

Enhancing Research Reproducibility:

Recommendations from the
Federation of American Societies for Experimental Biology



FASEB

Federation of American Societies
for Experimental Biology

Acknowledgments

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FASEB Member Societies

The American Physiological Society (APS)
American Society for Biochemistry and Molecular Biology (ASBMB)
American Society for Pharmacology and Experimental Therapeutics (ASPET)
American Society for Investigative Pathology (ASIP)
American Society for Nutrition (ASN)
The American Association of Immunologists (AAI)
American Association of Anatomists (AAA)
The Protein Society (PS)
Society for Developmental Biology (SDB)
American Peptide Society (APEPS)

The Association of Biomolecular Resource Facilities (ABRF)
American Society for Bone and Mineral Research (ASBMR)
The American Society for Clinical Investigation (ASCI)
Society for the Study of Reproduction (SSR)
The Teratology Society (TS)
Endocrine Society (ES)
The American Society of Human Genetics (ASHG)
International Society for Computational Biology (ISCB)
American College of Sports Medicine (ACSM)

Biomedical Engineering Society (BMES)
Genetics Society of America (GSA)
American Federation for Medical Research (AFMR)
The Histochemical Society (HCS)
Society for Pediatric Research (SPR)
Society for Glycobiology (SfG)
Association for Molecular Pathology (AMP)
Society for Redox Biology and Medicine (SFRBM)
Society for Experimental Biology and Medicine (SEBM)
American Aging Association (AGE)
U.S. Human Proteome Organization (US HUPO)



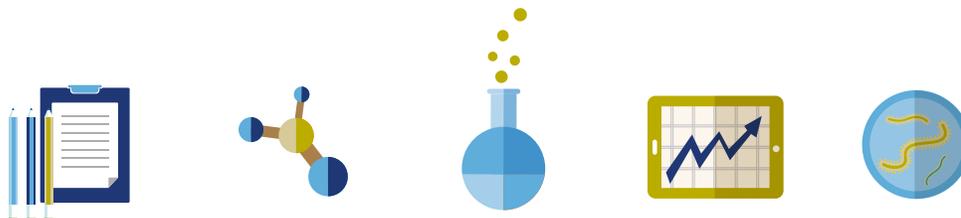
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Science advances through the publication of novel results, followed by efforts to reproduce them. Such replication of experimental findings distinguishes science from other forms of intellectual inquiry. Today, as we learn more about the complexity of living organisms, both successful and failed attempts to replicate a given study can provide valuable insights into biological processes. We are also gaining greater understanding of the many factors that can affect the outcomes of experiments. Variability of reagents, methods, and resources is difficult to avoid—particularly in biology—and can have a sizeable effect on experimental outcomes.

Recently, well publicized allegations of the inability to reproduce published biomedical research^{1,2} have raised questions within the research community and among public stakeholders. Federal agencies that support research activities, including the National Institutes of Health (NIH)^{3,4,5} and the National Science Foundation⁶, are in the process of implementing new policies to address these concerns and improve communication of critical experimental details, including materials and methods and study limitations,

¹ **The Economist.** [Trouble at the lab](#). 19 Oct 2013

² **Landis SC, Amara SG, Asadullah K, Austin CP, et al.** [A Call for Transparent Reporting to Optimize the Predictive Value of Preclinical Research](#). *Nature*. 2012; 490 187-191

³ **Collins F, Tabak L.** [NIH plans to enhance reproducibility](#). *Nature*. 2014; 505 612-613

⁴ **National Institutes of Health.** [Principles and Guidelines for Reporting Preclinical Research](#).

⁵ **National Institutes of Health.** [Implementing Rigor and Transparency in NIH & AHRQ Research Grant Applications](#).

⁶ **National Science Foundation.** [A Framework for Ongoing and Future National Science Foundation Activities to Improve Reproducibility, Replicability, and Robustness in Funded Research](#). 2014.

within the research community and to the public. Recognizing the critical role of individual researchers to ensuring the success of such initiatives, the Federation of American Societies for Experimental Biology (FASEB) worked with its member societies to develop recommendations to improve reporting of research materials and methods and ensure robust training of researchers in rigorous experimental design.

