NIH Update Following ACD Recommendations on Enhancing Rigor, Transparency, and Translatability in Animal Research

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NIH Advisory Committee to the Director (ACD) Meeting (Virtual)
June 9, 2022

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Recommendations: Five Themes

1. Improve Study Design and Analytic Rigor

2. Address Bias, Incomplete Reporting and Questionable Research Practices

5. Measure and Evaluate Effectiveness and Costs

3. Improve Relevance and Use of Animal Models

4. Improve Methodologic and Results Reporting

Overview

- EAWG detailed review of recommendations
- DPCPSI ORIP NOSI and concept clearance on rigor, reproducibility, and translatability of animal research
- Planned workshops
- Existing resources and opportunities to better leverage them
- Ongoing efforts to enhance rigor and peer review
- Shorter-term considerations for discussion

EAWG = Extramural Activities Working Group
DPCPSI ORIP = Division of Program Coordination, Planning, and Strategic Initiatives
NOSI = Notice of Special Interest

Notice of Special Interest (NOSI): Development of Resources and Technologies for Enhancing Rigor, Reproducibility, and Translatability of Animal Models in Biomedical Research

Notice Number:

NOT-OD-22-039

Key Dates

Release Date:	December 7, 2021
First Available Due Date:	February 16, 2022
Expiration Date:	May 08, 2024

Related Announcements

PAR-21-167 - Development of Animal Models and Related Biological Materials for Research (R21 Clinical Trial Not Allowed)

Issued by

Division of Program Coordination, Planning and Strategic Initiatives, Office of Research Infrastructure Programs (ORIP)

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-039.html

ORIP NOSI Goals

- Exploratory/developmental and highly innovative projects aimed at developing broadly applicable technologies, tools, and resources for validating animal models and enhancing the rigor, reproducibility, and translatability of animal research
- [Proposals] … must either address research interests of multiple NIH ICs, explore multiple body or organ systems, or be applicable to diseases and processes that impact multiple body or organ systems.

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-039.html

Concept Clearance

- DPCPSI ORIP presented to Council of Councils on May 19, 2022
- Grant mechanisms
  - 2-year R21
  - 5-year R01
  - 4-year R24 and U24
  - Small business
- Proposed projects must demonstrate how proposed resources and technologies will impact rigor and reproducibility of animal studies

https://dpcpsi.nih.gov/sites/default/files/Day1-1150AM-ORIP-Concept-Rigor-Reproducibility-Zou-slidesREV.pdf
https://dpcpsi.nih.gov/sites/default/files/Day1-1150AM-ORIP-Concept-Rigor-Reproducibility-Zou-background-508.pdf

Other Planned Workshops

- ORIP: animal models and related resources for COVID research
  - Leverages NIH-wide portfolio analysis
- ORIP: enhance rigor and reproducibility by managing extrinsic factors
  - Assess equipment, instrumentation, and extramural construction projects
- National Academies Institute for Laboratory Animal Research (ILAR) project on effective communication with the general public about scientific research that requires work with animals

Existing Resources

Statistical Topics for Reproducible Animal Research

Andrew W. Brown and David B. Allison, Indiana University School of Public Health-Bloomington; Tapan Mehta and Stephen Watts, University of Alabama at Birmingham, R25 GM116167

Preclinical research involving animal models can be improved when appropriate experimental, analytical, and reporting practices are used. We produced a series of animated vignettes with quantitative experts and laboratory scientists discussing aspects of study design, interpretation,

Controls in Animal Studies for Rigor and Reproducibility

Christina N. Bennett and Marsha Lakes Matyas, American Physiological Society, R25 GM116166

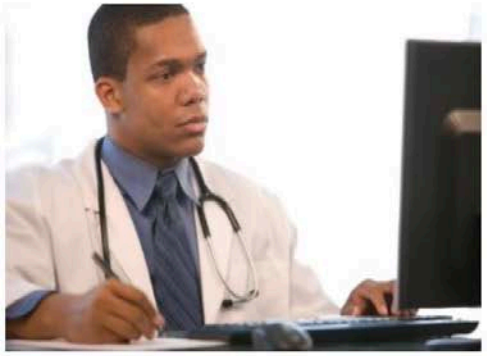
This teaching module was designed to help biomedical researchers understand the changing standards of practice for studies using animals as research models. This module is comprised of three sections that focus on developing strong skills in designing animal studies, analyzing results from those studies, and reporting findings that are reproducible. Modules are designed to be used by higher education institutions, laboratory groups, individuals, and professional societies.

