Reviewer Guidance on Rigor and Transparency: Research Project Grant and Mentored Career Development Applications

The goal of this initiative is to enhance reproducibility of research through rigor and transparency. NIH recently updated application instructions and review language for research grant (NOT-OD-16-011) and mentored career development award (NOT-OD-16-012) applications submitted for due dates of January 25, 2016 and beyond. Implementation of rigor and transparency for individual fellowship, institutional career development, and institutional training grant applications will be announced in advance, on a different timeline that allows for training in rigor and transparency to be developed (NOT-OD-16-034).

The four areas of the current rigor and transparency initiative are explained below.

- **Scientific Premise** refers to the quality and strength of the prior research used as the basis for the proposed research question or project; this is distinct from the hypothesis or justification.
  - The applicant should discuss the strengths and weaknesses of the prior research used to support the application and describe how the proposed research will address weaknesses or gaps identified by the applicant. For example, a discussion of scientific premise might include attention to the rigor of previous experimental designs, either conducted by the applicant or reported in the literature.
  - Reviewers will evaluate scientific premise as part of the Significance criterion for research grant applications or the Research Plan criterion for mentored career development award applications.
    - Consider whether the applicant has discussed the strengths and weaknesses of the foundational data.
    - A weak scientific premise, or the failure to address scientific premise adequately, may affect criterion and overall impact scores.
    - The page limit is not an acceptable excuse for an applicant to not address scientific premise.
- **Scientific Rigor** is the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation and reporting of results. Whereas scientific premise pertains to supporting data, scientific rigor pertains to the proposed research.
  - The applicant should describe experimental controls, plans to reduce bias (blinding, randomization, subject inclusions and exclusion criteria, etc.), power analyses, and statistical methods, as appropriate.

- Reviewers will assess scientific rigor as part of the Approach criterion for research grant applications and the Research Plan criterion for mentored career development award applications, as well as the overall impact score.
    - The Vertebrate Animal Section no longer requires a justification of animal numbers (NOT-OD-16-006). Inadequate vertebrate animal numbers should be reflected in the score and will not result in a block to funding.
    - Reviewers will assess information concerning numbers of animals according to the section where it is included in the application.

	Scientific Premise	**Scientific Rigor**
Pertains to:	Supporting data	Proposed research
Review Criterion – Research Grants	Significance	Approach
Review Criterion – Mentored Career Development Grants	Research Plan	Research Plan

- **Consideration of Sex and Other Biological Variables** includes the critical factors affecting health or disease in vertebrate animals or human subjects. Biological variables, such as sex, age, weight, and underlying health conditions, are often critical factors affecting health or disease.
    - Applicants are expected to factor Sex as a Biological Variable (SABV) into research designs, analyses, and reporting in vertebrate animal and human studies.
        - Consideration of SABV does not necessarily mean sex differences research. See Figure 1 in "Studying both sexes = A guiding principle for biomedicine" for further detail.
        - A justification is expected if the application proposes to study one sex, for example in the case of a sex-specific condition or phenomenon (e.g., ovarian or prostate cancer), acutely scare resources, or sex-specific hypotheses when there are known differences between males and females.
        - Cost and absence of known sex differences are inadequate justifications for not studying both sexes.
    - Reviewers will assess the applicant's plans to address relevant biological variables, such as sex, as part of the Approach (or Research Plan) criterion score and the overall impact score, and comment on the adequacy of those plans in their written critiques and in meeting discussions.
        - Reviewers will assess justifications for numbers of animals according to the section where it is included in the application.
        - See additional reviewer guidance for evaluating sex as a biological variable: https://grants.nih.gov/grants/peer/guidelines_general/SABV_Decision_Tree_for_Reviewers.pdf.
- **Authentication of Key Biological and/or Chemical Resources.** Key biological and/or chemical resources are those that 1) may differ from laboratory to laboratory or over time; 2) may have qualities and/or qualifications that could influence the research data; and 3) are integral to the proposed research. These include, but are not limited to, cell lines, specialty chemicals, antibodies, and other biologics, not standard laboratory reagents.

- Applicants should provide a brief plan (one page or less).
  - The plan should not include authentication data.
  - The plan may reflect existing guidelines or standards for authentication of a resource when such standards exist.
- Reviewers will discuss the authentication plan after scoring; comments on key resource authentication should not affect scores.
  - Reviewers will comment in their written critiques and discussion at the meeting on the adequacy of the plan for key resource authentication; comments can be addressed by the applicant prior to award for meritorious applications.
  - Reviewers should note if the authentication plan is missing from the application.

Not all activity codes are included in the rigor and transparency initiative. Therefore, reviewers need to follow the correct review criteria and use the appropriate and current critique template for each application. Your Scientific Review Officer (SRO) should provide or direct you to the appropriate templates and guidance.

Page limits have not changed. SROs and reviewers need to be alert for over-stuffed applications.

You may submit your comments/questions about the NIH policy to reproducibility@nih.gov.

OVERVIEW: RESEARCH PROJECT GRANT (RPG) APPLICATIONS

Element of Rigor and Transparency	Section of Application	Criterion Score	Additional Review Consideration	Contribute to Overall Impact Score?
Scientific Premise	Research Strategy	Significance	NA	Yes
Scientific Rigor	Research Strategy	Approach	NA	Yes
Consideration of Relevant Biological Variables, such as Sex	Research Strategy	Approach	NA	Yes
Authentication of Key Biological and/or Chemical Resources	New Attachment	NA	Yes	No

OVERVIEW: MENTORED CAREER DEVELOPMENT AWARD (K) APPLICATIONS

Element of Rigor and Transparency	Section of Application	Criterion Score	Additional Review Consideration	Contribute to Overall Impact Score?
Scientific Premise	Research Strategy	Research Plan	NA	Yes
Scientific Rigor	Research Strategy	Research Plan	NA	Yes
Consideration of Relevant Biological Variables, such as Sex	Research Strategy	Research Plan	NA	Yes
Authentication of Key Biological and/or Chemical Resources	New Attachment	NA	Yes	No

Additional Resources

- NIH Extramural website on Rigor and Reproducibility
- Nature Perspectives: "A call for transparent reporting to optimize the predictive value of preclinical research" Landis, et al., 10/10/2012
- Nature Commentary: "Policy: NIH plans to enhance reproducibility" Collins & Tabak, 01/27/2014
- Nature Commentary: "Policy: NIH to balance sex in cell and animal studies" Clayton & Collins, 05/14/2014
- Science Editorial: "Journals Unite for Reproducibility" 11/07/2014
- Science Perspectives: "Fixing problems with cell lines" Lorsch, Collins & Lippincott-Schwartz, 12/19/2014
- FASEB Journal Life Sciences Forums: "Studying both sexes: a guiding principle for biomedicine" Clayton 10/29/2015
- Narrated overview of the NIH policy and why it's important: https://grants.nih.gov/reproducibility/module_1/presentation.html
- The FASEB Journal: "Studying both sexes: a guiding principle for biomedicine" Clayton 2/30/2016
- The FASEB Journal: "Considering sex as a biological variable in preclinical research" Miller 9/28/2016