Earlier this year, FASEB convened a series of dialogs involving delegates from FASEB member societies, federal agency representatives, society staff, and invited experts to consider strategies researchers could adopt to enhance reproducibility of research findings and address public concerns. Recognizing the ongoing and complementary efforts of other organizations, FASEB's discussions focused on two key tools critical to basic research: mouse models and antibodies. Although the initial goal of this effort was to develop recommendations to assist individual researchers in fulfilling new policies for federal funding, the final recommendations include actions for stakeholders across the research enterprise, including researchers, institutions, professional societies, journals, and federal agencies.

Overarching Recommendations



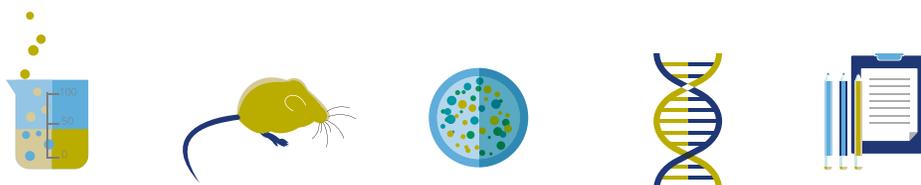
Participants in FASEB's roundtable discussions agreed that three general factors impede the ability to reproduce experimental results: lack of uniform definitions to describe the problem, insufficient reporting of key experimental details, and gaps in scientific training. Clear definitions and parameters need to be established to describe the issue, and stakeholders must be engaged in discussions and activities to enhance reproducibility and transparency of research.

1. Scientists, policy makers, and journalists should use precisely defined terms and definitions when discussing research rigor and transparency to promote uniform understanding.
 - a. **Replicability:** the ability to duplicate (i.e., repeat) a prior result using the same source materials and methodologies. This term should only be used when referring to repeating the results of a specific experiment rather than an entire study
 - b. **Reproducibility:** the ability to achieve similar or nearly identical results using comparable materials and methodologies. This term may be used when specific findings from a study are obtained by an independent group of researchers
 - c. **Generalizability:** the ability to apply a specific result or finding more broadly across settings, systems, or other conditions
 - d. **Translatability:** the ability to apply research discoveries from experimental models to human health applications
 - e. **Rigor:** the use of unbiased and stringent methodologies to analyze, interpret, and report experimental findings
 - f. **Transparency:** the reporting of experimental materials and methods in a manner that provides enough information for others to independently assess and/or reproduce experimental findings

It is important to recognize that variations in experimental results may signal unexpected phenomena leading to new scientific understanding. Lack of reproducibility, generalizability, and translatability are distinct from and do not imply error or scientific misconduct.

2. The inability to reproduce research findings among laboratories may result from a lack of sufficient detail in the reporting of critical materials or methods. FASEB recommends that professional societies, commercial reagent vendors, scientific journals, and funding agencies engage in a dialog to develop expectations for describing reagents, laboratory tools, and protocols in publications and grant applications.
3. Rigorous and transparent research is dependent upon adherence to good research practices by all research team members, including but not limited to principal investigators/faculty members, staff scientists, postdoctoral scholars, graduate and undergraduate students, core facility staff, and institutional leadership. Therefore, research training should review and reinforce good practices for:
 - a. Maintenance of experimental records and laboratory notebooks
 - b. Use of precise definitions and standard nomenclature for the field or experimental model
 - c. Critical review of experimental design, including variables, metrics, and data analysis
 - d. Application of appropriate statistical methods
 - e. Complete and transparent reporting of findings.