https://www.nigms.nih.gov/training/pages/clearinghouse-for-training-modules-to-enhance-data-reproducibility.aspx#statistical-topics-for-reproducible-animal-research

Highlighting Other Resources

Resources for Preparing Your Application

Learn how to prepare a rigorous application with select excerpts of rigor from awarded applications, authentication plan examples, and resources like the experimental design assistant (EDA), guidance on sample size calculation, and more.



Training and Other Resources

Resources and training on many aspects of rigor and reproducibility, including sex as a biological variable, research methods, reviewer guidance and more.

OFFICE-LED PROJECT

The Experimental Design Assistant - EDA

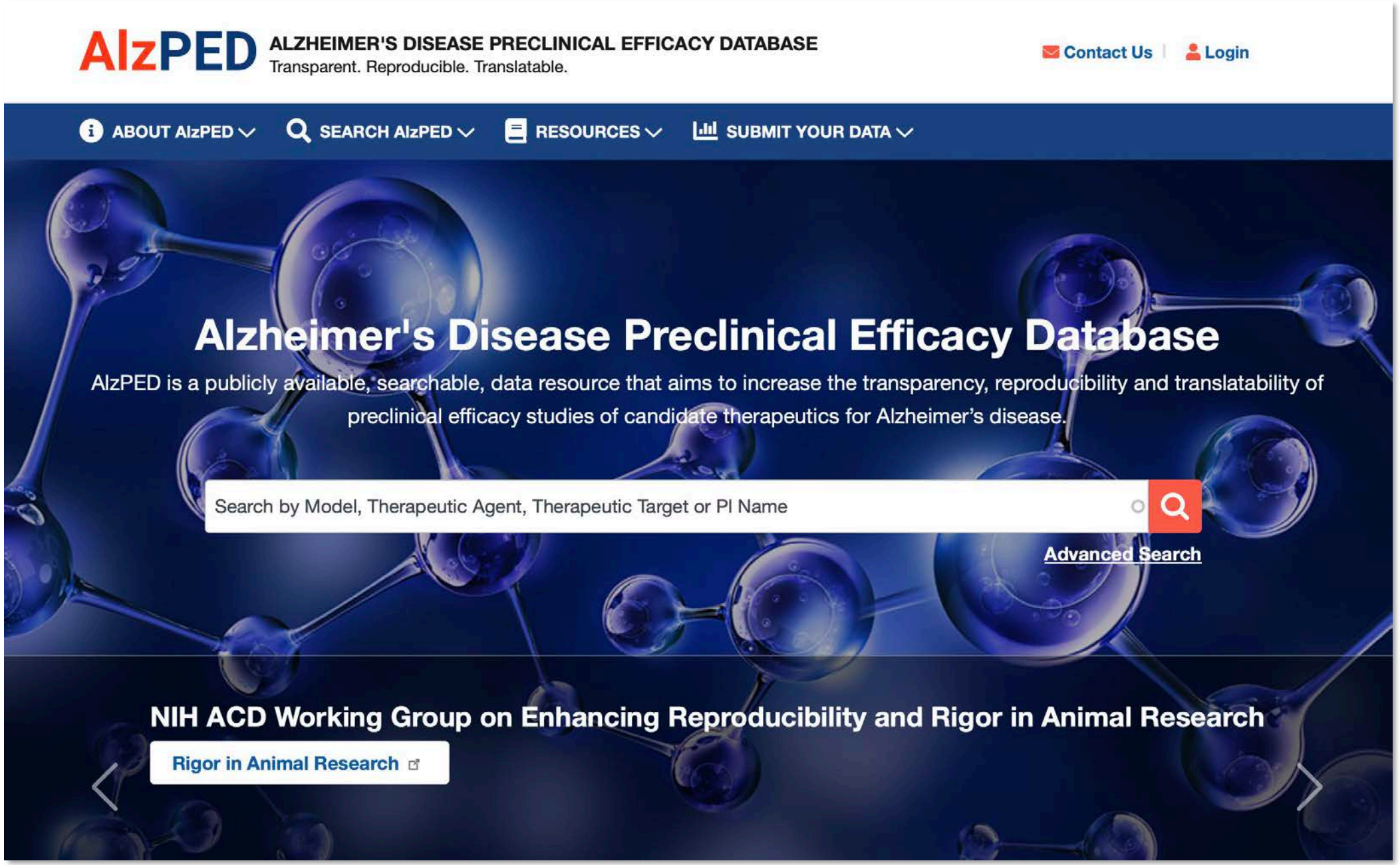
Contents

- Overview
- Publications

Overview

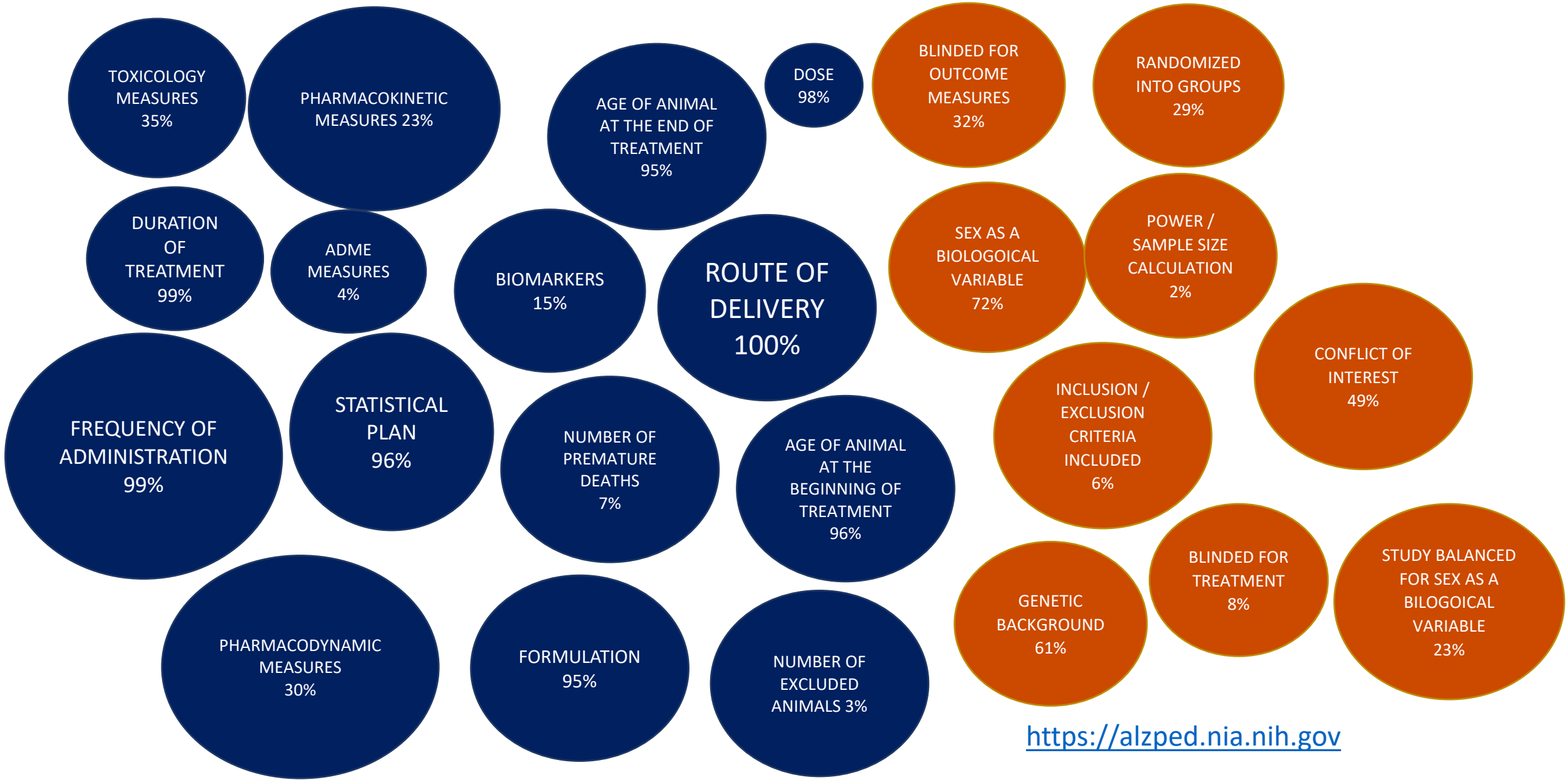
EDA

https://grants.nih.gov/policy/reproducibility/index.htm
https://www.nc3rs.org.uk/our-portfolio/experimental-design-assistant-eda



https://alzped.nia.nih.gov

View Reporting for Experiment Design



https://alzped.nia.nih.gov

Preclinical validation of a potent γ-secretase modulator for Alzheimer's disease prevention

BIBLIOGRAPHIC | THERAPEUTIC AGENT | ANIMAL MODEL | EXPERIMENTAL DESIGN | OUTCOMES

Bibliographic

Year of Publication: 2021

Experimental Design

Is the following information reported in the study?:

