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

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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**

#### 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:
   - The research strategy guidelines require that you:
     - 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.
     - Elaborate on relevant biological variables, such as sex, for studies in vertebrate animals or human subjects.

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
     - Antibodies
     - Specialty chemicals
     - Other biologics
     - Standard laboratory reagents that are not expected to vary but may need to be included in the plan. Examples are buffers and other common biologicals or chemicals.

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?

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### Enhancing Reproducibility in NIH Applications: Resource Chart

**NIH-Grants Policy Website:** [http://grants.nih.gov/grants/research/reputation.htm](http://grants.nih.gov/grants/research/reputation.htm)

**NIH Website:** [https://nih.gov/research/reproducibility](https://nih.gov/research/reproducibility)

**4 AREAS OF REVIEW**

<table>
<thead>
<tr>
<th>Area of Review</th>
<th>What Does It Mean?</th>
<th>Where Should It Be Included in the Application?</th>
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</thead>
<tbody>
<tr>
<td>Rigor of the Prior Research</td>
<td>A specific assessment of the rigor of the prior research that serves as the key support for a proposed project, which also applies to identify any weaknesses or gaps in the rigor of research.</td>
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<tr>
<td></td>
<td>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.</td>
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<td></td>
<td>Describe plans to address weaknesses in the rigor of the prior research that serves as the key support for the proposed project.</td>
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<td><strong>Note:</strong> Follow the format.</td>
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<tr>
<td>Scientific Rigor (Design)</td>
<td>Scientific rigor is the critical application of the experimental methods to achieve robust and unbiased experimental design, methodology, analysis, interpretation, and reporting of results.</td>
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<tr>
<td></td>
<td>Emphasis here is the experimental design and method used to achieve robust and unbiased results.</td>
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<td><strong>Note:</strong> Follow the format.</td>
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<tr>
<td>Biological Variants</td>
<td>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 outcomes.</td>
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<td></td>
<td>Explain how relevant biological variables, such as the ones listed above, are fostered into research designs, analyses, and reporting in vertebrate animal and human studies. Stipulation from the scientific literature, preliminary data, or other relevant considerations must be provided for applications proposing to study sex or age.</td>
<td></td>
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<tr>
<td></td>
<td><strong>Note:</strong> Follow the format.</td>
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<tr>
<td>Authentication</td>
<td>Key biological and/or chemical resources are crucial, but are not included, cell lines, specialty chemicals, antibodies, and other biologicals.</td>
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<tr>
<td></td>
<td>Briefly describe methods to ensure the identity and validity of any biological and/or chemical resources used in the proposed studies. These resources may be obtained from commercial sources.</td>
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<tr>
<td></td>
<td>Include as an attachment if not described in the text.</td>
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</tbody>
</table>

**Notes:**

- The resource chart is based on general instructions for research grant applications submitted for January 24, 2022 due dates and should only be used as a guide.
- For additional instructions, please refer to the applicable Funding Opportunity Announcement (FOA) & Application Guide for specific instructions.
Improving Reproducibility in Research

I. 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 Videos

Instructional Resources

Instructional Videos

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

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 Video

Instructional Resources

Instructional Resources

Sample Articles

Blainey, Krzywinski, & Altman, 2014

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

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