Recommendations Specific to Research Using Mouse and Other Animal Models



FASEB's deliberations on factors that contribute to variability of results in research using mouse models identified opportunities for action by both institutions/research organizations and individual investigators. Institutions and research organizations should work with investigators to increase awareness and utilization of existing guidelines for reporting animal care and use. Closer collaboration between investigators and animal facility staff provides opportunities to improve existing animal husbandry practices, and individual investigators are encouraged to expand the definition of their laboratory and research team to include animal facilities and staff. Although standard nomenclatures exist for most animal models, FASEB roundtable participants agreed that the use of standard terminology in research publications and protocols could be improved.

Recommendations for Institutions/ Research Organizations

4. In 2010, two independent groups—the National Centre for the Replacement, Refinement, and Reduction of Animals in Research (NC3Rs) and the Institute for Laboratory Animal Research (ILAR) published guidelines to improve the reporting of research using animals, maximizing the utility of published studies and minimizing the need for additional studies. NC3Rs's *Animal Research: Reporting of In Vivo Experiments (ARRIVE) Guidelines*⁷ and ILAR's *Guide for the Care and*

⁷ Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PLOS Biology*. 2010; 8(6): e1000412

*Use of Laboratory Animals*⁸ and *Guidance for the Description of Animal Research in Scientific Publications*⁹ serve as useful references. FASEB recommends that institutional animal facilities, Institutional Animal Care and Use Committees (IACUCs), and professional societies work together to promote awareness and use—as appropriate—of the ARRIVE and ILAR guidelines in animal research.

5. As their research roles expand or change, research team members may require additional training to understand, implement, and report animal husbandry practices and genetic backgrounds of animal subjects. Access to statisticians or additional statistical training may also be necessary to ensure that animal sample sizes are sufficient for the required analyses. FASEB recommends that training resources be made available to the research community on a regular, on demand basis.

Recommendations for Individual Investigators

6. The organization, daily operation, environment, and staffing of an animal facility can affect the outcomes of experiments. Therefore, animal facilities and staff should be considered extensions of an investigator's laboratory and research team. FASEB recommends that investigators include animal facility staff in discussions of relevant aspects of experimental design. FASEB also recommends development of checklists to facilitate review of animal care variables and to denote study-specific variations.
7. Animal models provide critical insights into human biology and health. When communicating to the public about preclinical studies, researchers should clearly articulate the rationale for the choice of an animal model as well as its value and limitations in recapitulating human disease and its treatment.
8. Investigators and animal facility staff ensure humane treatment and care of animal subjects by adhering to established guidelines and federal regulations. To minimize environmental effects on experimental outcomes and continue to improve animal care standards, FASEB encourages institutions, veterinarians, and researchers to identify, understand, and promote the adoption of evidence-based husbandry practices. Reporting of animal care practices and study-specific variations will enhance reproducibility.
9. FASEB recommends that researchers, professional societies, and journals use standard nomenclature^{10, 11, 12} when reporting animal husbandry practices, breeding practices, and genetic backgrounds of study subjects in grant applications and publications.

⁸ **Institute for Laboratory Animal Research.** *Guide for the Care and Use of Laboratory Animals*. 2010. The National Academies Press.

⁹ **Institute for Laboratory Animal Research.** *Guidance for the Description of Animal Research in Scientific Publications*. 2011. The National Academies Press.

¹⁰ **Jackson Laboratories.** *Quick Guide to Mouse Nomenclature*. Accessed January 6, 2016.

¹¹ **Institute for Laboratory Animal Research.** *Guidance for the Description of Animal Research in Scientific Publications*. 2011. The National Academies Press.

¹² **Phelan J. A** *Mouse By Any Other Name: Nomenclature Tutorial*. Taconic. 2015

Recommendations Specific to Research Using Antibodies



FASEB's discussions of ways to enhance reproducibility of research using antibodies were animated and reflected the diversity of fields and methodologies that use these common reagents. The key challenge to developing recommendations in this area was to identify ways to enhance transparency of research methods without being overly prescriptive and limiting scientific exploration. The need to adopt a standard format for reporting antibody information, both by vendors and researchers using the product, was one area in which there was agreement. Although the information necessary to select proper antibodies will vary by experimental technique, model, and specific research question, FASEB proposes recommendations for both vendors and researchers for reporting validation and experimental methods and enhancing transparency of research findings.