✗ Power/Sample Size Calculation	✓ Randomized into Groups
✓ Blinded for Treatment	✓ Blinded for Outcome Measures
✓ Pharmacokinetic Measures	✓ Pharmacodynamic Measures
✓ Toxicology Measures	✓ ADME Measures
✓ Biomarkers	✓ Dose
✓ Formulation	✓ Route of Delivery
✓ Duration of Treatment	✓ Frequency of Administration
✓ Age of Animal at the Beginning of Treatment	✓ Age of Animal at the End of Treatment
✓ Sex as a Biological Variable	✓ Study Balanced for Sex as a Biological Variable
✗ Number of Premature Deaths	✗ Number of Excluded Animals
✓ Statistical Plan	✓ Genetic Background
✗ Inclusion/Exclusion Criteria Included	✓ Conflict of Interest

https://alzped.nia.nih.gov/preclinical-validation-potent

Ongoing Rigor Efforts

- CSR Advisory Council Workgroup on Simplifying Review Criteria
  - Focus on what's important: five to three criteria
    - Should it be done? → Importance of the science
    - Can it be done well? → Feasibility and rigor
    - Will it be done? → Investigators and environment
  - Further ACD discussion later this year
- NIH Data Management and Sharing Policy (later this ACD)

https://public.csr.nih.gov/sites/default/files/presentations/200330/Simplifying_Review_Criteria_Workgroup_Interim_Rpt_final.pdf

NINDS Activities

Funding Opportunity Title	Creating an Educational Nexus for Training in Experimental Rigor (CENTER) (UC2 Clinical Trial Not Allowed)

