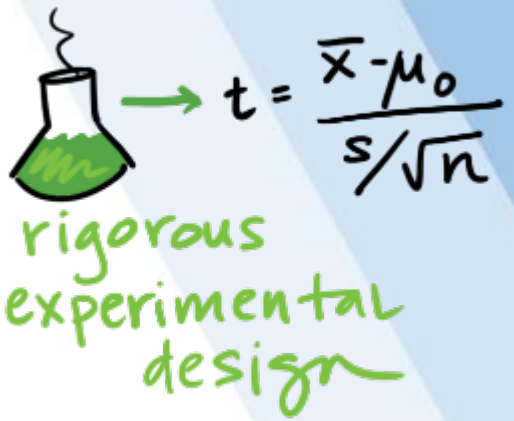
FAQ: WILL ATTENTION TO SCIENTIFIC PREMISE IMPEDE INNOVATION?

- Scientific premise refers to the key data introduced by the applicant to justify the project

- If preliminary data are not provided in an application, a critical assessment of the scientific literature that supports and/or contradicts the research question(s) can be provided

- Consideration of scientific premise can help investigators identify the risks and develop a research strategy that enhances the opportunity for success

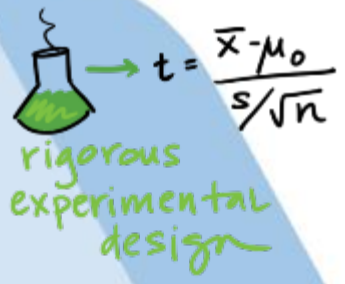
SCIENTIFIC RIGOR



- The strict application of the scientific method

- Robust results
  - obtained with solid, well-controlled experiments
  - capable of being reproduced under well-controlled conditions, using reported experimental details.
- Methods to reduce bias (examples)
  - multiple individuals record assessments,
  - define terminology in advance,
  - independent, blinded assessors, etc.

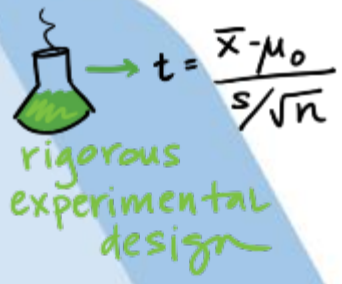
SCIENTIFIC RIGOR
RESEARCH STRATEGY: APPROACH



- Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project.
  Describe the experimental design and methods proposed and how they will achieve robust and unbiased results.

  Unless addressed separately in Item 15 (Resource Sharing Plan), include how the data will be collected, analyzed, and interpreted as well as any resource sharing plans as appropriate.
- Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.
- If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high risk aspects of the proposed work.

FAQ: HOW MUCH DETAIL DO I NEED TO INCLUDE TO ADDRESS SCIENTIFIC RIGOR?



- Succinctly state what is planned
  - Include information on samples numbers, blinding, powered studies, statistical analyses…
- Be transparent about your plans for analysis
- Stay within page limits

CONSIDERATION OF RELEVANT BIOLOGICAL VARIABLES, SUCH AS SEX

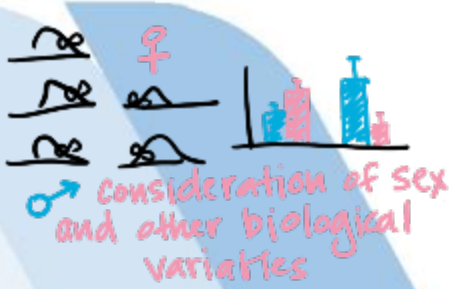
- Affect health or disease
  - sex,
  - age,
  - weight, and
  - underlying health conditions

- Should be factored into research designs, analyses, and reporting in vertebrate animal and human studies.
- Proposing to study one sex?
  - Need strong justification from the scientific literature, preliminary data, or other relevant considerations

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.
- If your study(s) involves human subjects, the sections on the Inclusion of Women and Minorities and Inclusion of Children can be used to expand your discussion on inclusion and justify the proposed proportions of individuals (such as males and females) in the sample, but it must also be addressed here in the Approach section.
- Please refer to NOT-OD-15-102 for further consideration of NIH expectations about sex as a biological variable.

