

Rigor and Reproducibility: A Resource for the NIH Training Plan

Resources Compiled by the
Office of Research Integrity
Office of Research, Economic Development, and Knowledge Enterprise
The University of Texas at San Antonio

Questions? Contact Dr. Michelle Stevenson:
michelle.Stevenson@utsa.edu
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Background

- Problem: Difficulty in interpreting and reproducing studies due to lack of transparency and scientific rigor.
- Many NIH workshops; led to consensus of key principles
- Incorporated into research grants, career development awards, training grants, and fellowships (5/25/2020)
 - Rigor of the Prior Research (*Research Strategy: Significance, Approach*)
 - Scientific Rigor of the Proposed Research (*Research Strategy, Approach*)
 - How will the proposed research achieve robust and unbiased results?
 - Biological Variables (*Research Strategy, Approach*)
 - How are relevant biological variables, such as sex, factored into research designs and analyses?
 - Authentication of Biological and/or Chemical Resources (*Other Research Plan*)
 - Examples: cell lines, specialty chemicals antibodies, other biologics
- Funding Opportunity Announcements may have different requirements
- Questions? Email reproducibility@nih.gov

Topics for Training Modules

- Preparing your NIH Grant Proposal
- Improving Reproducibility in Research
- Importance of Transparency
- Blinding and Randomization
- Biological and Technical Replicates
- Sample Size, Outliers, and Exclusion Criteria
- Integrating Sex into Research Design to Improve Scientific Rigor
- Controls in Animal Studies for Rigor and Reproducibility
- Group Randomized Trials in Public Health and Medicine

Preparing Your NIH Grant Proposal

- [Examples of Scientific Rigor and Authentication Plans](#)
- [NIH's FAQs on Rigor and Reproducibility](#)
- [Policy on the Inclusion of Women in Clinical Research](#)
- [The Experimental Design Assistant](#)
- [The EQUATOR Network](#) for Quality and Transparency in Publications

NIH ENHANCING REPRODUCIBILITY GUIDELINES

what you need to know

WHAT ARE THE FOUR ELEMENTS OF RIGOR?

1

RIGOR OF THE PRIOR RESEARCH

2

RIGOR OF THE PROPOSED RESEARCH

3

BIOLOGICAL VARIABLES

4

AUTHENTICATION


Send inquiries to reproducibility@nih.gov

See also NIH Notice NOT-OD-18-228 <https://grants.nih.gov/grants/guide/notice-files/NOTOD-18-228.html>


WHERE IN THE APPLICATION?

1 RESEARCH STRATEGY


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




Introduction to Resubmission and Revision Applications




Specific Aims



Research Strategy



Progress Report Publication List



Vertebrate Animals

- Describe the strengths and weaknesses in the rigor of the prior research that serves as key support.
- Describe plans to address weaknesses in the rigor of the prior research.
- Describe how your experimental design and methods will achieve robust and unbiased results.
- Explain how relevant biological variables, such as sex, are factored into research designs and analyses.

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

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

SPECIALTY CHEMICALS

ANTIBODIES

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 REVIEW GUIDELINES

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

- Is the prior research that serves as the key support for the proposed project rigorous?
- Have the investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project?
- Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed?
- Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

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

Enhancing Reproducibility in NIH Applications: Resource Chart

NIH Grants Policy Website: <https://grants.nih.gov/reproducibility/index.htm>
 NIH Website: <https://www.nih.gov/research-training/type-reproducibility>

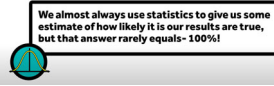
4 AREAS OF FOCUS	WHAT DOES IT MEAN?	WHERE SHOULD IT BE INCLUDED IN THE APPLICATION?
Rigor of the Prior Research	<p>A careful assessment of the rigor of the prior research that serves as the key support for a proposed project will help applicants identify any weaknesses or gaps in the line of research.</p> <p>Describe the strengths and weaknesses in the rigor of the prior research (both published and unpublished) that serves as the key support for the proposed project.</p> <p>Describe plans to address weaknesses in the rigor of the prior research that serves as the key support for the proposed project.</p> <p style="font-size: x-small;">*See related FAQs, blog post</p>	<p>Research Strategy</p> <ul style="list-style-type: none"> ➢ Significance ➢ Approach
Scientific Rigor (Design)	<p>Scientific rigor is the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation and reporting of results.</p> <p>Emphasize how the experimental design and methods proposed will achieve robust and unbiased results.</p> <p style="font-size: x-small;">*See related FAQs, blog post, examples from pilots</p>	<p>Research Strategy</p> <ul style="list-style-type: none"> ➢ Approach
Biological Variables	<p>Biological variables, such as sex, age, weight, and underlying health conditions, are often critical factors affecting health or disease. In particular, sex is a biological variable that is frequently ignored in animal study designs and analyses, leading to an incomplete understanding of potential sex-based differences in basic biological function, disease processes and treatment response.</p> <p>Explain how relevant biological variables, such as the ones noted above, are factored into research designs, analyses, and reporting in vertebrate animal and human studies. Strong justification from the scientific literature, preliminary data or other relevant considerations must be provided for applications proposing to study only one sex.</p> <p style="font-size: x-small;">*See related FAQs, blog posts, article</p>	<p>Research Strategy</p> <ul style="list-style-type: none"> ➢ Approach
Authentication	<p>Key biological and/or chemical resources include, but are not limited to, cell lines, specialty chemicals, antibodies and other biologics.</p> <p>Briefly describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies. These resources may or may not have been generated with NIH funds and:</p> <ul style="list-style-type: none"> • may differ from laboratory to laboratory or over time; • may have qualities and/or qualifications that could influence the research data; • are integral to the proposed research. <p>The authentication plan should state in one page or less how you will authenticate key resources, including the frequency, as needed for your research. Note: Do not include authentication data in your plan.</p> <p style="font-size: x-small;">*See related FAQs, blog post, examples</p>	<p>Other Research Plan Section</p> <ul style="list-style-type: none"> ➢ Include as an attachment ➢ Do not include in the Research Strategy.