Recommendations for All Stakeholders

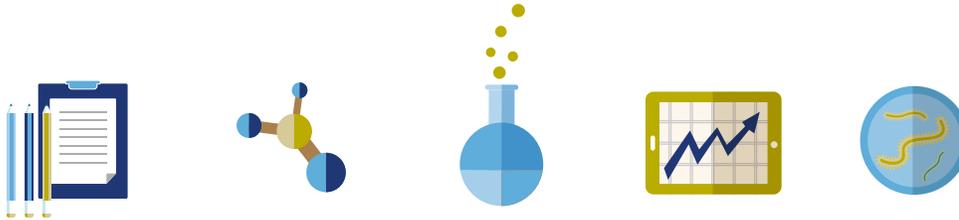
10. FASEB strongly recommends that researchers, journals, and funding agencies work together to develop and adopt a standard format for citing antibodies¹³ in grant applications and publications. At minimum, this standard format should include the complete product name, catalog number, antibody type (monoclonal, polyclonal, or recombinant), vendor, target, lot number, and dilution/concentration.
11. There is a growing concern that all lab personnel may not fully appreciate the underlying science or limitations of commercially available antibodies or antibody-based kits. Although vendor-supplied technical information may help investigators select reagents such as antibodies, this information is insufficient for validation. Therefore, FASEB recommends that stakeholders—including researchers, funding agencies, product vendors, and journals—convene an impartial advisory body to determine information needed for high quality technical bulletins. This might include immunogenic sequence, epitope sequence, cross-species reactivity, and methodologies for which the antibody is validated.

Recommendation for Individual Investigators

12. To achieve uniform reporting of research findings, FASEB recommends that investigators, funding agencies, and journals adopt best practices for experiments using antibodies. Best practices may vary by field and technique. Some core suggestions include:
 - a. Images should show as much of a blot or tissue section as reasonable to demonstrate findings. Blot images should show all key experimental samples, appropriate positive and negative controls, and size markers
 - b. Methods sections should include descriptions of sample preparation and blocking procedures (e.g., tissue retrieval, fixation, and processing parameters)
 - c. Details regarding reagents and equipment used (see Recommendation 1) should be described in the methods section
 - d. Results should include descriptions of the positive and negative controls used, including justification of appropriateness for technique, experimental system, and research query.

¹³ **Chawla DS.** [Researchers Argue for Standard Format to Cite Lab Resources.](#) *Nature News*. 2015

Potential Strategies for Professional Societies/Organizations to Pursue



Enhancing the reproducibility and transparency of biological and biomedical research is a discussion that includes a broad range of stakeholders, including individual investigators, institutions, professional societies, scientific journals, and journalists. Throughout its deliberations, FASEB sought to expand the discussion beyond its member societies and work with other organizations to identify opportunities in which coordinated effort would facilitate adoption of recommended practices. Professional societies are poised to play a unique role in the discussion and implementation of recommendations to enhance the reproducibility and transparency of research results, as many provide professional/career development information and training through member services and also serve as publishers of research findings through society-managed scientific journals. FASEB recognizes that many professional societies are already engaged in efforts to enhance the transparency of experimental methods¹⁴,^{15, 16} and the following recommendations are intended to encourage and expand these efforts.

¹⁴ **American Society for Cell Biology.** [How Can Scientists Enhance Rigor in Conducting Basic Research and Reporting Research Results?](#) 2015.

¹⁵ **Biophysical Society.** [Guidelines for the Reproducibility of Biophysics Research.](#) 2015.

¹⁶ **Society for Neuroscience.** [Research Practices for Scientific Rigor: A Resource for Discussion, Training and Practice.](#) 2015.