FAQ: WILL I HAVE TO DOUBLE MY ANIMAL NUMBERS?



- Policy requires that you *consider* sex as a biological variable
- Justification should be provided if the application proposes to study one sex
  - sex-specific condition of phenomenon (e.g., ovarian or prostate cancer),
  - acutely scarce resources, or
  - sex-specific hypotheses possible due to known differences between males and females.
- Cost and absence of known sex differences are inadequate justifications for not addressing sex.

AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES

- Quality of resources is critical to the ability to reproduce results
- Key biological and/or chemical resources should be regularly authenticated to ensure identity and validity

- Key biological and/or chemical resources may or may not be generated with NIH funds and:
  - may differ from laboratory to laboratory or over time;
  - may have qualities and/or qualifications that could influence the research data; and
  - are integral to the proposed research.

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 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.
- Reviewers will assess the information provided in this Section. Any reviewer questions associated with key biological and/or chemical resource authentication will need to be addressed prior to award.

FAQ: WHAT SHOULD I INCLUDE IN MY AUTHENTICATION PLAN?

- Each investigator determines which resources are key to the proposed research
- Scientific societies and the research community encouraged to develop standard approaches
- Key resources refer to *established resources*
- If key resources have been obtained from an outside source, the investigator is still expected to provide their own plans
- Authentication plan is not scored, so if the application is meritorious, applicant may work with PO to address any deficiencies prior to award

RPPR

- NOT-OD-16-031 (published12/15/2015)
- Rigor addition to RPPR instructions: 1/25/2016
  - B.2 What was accomplished under these goals?
  - B.6 What do you plan to do for the next reporting period to accomplish the goals?
- These RPPR updates for rigor and transparency:
  - Prepare non-competing renewals for the next competitive renewal, and
  - Will help NIH implement and evaluate the policy for both current and new awards.

OVERVIEW

- Why the concern about reproducibility?
- The NIH response
- Training and Resources

TRAINING

- Need for more training on day-to-day basis
- Focus on rigor & transparency
- Separate from RCR

TRAINING

- NIH will require a description of instruction in the design and conduct of rigorous experiments.
  - Institutional training
  - Institutional career development
  - Individual fellowships

- Additional guidance on training requirements will be forthcoming for FY17, see NOT-OD-16-034

Clearinghouse for Training

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

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Basic Discoveries for Better Health

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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

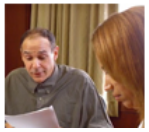
In order to reproduce someone else's findings adequately, the experimental methods, rationale and other pertinent information must be accessible and understandable. This module highlights the need to include all relevant details in publications to ensure that other studies are able to build upon the 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 in permitting reliable statistical testing. This module presents the importance of blinding and randomization, as well as the impact of issues that may introduce bias, such as pressure to publish.

Blinding and Randomization Discussion Material [PDF, 104KB]



Module 3: Biological and Technical Replicates

Including replicates in the experimental process is essential to ensuring the most rigorous research approach. In this module, reviewers discuss a figure included in a grant application and the potential significance of the finding, which leads to a brief conversation about the differences between biological and technical replicates.

