



Center for
Scientific Review

RIGOR AND REPRODUCIBILITY IN RESEARCH

GUIDANCE FOR REVIEWERS

Goal: To support the **highest quality science, public accountability, and social responsibility in the conduct of scientific research.**

NIH's Rigor and Transparency efforts are intended to clarify expectations and highlight attention to four areas that may need more explicit attention by applicants and reviewers:

- Scientific premise
- Scientific rigor
- Consideration of relevant biological variables, such as sex
- Authentication of key biological and/or chemical resources

- To assess the scientific merit of each application based on current best practices in the field.
- To emphasize longstanding NIH expectations regarding Rigor and Reproducibility.
- Inform the NIH on rigor and reproducibility.
- Develop consensus and standards for assessing the four components
 - Scientific premise
 - Scientific rigor
 - Consideration of relevant biological variables, such as sex
 - Authentication of key biological and/or chemical resources

- May differ for specific fields of research
- May differ for different study sections

Reviewing Rigor and Transparency of Research

	Applies to which applications?	Where will I find it in the application?	Where do I include it in my critique?	Addition to review criteria	Affect overall impact score?
Scientific Premise	All	Research Strategy (Significance)	Significance	Is there a strong scientific premise for the project?	Yes
Scientific Rigor	All	Research Strategy (Approach)	Approach	Are there strategies to ensure a robust and unbiased approach?	Yes
Consideration of Relevant Biological Variables, Such as Sex	Projects with vertebrate animals and/or human subjects	Research Strategy (Approach)	Approach	Are adequate plans to address relevant biological variables, such as sex, included for studies in vertebrate animals or human subjects?	Yes
Authentication of Key Biological and/or Chemical Resources	Project involving key biological and/or chemical resources	New Attachment	Additional review considerations	Comment on plans for identifying and ensuring validity of resources.	No

Scientific Premise

GOAL: Ensure that the underlying **scientific foundation** of the project—concepts, previous work, and data (when relevant)—is sound.

Reviewers will need to mention in their critiques under **SIGNIFICANCE** section how strong or weak the scientific premise is by assessing whether the applicant has:

- Provided sufficient justification for the proposed work.
- Provided a strong argument for their hypothesis or research project.
- Cited appropriate published work and/or provided strong preliminary data.
- Appropriately identified strengths and weaknesses in prior work in the field.
- Proposed to fill broad gaps in the related research field.
- **OR has the applicant provided justification why this is not possible.**

Scientific Rigor

GOAL: Ensure a strict application of scientific method that supports robust and unbiased design, analysis, interpretation, and reporting of results, and sufficient information for the study to be assessed and reproduced. Give careful consideration to the methods and issues that matter in your field.

Reviewers will need to mention in their critiques under **APPROACH** how strongly or weakly the scientific rigor has been emphasized in the application by basing their assessment on whether the applicant has:

- Discussed strategies to ensure a robust and unbiased approach, as appropriate for the work proposed.
- Provided sufficient information to allow independent confirmation or analysis.
- Powered the study appropriately or based on reasonable assumptions.
- Presented plans for handling outliers, unintended consequences, etc.
- Provided statistical procedures to determine appropriate group sizes, numbers of animals, etc.
- Presented procedures to ensure independent, blinded measurements.
- Presented procedures to improve precision and minimize variability.
- Provided criteria for subject inclusion or exclusion.

All possible considerations may or may not be appropriate for the scientific field and research question of every application



Relevant Biological Variables

GOAL: Ensure that the research accounts for sex and other relevant biological variables in developing research questions and study designs. The ways in which sex and other biological variables need to be accounted for will differ across research questions and fields of study.

Reviewers will need to address in their critiques under **APPROACH** whether the applicant has provided adequate plans to address relevant biological variables for studies in vertebrate animals or human subjects.