Strategies to Increase Awareness among Scientists

13. Rigor and reproducibility are critical for the advancement of science. To improve awareness within the scientific community regarding concerns about the translatability of basic research discoveries to clinical applications, strategies to enhance transparent reporting of research findings, and the new NIH policy that will go into effect on January 25, 2016, FASEB recommends that professional societies emphasize proactive efforts demonstrating the research community's commitment to rigorous and transparent research.¹⁷ This could take several forms, including editorials in scientific journals, press releases, and development of uniform talking points. These efforts should acknowledge the distinction between strategies to enhance scientific rigor and transparency versus identification of scientific misconduct.

14. To facilitate investigator access to resources intended to enhance scientific rigor and transparency, FASEB recommends the establishment of a publicly accessible clearinghouse website. This website would aggregate existing training resources and best practices to enhance scientific rigor and transparency, such as those developed by NIH¹⁸,¹⁹, professional societies²⁰, and research consortia. A resource hosted by a third-party such as FASEB would allow distribution of uniform information regardless of discipline or funding agency.

¹⁷ The American Physiological Society is developing an on-demand educational module to help researchers design, perform, analyze, and report well-controlled animal studies to enhance accuracy and reproducibility. Controls in Animal Studies Professional Skills Course (Grant: 1R25GM116166-01) is funded by the National Institute of General Medical Sciences. Additional information is available through the National Institutes of Health [RePORTER](#).

¹⁸ **National Institute of General Medical Sciences.** [Clearinghouse for Training Modules to Enhance Data Reproducibility](#).

¹⁹ **Clayton, JA.** [Studying both sexes: a guiding principle for biomedicine](#). *FASEB Journal*. 2016; 30 1-6. (Published online October 29, 2015).

²⁰ The Association of Biomolecular Resource Facilities (ABRF) hosts the [ABRF Marketplace](#), a free, searchable registry for core facility services that encourages resource sharing among individual researchers as well as across core facilities.

Suggestion/Consideration for Society Publications Committees/Journals

15. While the goal of FASEB's rigor and reproducibility roundtables was to develop strategies to assist individual investigators in addressing the NIH policy²¹ that will go into effect on January 25, 2016, several opportunities for journals and society publications committees were also identified. Many journals have taken significant actions to address concerns about rigor and reproducibility. FASEB encourages professional societies to continue to enhance scientific rigor and transparency within their specific disciplines and share alternative strategies developed to address these issues. Opportunities include:
 - a. Engagement of society publications committees and journal boards in discussion of issues related to rigor and transparency
 - b. Support of simple, common guidelines for reporting methods and reagents in publications and grant applications
 - c. Promotion of common guidelines to reflect needs of specific disciplines and fields of research
 - d. Development of uniform instructions to authors regarding transparent reporting of materials and methods
 - e. Publication of null or negative results
 - f. Development of training modules or programs on rigor and reproducibility by individual societies related to the needs of their respective disciplines.

Role of FASEB

FASEB appreciates that implementation of the NIH policy²² to enhance scientific rigor and research transparency will be an iterative process. Stakeholders including investigators, scientific administrators, program officers, scientific review officers, study section members and chairs, professional societies, and journals can provide critical insights regarding ways in which implementation of the policy could be improved. Representing over 125,000 individual scientists, FASEB will continue to facilitate the dialog on enhanced rigor and reproducibility by synthesizing the views of the research community regarding clarity of the policy, challenges encountered, and resources that could help streamline compliance.

²¹ **National Institutes of Health.** [Implementing Rigor and Transparency in NIH and AHRQ Research Grant Applications.](#)

²² Ibid.

Conclusion



Concerns regarding the inability to reproduce published pre-clinical studies and forthcoming policy changes from federal funding agencies presented an opportunity for the scientific community to highlight existing efforts and resources to enhance the reproducibility and transparency of research and identify areas in which more attention is needed. Engaging its membership in a series of discussions, FASEB developed consensus recommendations to increase researchers' awareness of strategies to enhance reproducibility and transparency of research utilizing animal models and antibodies. These discussions also explored ways in which professional societies could support members as new policies to enhance scientific rigor of federally funded research are implemented in 2016. This approach builds upon longstanding practices for the development and adoption of standards for reporting methods and results for publications and applications for funding. 



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