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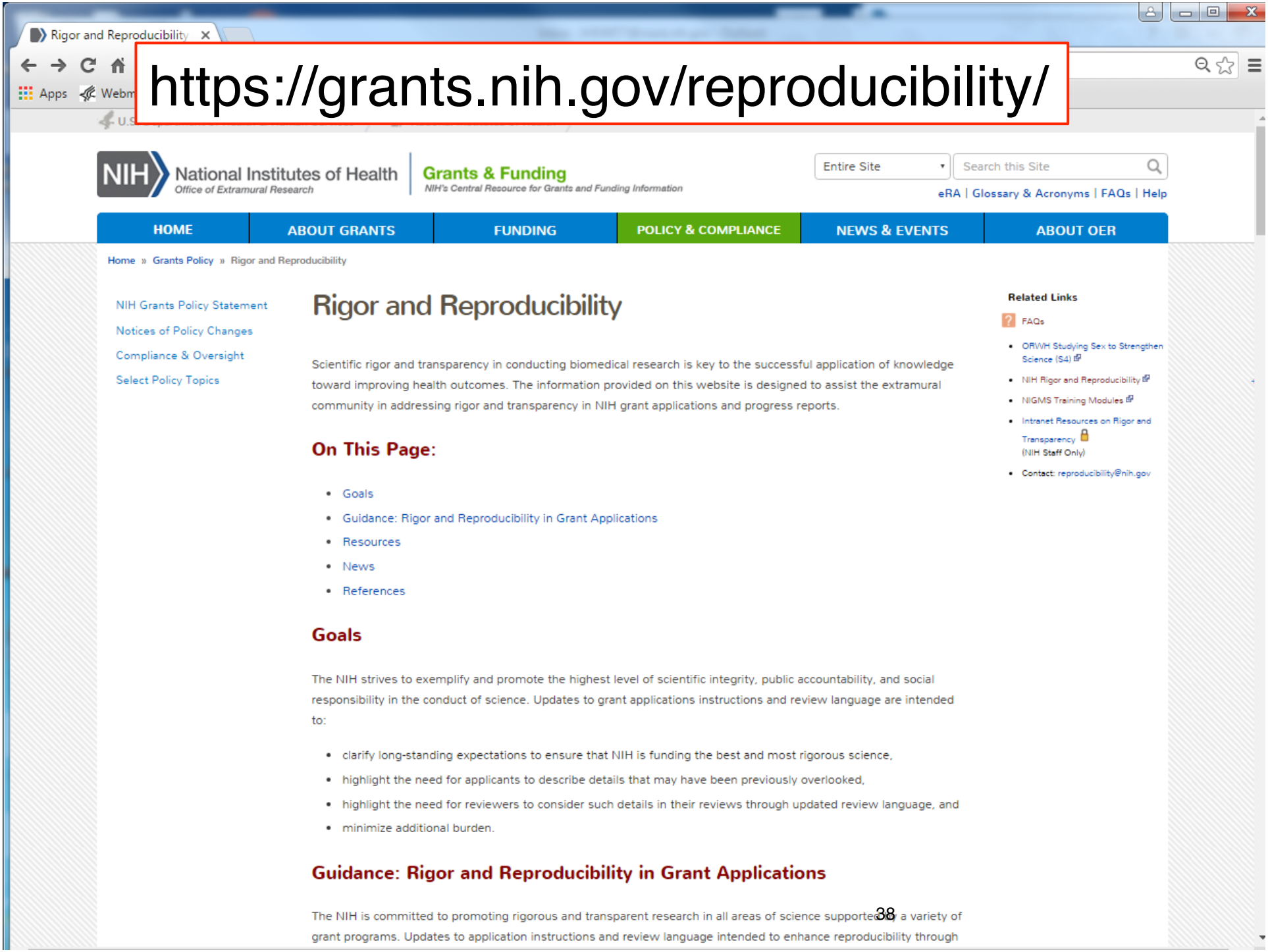
Related Information

NIH Reproducibility Workshops on Modern Technologies: Potentials and Pitfalls

- Cell Biology
- Structural Biology


Rigor and Reproducibility
https://grants.nih.gov/reproducibility/
NIH National Institutes of Health
Office of Extramural Research
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Home » Grants Policy » 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.
Guidance: Rigor and Reproducibility in Grant Applications
The NIH is committed to promoting rigorous and transparent research in all areas of science supported by a variety of grant programs. Updates to application instructions and review language intended to enhance reproducibility through
Related Links
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

RIGOR UPDATES INFOGRAPHIC

NEW GRANT GUIDELINES

what you need to know

WHY UPDATE THE GUIDELINES?