- Applies broadly to all biological variables relevant to the research such as sex, age, source, weight, or genetic strain or any relevant biological variables that could affect experimental outcome.
- Specific considerations to assess include:
 - Has the applicant considered biological variables, such as sex, that are relevant to the experimental design?
 - Will relevant biological variables be controlled or factored into the study design appropriately.
 - Consideration of sex is required in all studies involving human subjects or vertebrate animals

Consideration of sex, included under the umbrella of “Relevant Biological Variables”, is required in all studies involving human subjects or vertebrate animals.

NIH expectations for applicants:

- If little is known about sex differences, the application should include both sexes.
 - Sufficient numbers should be provided to inform the presence or absence of sex differences. Statistically powered comparisons between sexes may not be warranted.
 - Specific hypotheses about sex differences may not be possible.
 - Findings should be reported separately by sex in progress reports and publications.
- If sex differences are known not to exist, a strong justification should be provided if the application proposes to study one sex.
- If sex differences are known, experiments should be designed with appropriate group sizes to detect sex differences.

NIH expectations for reviewers:

- As part of the Consideration of Relevant Biological Variables, assess whether the plans to address sex as a biological variable are adequate (for studies in vertebrate animals or human subjects).
- If the study involves only one sex, is this justified scientifically?
- Assess within the context of the research question and current scientific knowledge.

Plan for Resource Authentication

GOAL: Ensure processes are in place to identify and regularly validate key resources used in their research and avoid unreliable research as a result of misidentified or contaminated resources.

Reviewers will comment on the brief plans proposed for identifying and ensuring the validity of key research resources under new “Authentication of Key Biological and/or Chemical Resources section”

- Applies broadly to all key research resources such as cell lines, specialty chemicals, antibodies, biologics or any relevant biological resource that could affect experimental outcome.
- Adequate authentication of key biological and/or chemical resources used in their research is needed to ensure that the resources are genuine.
- Rate as acceptable/unacceptable (provide brief explanation if unacceptable)
- Does not affect criterion scores or overall impact score



Related Review Issues

- Different research fields may have different best practices and reach different conclusions about scientific premise and rigor. Assess based on best practices in the field.
- Rigor and transparency considerations also applies to R21, R03, and R15 applications. Since these mechanisms do not require preliminary data and the extent to which approach details can be provided may differ. Reviewers should evaluate the scientific merit of these applications, including rigor and transparency, in light of the goals and reviewer guidelines for these activities.
- Whether rigor and transparency is embedded in the research plan or presented in a separate section should not matter, reviewers should focus their evaluation on the likely outcome, not grant writing preferences.

Related Review Issues

- An application that does not include premise, rigor, relevant biological variables, or an authentication plan will proceed to review.
- Page limits have not changed. Be alert for page limit violations (e.g. inappropriate use of appendices or other application sections). Alert the SRO if you see a potential issue.
- Page limits, cost and time are not valid reasons to disregard attention to these issues.
- The elements of rigor and reproducibility are not acceptable post-submission materials.
- A weak premise, lack of rigor, etc. does not meet the definition of research misconduct.
- **Scientific justifications may be acceptable in certain circumstances**



Additional resources

- Rigor and Reproducibility in grant applications (OER site):
<http://grants.nih.gov/reproducibility/index.htm>
- NIH presentation of background and goals of Rigor and Transparency (video)
https://grants.nih.gov/reproducibility/module_1/presentation.html
- Reviewer Guidance on Rigor and Transparency:
[http://grants.nih.gov/grants/peer/guidelines_general/Reviewer Guidance on Rigor and Transparency.pdf](http://grants.nih.gov/grants/peer/guidelines_general/Reviewer_Guidance_on_Rigor_and_Transparency.pdf)
- Consideration of Sex as a Biological Variable in NIH-funded Research
http://orwh.od.nih.gov/sexinscience/overview/pdf/NOT-OD-15-102_Guidance.pdf
- Rigor and transparency do not apply to all applications. See List of Eligible Activity Codes:
<https://nih-extramural-intranet.od.nih.gov/d/sites/default/files/RigorActivityCodes-20151006.pdf>. Also, certain Funding Opportunity Announcements are exempt from Rigor and Transparency, by request from the ICs.
- Questions about the NIH policy should be directed to reproducibility@nih.gov