Funding Opportunity Title	Materials to Enhance Training in Experimental Rigor (METER) (UE5 Clinical Trial Not Allowed)

[These] Funding Opportunity Announcements (FOAs) … together aim to facilitate teaching of fundamental principles of rigorous biomedical research by developing an innovative online educational resource for use by a broad range of researchers in an array of learning environments.

https://grants.nih.gov/grants/guide/rfa-files/RFA-NS-21-009.html
https://grants.nih.gov/grants/guide/rfa-files/RFA-NS-21-033.html

Catalyzing Communities of Research Rigor Champions

A Workshop Hosted by the NINDS Office of Research Quality

May 23-24, 2022
NIH Campus, Bethesda, MD

https://www.infinityconferences.org/ResearchRigorChampions

Co-Chairs:

Steven Goodman, Stanford University

Veronique Kiermer, PLOS

https://www.ninds.nih.gov/news-events/events/ninds-workshop-catalyzing-communities-research-rigor-champions
https://videocast.nih.gov/watch=45245; https://videocast.nih.gov/watch=45247

Possible Short to Intermediate Efforts

- Guide Notice to encourage use of ARRIVE Guidelines when reporting results of NIH-funded animal research
  - Many journals already encourage or require ARRIVE
- Fund statistical cores to support animal researchers at under-resourced institutions
- Non-monetary prize to highlight exemplary work in study design and analysis in animal research