The updates focus on four areas deemed important for enhancing rigor and transparency:

1. **PREMISE** — The scientific premise forming the basis of the proposed research
2. **DESIGN** — Rigorous experimental design for robust and unbiased results
3. **VARIABLES** — Consideration of relevant biological variables
4. **AUTHENTICATION** — Authentication of key biological and/or chemical resources

Send inquiries to reproducibility@nih.gov

See also NIH Notice NOT-OD-16-011
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-011.html

WHAT ARE THE UPDATES?

1 UPDATES TO RESEARCH STRATEGY GUIDANCE

The research strategy is where you discuss the significance, innovation, and approach of your research plan. Let's look at an R01, for example:

The new **research strategy** guidelines require that you:

- State the strengths and weakness of published research or preliminary data crucial to the support of your application
- Describe how your experimental design and methods will achieve robust and unbiased results
- Explain how biological variables, such as sex, are factored into research design and provide justification if only one sex is used

2 NEW ATTACHMENT FOR AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES

From now on, you must briefly describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies.

These include, but are not limited to:

CELL LINES · ANTIBODIES · SPECIALTY CHEMICALS · 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.

- **DO NOT** put experimental methods or preliminary data in this section
- **DO** focus on authentication and validation of key resources

3 NEW REVIEWER GUIDELINES

Here are the additional criteria the reviewers will be asked to use:

- Is there a **strong scientific premise** for the project?
- Have the investigators presented adequate plans to address **relevant biological variables**, such as sex, for studies in vertebrate animals or human subjects?
- Have the investigators presented strategies to ensure a **robust and unbiased approach**, as appropriate for the work proposed?

Reviewers will also be asked to comment on that new attachment (see **Update 2**)!

NIH POLICY: ENHANCING REPRODUCIBILITY THROUGH RIGOR AND TRANSPARENCY

Module 1: General Policy Overview

THANK YOU!

QUESTIONS?

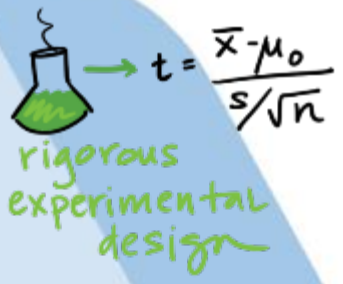
reproducibility@nih.gov

ADDITIONAL INFORMATION

SCIENTIFIC PREMISE
SIGNIFICANCE – REVIEW QUESTIONS

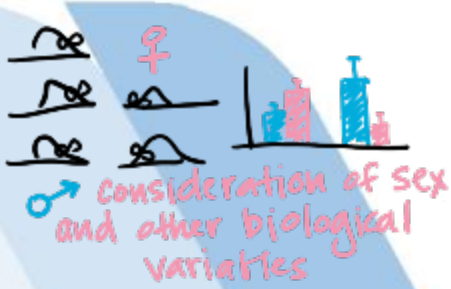
- Does the project address an important problem or a critical barrier to progress in the field?
- Is there a strong scientific premise for the project?
- If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved?
- How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

SCIENTIFIC RIGOR
APPROACH – REVIEW QUESTIONS



- Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project?
- Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed?
- Are potential problems, alternative strategies, and benchmarks for success presented?
- If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed?

