**Research Strategy**

Blue Text = Guidance from [NIH SF424 R&R](https://grants.nih.gov/grants/how-to-apply-application-guide/forms-f/fellowship-forms-f.pdf)

Brown Text and Outline = Adapted from [*The Grant Application Writer’s Workbook*](http://www.grantcentral.com/workbooks/national-institutes-of-health/).

Organize the Research Strategy in the specified order and use the instructions provided below, unless otherwise specified in the FOA. Start each section with the appropriate section heading – Significance, Approach, etc. Cite published experimental details in the Research Strategy and provide the full reference in F.220 - R&R Other Project Information Form, Bibliography and References Cited.

Limited to 6 pages unless otherwise noted in the Funding Opportunity Announcement (FOA).

**Note for Applications Proposing the Involvement of Human Subjects and/or Clinical Trials:**

* Use the Research Strategy section to discuss the overall strategy, methodology, and analyses of your proposed research, but do not duplicate information collected in the PHS Human Subjects and Clinical Trials Information form.
* The PHS Human Subjects and Clinical Trials Information form will capture detailed study information, including eligibility criteria; inclusion of women, minorities, and children; and protection and monitoring plans.
* You are encouraged to refer to information in the PHS Human Subjects and Clinical Trials Information form as appropriate in your discussion (e.g., see Question 2.4 Inclusion of Women, Minorities, and Children).

**Note for Applicants with Multiple Specific Aims:** you may address the Significance and Approach either for each Specific Aim individually or for all of the Specific Aims collectively.

**1. Significance** *(suggested length 1-1.5 pages)*

* Explain the importance of the problem or critical barrier to progress that the proposed project addresses.
* Describe the strengths and weaknesses in the rigor of the prior research (both published and unpublished) that serves as the key support for the project.
* Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
* Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

**Suggested Outline**

Importance of the problem: *(1 paragraph,~0.25 pages) An extension of the information provided in first paragraph of Specific Aims page, e.g., what problem or critical barrier your research addresses (substantiated with documentation from the literature) and the negative consequences of not meeting the need. Be sure to go from* ***broad to specific****; do not interrupt the flow with a statement of what you plan/expect to accomplish—save this for the* ***Significance of the expected research contribution*** *subsection below.*

* Opening sentence/problem being addressed…
* “It is widely appreciated that…”
* “There is a clear lack of…”
* “Thus, there is an *urgent need*…”

Scientific premise and rigor of prior research (previously, scientific premise): *(several paragraphs, ~0.5–0.75 pages) The foundation on which your proposal is built and the reliability and rigor or prior research.* ***Organize by aim or overall.*** *Discuss: the strengths and weaknesses in the rigor of prior research (both published studies and unpublished preliminary data) that serves as the key support for the proposed project. Note that it may be more appropriate to discuss limitations rather than issues with rigor. End this by including general statements (leave details for Approach section) about how weaknesses of prior research will be overcome. Cite only the strongest supporting publications.*

* “Numerous studies have…”
* “However, studies X and Y have important limitations…”
* “In addition, the rigor of study Z is not sufficient in that the antibody”
* “To overcome these gaps in rigor, we will…” **[keep this general]**
* “Thus, our proposed studies will circumvent the limitations of…by…”

Significance of the expected research contribution: *(1 paragraph, ~0.25 pages) The research contributions you expect to make; these should be relevant to the mission of the funding agency. Write about contributions to science in general vs. your field separately as suggested below, or in a single paragraph. In each paragraph your argument should go from* ***specific to broad****.*

Impact of the project on scientific knowledge: *How the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more fields.*

Impact of the project on the field: *How the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be advanced (vertically) if the proposed aims are achieved.*

**2. Approach**

* Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project. Describe the strengths and weaknesses in the rigor of the prior research (both published and unpublished) that serves as the key support for the project. Unless addressed separately in the Resource Sharing Plan attachment, include how the data will be collected, analyzed, and interpreted, as well as any resource sharing plans as appropriate. Resources and tools for rigorous experimental design can be found at [Enhancing Reproducibility through Rigor and Transparency.](https://grants.nih.gov/reproducibility/index.htm)
* For trials that randomize groups or deliver interventions to groups, describe how your methods for analysis and sample size are appropriate for your plans for participant assignment and intervention delivery. These methods can include a group- or cluster- randomized trial or an individually randomized group-treatment trial. Additional information is available at the [Research Methods Resources](https://researchmethodsresources.nih.gov/) webpage.
* Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.
* If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high risk aspects of the proposed work.
* Explain how relevant biological variables, such as sex, are factored into research designs and analyses for studies in vertebrate animals and humans. For example, strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex. Refer to NIH Guide Notice on Sex as a Biological Variable in NIH-funded Research for additional information.
* Point out any procedures, situations, or materials that may be hazardous to personnel and the precautions to be exercised.
* If research on Human Embryonic Stem Cells (hESCs) is proposed, but an approved cell line from the NIH [hESC Registry](https://grants.nih.gov/stem_cells/registry/current.htm) cannot be chosen, provide a strong justification for why an appropriate cell line cannot be chosen from the registry at this time.
* If you are proposing to gain [clinical trial research experience](https://grants.nih.gov/grants/glossary.htm#ClinicalTrialResearchExperience) (i.e., you will not be leading an independent clinical trial), briefly describe your role on the clinical trial.