**This chart is based on general instructions for research grant applications submitted for January 25, 2019 due dates and beyond. It should only be used as a guide. For all applications, please read the applicable Funding Opportunity Announcement (FOA) & Application Guide for specific instructions.

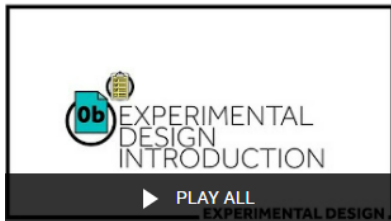
Improving Reproducibility in Research

I. Introduction

SERIES INTRODUCTION



II. Experimental Design (18 videos)



III. Analysis & Reporting (13 videos)



Credit: Aaron Carroll, Indiana University School of Medicine, R25 GM116146; @aaronecarroll

Importance of Transparency

Instructional Video



Instructional Resources

[Instructor's Guide](#)

Sample Articles

[Landis et al., 2012](#)

[Prager et al., 2019](#)

[Percie du Sert et al., 2020](#)

Credit: National Institutes of Health Office of the Director, Rigor & Reproducibility Training Modules

Blinding and Randomization

Instructional Video



Instructional Resources

[Instructor's Guide](#)

Sample Articles

[Monaghan et al., 2021](#)

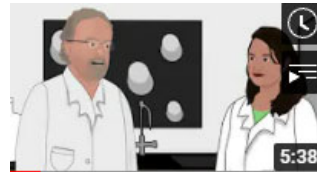
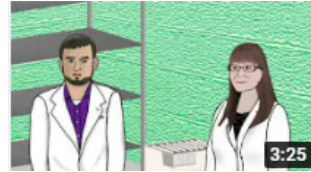
[Suresh, 2011](#)

[Festing & Altman, 2002](#)

[Schulz & Grimes, 2002](#)

Credit: National Institutes of Health Office of the Director, Rigor & Reproducibility Training Modules

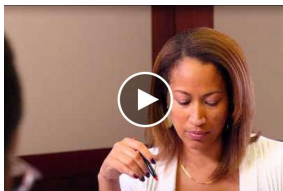
Instructional Videos



Credit: Stats in the Lab vignettes; Indiana University School of Public Health-Bloomington & University of Alabama – Birmingham; R25 GM116167

Biological and Technical Replicates

Instructional Video



Instructional Resources

[Instructor's Guide](#)

Sample Articles

[Blainey, Krzywinski, & Altman, 2014](#)

Credit: National Institutes of Health Office of the Director, Rigor & Reproducibility Training Modules

Instructional Video



Credit: Stats in the Lab vignettes; Indiana University School of Public Health-Bloomington & University of Alabama – Birmingham; R25 GM116167

Sample Size, Outliers, and Exclusion Criteria

Instructional Video



Instructional Resources

[Instructor's Guide](#)

Credit: National Institutes of Health Office of the Director, Rigor & Reproducibility Training Modules

Integrating Sex into Research Design to Improve Scientific Rigor

1. [Advancing Understanding of Health and Disease](#) - Dr. Chloe Bird, 9/26/2017
2. [Importance of Sex as a Variable](#) – Dr. Gillian Einstein, 4/2/2015
3. [Understanding Disease in Males and Females](#) – Dr. Arthur Arnold, 4/2/2015
4. [Challenging Assumptions about Sex](#) – Dr. Larry Cahill, 4/22/2015
5. [Understanding Gender in Research](#) – Dr. Londa Schiebinger, 4/22/2015
6. [Avoiding the Pitfalls of Selection Bias in BSSR](#) – Dr. Carl Bergstrom, 1/21/21
7. [NIH Review Standard for SABV](#) (Sex as a Biological Variable)
8. [Relevant Journal Articles](#)

Credits: 1-5, 8: NIH Office of Research on Women's Health; 6: NIH Office of Behavioral and Social Sciences Research

Controls in Animal Studies for Rigor & Reproducibility

- [Complete Instructional Handbook](#) (202 pages)
 - Lesson plan, lecture notes, slides, handouts, activities
- [Student Guide](#) (76 pages)
 - Editable student companion to the Instructional Handbook
- Experimental Design
 - [ppt slides](#)
 - [video](#)
- Analyzing Results
 - [ppt](#)
 - [video](#)
- Reporting Results
 - [ppt](#)
 - [video](#)

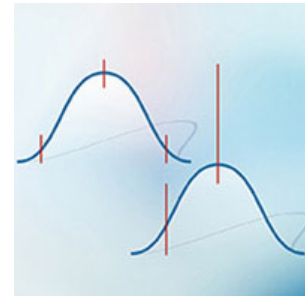
Credit: American Physiological Society, R25 GM116166, January 2019; Hosted by LifeSciTRC.org

Group-Randomized Trials in Public Health & Medicine

Access the 7-part course [here](#), including videos and activities

1. [Introduction and Overview](#)
2. [Designing the Trial](#)
3. [Analysis Approaches](#)
4. [Power and Sample Size](#)
5. [Examples](#)
6. [Review of Recent Practices](#)
7. [Alternative Designs](#)

[Course References and Suggested Reading](#)



Credit: NIH Office of Disease Prevention