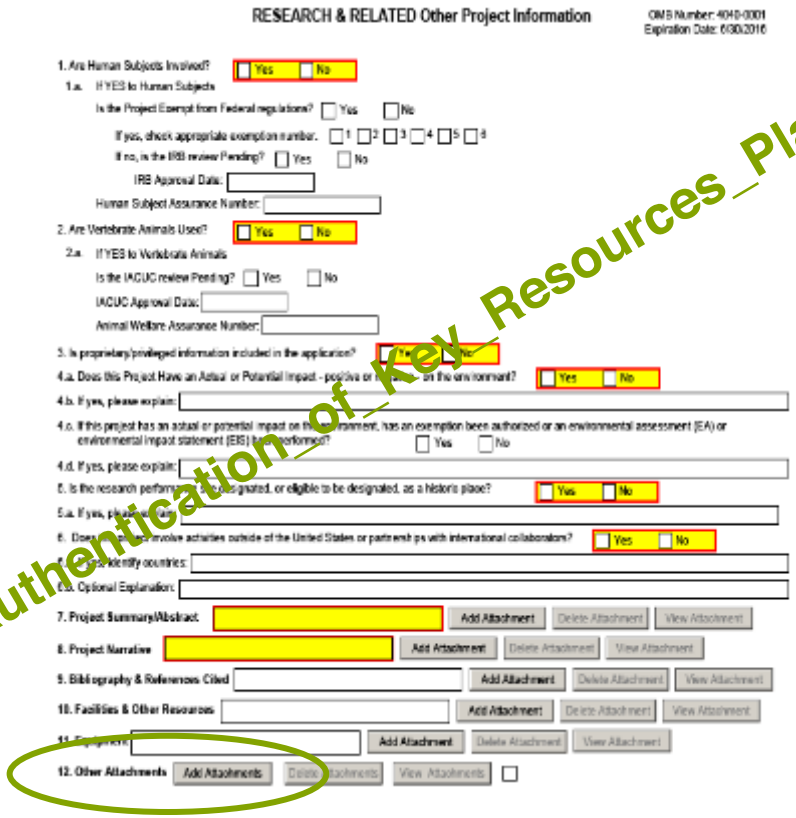
RELEVANT BIOLOGICAL VARIABLES
APPROACH – REVIEW QUESTIONS



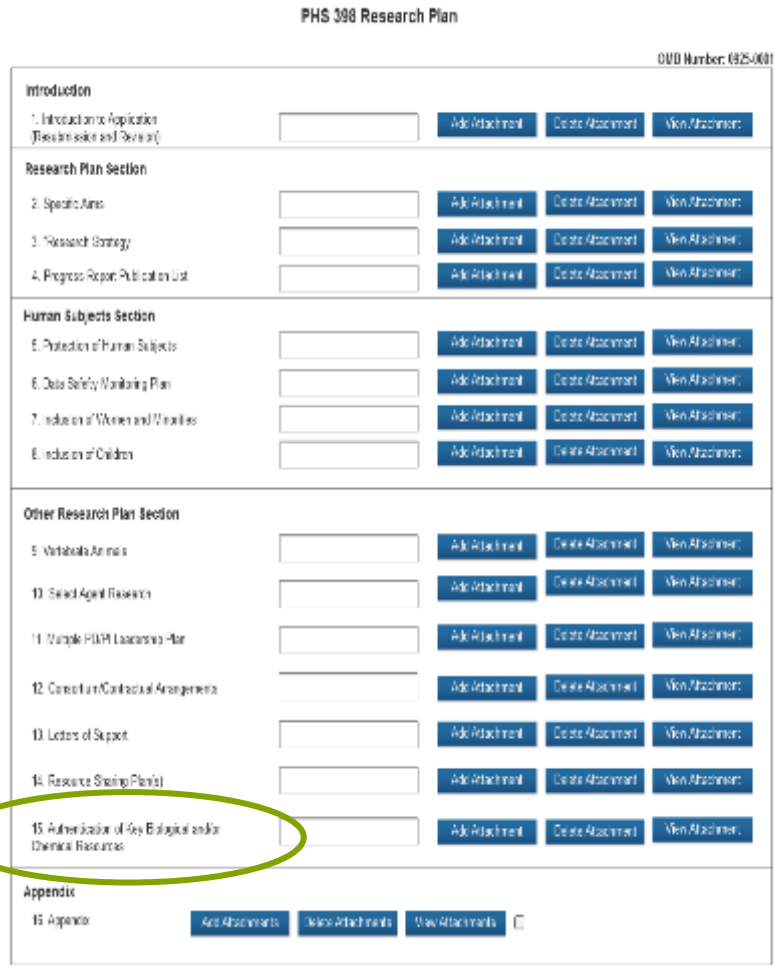
- Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

AUTHENTICATION PLAN ATTACHMENT

01/25/16 – 05/24/16



05/25/2016 & BEYOND



Authentication_of_Key_Resources_Plan.pdf

AUTHENTICATION OF KEY RESOURCES

ADDITIONAL REVIEW CONSIDERATION

- 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.