# As applicable, also include the following information as part of the Research Strategy, keeping within the two sections (Significance and Approach) listed above.

**Preliminary Studies for New Applications:**

For new applications, include information on preliminary studies (including data collected by others in the lab), if any. Discuss the applicant's preliminary studies, data, and/or experience pertinent to this application.

Note that the Progress Report falls within the Research Strategy and is therefore included in the page limits for the Research Strategy. If you are submitting a renewal application, provide a Progress Report. Provide the beginning and ending dates for the period covered since the last competitive review. In the Progress Report, you should:

* Summarize the specific aims of the previous project period and the importance of the findings, and emphasize the progress made toward their achievement.
* Explain any significant changes to the specific aims and any new directions, including changes resulting from significant budget reductions.
* Discuss previous participant enrollment (e.g., recruitment, retention, inclusion of women, minorities, children, etc.) for any studies meeting the NIH Glossary definition for clinical research. Use the Progress Report section to discuss, but do not duplicate information collected elsewhere in the application.

Do not include a list of publications, manuscripts accepted for publication, patents, or other printed materials in the Progress Report. That information will be included in the "Progress Report Publication List" attachment.

**Suggested Outline**

**Issues related to rigor and reproducibility:** *For paragraphs on* ***Addressing weaknesses in rigor of prior research,******Strategies to ensure rigor of the proposed research*** *and* ***Considerations of biological variables including sex****, authors should provide relevant information that clearly addresses all points. This can be done:*

* *at the beginning (as shown below) or end of the Approach subsection (advisable if applicable to all aims), or*
* *in each aim (if information differs by aim).*

*The key is to make all information on the topic of R&R easy to find, i.e.* ***the paragraphs should be labeled****.*

Addressing weaknesses in rigor of prior research **–** *(0.25 pages)*

*Describe plans to address weaknesses in rigor of the prior research that serves as the key support for the proposed project.*

* “As described under Significance, the key weaknesses of past studies of xxx are yyy.”
* “In the current study, we will address xxx.”
* “In addition, we will ensure the proposed research is performed rigorously, as described below.”

Strategies to ensure rigor of the proposed research – *(0.25 pages)*

*Describe how you will ensure a robust and unbiased approach appropriate for the work proposed. Strategies may include:*

* *Randomization protocol for sample groups*
* *Blinded data recording and analysis*
* *Controls and replicates needed*
* *Sample size estimation/power analysis (critical for studies using human subjects or higher vertebrates)*
* *Principles of Good Laboratory Practice*
* *Essential reagents and their authentication*
* *Statistical analyses to be used*

[Adapted from Landis SC et al. (2012) A call for transparent reporting to optimize the predictive value of preclinical research. *Nature* Oct. 11; 490(7419):181-91.](https://www.ncbi.nlm.nih.gov/pubmed?term=nature%5BJour%5D+AND+2012%5Bpdat%5D+AND+landis%5Bauthor%5D&cmd=detailssearch)

Consideration of biological variables, including sex, in the proposed research – *(0.25 pages)*

*Include discussion of:*

* *Sex (required; e.g. inclusion of equal numbers of each; impact on results; separate analysis of results; karyotype of cell lines)*
* *Weight, age, and health status, if applicable*

**Aim** **1:** *Title to be repeated verbatim from Specific Aims page.*

Introduction: ***Include the following points, combined into one paragraph.***

* Justification: *The question/problem that needs to be addressed (a part of the overall need).*
* Objective of Aim: *Part of the overall objective stated on Specific Aims page; also how attaining this objective will help address/resolve the question posed above.*
  + “The *objective* of this aim is to…”
* Working hypothesis: *Repeated verbatim from Specific Aims.*
  + “To attain this objective, we will test the *working hypothesis* that…”
* Approach: *The approach you will use to test your working hypothesis.*
  + “Our *approach* to testing the working hypothesis will be…”

Justification and feasibility: *Preliminary data and findings from the literature that support the rationale of this aim.*

* Preliminary data/data from the literature:
* Rationale: *Future steps that will only be possible after the proposed work is completed. Include preliminary data that strengthen your rationale.* 
  + The *rationale* for this aim is…

Research design:

* Subaim 1*Possible details to include – not an exhaustive list. Details related to the rigor of (a) prior research and/or (b) the proposed research that are not covered above should be included here.*
* *Approach to be used*
* *Overview of methods*
* *Essential minor/major equipment*
* *Detailed expectations*
* *How results will be interpreted*
* Subaim 2*(as above)*

Expected outcomes:*Short paragraph that integrates outcomes from all proposed activities within this aim, and indicates how they will contribute to achieving your overall objective.*

Potential problems and alternative strategies:*Essential for every aim. Propose alternatives in case your hypothesis is proven invalid/critical reagents fail/approaches are inconclusive. These problems should not be fatal to your proposal; even if they occur, the alternatives described here should enable you to achieve the main objectives.*

**Repeat outline above for each aim**

**Timeline and benchmarks for success:** *Preferred in table format. Demonstrate that you have thoroughly considered how long it will take to complete each component proposed. Include when you expect to achieve certain benchmarks (be sure to specify what these are).*

**Future directions:** *Brief summary of where you expect the science to be at the conclusion of the proposed research. Include the next expected steps and why they are important.*