Don't Propose Too Much

Sharpen the focus of your application. Novice PI applicants often overshoot their mark, proposing too much. Make sure the scale of your hypothesis and aims fits your request of time and resources. Reviewers will quickly pick up on how well matched these elements are. Your hypothesis should be provable and aims doable with the resources you are requesting.

Address NIH Review Criteria

Significance. Does this study address an important problem? If the aims are achieved, how will scientific knowledge or clinical practice be advanced?

Approach. Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Does the PI applicant acknowledge potential problem areas and consider alternative tactics?

Innovation. Is the project original and innovative? For example: Does it challenge existing paradigms or address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or use novel concepts, approaches, methods, tools, or technologies?

Master the Application -- Formatting Requirements

Beware: NIH strictly enforces formatting requirements and may return improperly formatted applications!

Follow these font size and spacing requirements:

- Black Arial, Helvetica, Palatino, or Georgia typeface; font size 11 points or larger.
  - You can use a symbol font for special characters; all font requirements apply.
  - Font size in figures and tables may be smaller but must be easily readable.
- Type density, characters and spaces, no more than 15 characters in an inch.
- No more than six lines in a vertical inch.
- For electronic applications: paper size 8.5 by 11 inches; margins, at least one-half inch.
- For electronic applications:
  - Use one column only.
  - Do not add a header or footer -- they are generated automatically.
  - Put full-sized glossy photographs of materials such as gels in the Appendix; you must also include those images (or smaller versions) in the Research Plan.
  - Put other graphs and charts in the Research Plan only.

Develop Your Research Plan

Creating a top-quality Research Plan is critical to your application's success in peer review. Your plan describes what you are proposing to do, why it's important, and how you will do it.
The body of a Research Plan has four sections: (NOTE TO STUDENTS: YOU CAN IGNORE SECTION #3)

1. Specific Aims.
2. Background and Significance.

Design your research to answer the question posed by your hypothesis. Throughout the plan, you should give enough detail to convince the primary, secondary, and tertiary reviewers:

- Your hypothesis is sound and important.
- Your aims are logical and feasible.
- You understand potential problems.
- You can analyze the data.

How Will You Organize Your Research Plan?

By organizing effectively, you'll give reviewers guideposts to understand your plan.

- For the big picture, use the section letters and headers in the 398 for paper application or the Grant Application Guide for your Grant Application Package for electronic application.
- Depending what works best for you, fine tune the next level, organizing your material using by any of the following. Coordinate sections so they progress logically.
  - Review criteria.
  - Order of your experiments.
  - More and less technical material.
  - A mixture of the approaches listed above.
- No matter how you organize, list all experiments you plan to do for each specific aim, showing start and stop points for each one.
  - Always tell reviewers what staff you'll need to accomplish your aims.
  - Be sure to correlate the time you indicate it takes to complete the experiments with the budget and personnel you are requesting.
- For maximum effectiveness, include graphical timetables to illustrate the flow and timeframe for your experiments. In decision trees, show any overlap and what you plan to do if you get a negative result.
- To save time and space, you can use well-known references for the more technical material. If a citation is known in your field, reviewers will be familiar with it, so you can leave out details related to it.
- Don't put anything in your research you don't plan to do! Keep it streamlined. The more you put in, the greater your chances of making a mistake.

Specific Aims

Your specific aims are the objectives of your research project, what you want to accomplish, and your project milestones. Recommended length of this section is one page.
• Write this section for all your audiences, primary reviewers and other reviewers, since they'll all read it.

• Choose aims the reviewers can easily assess.
  o Your aims are the accomplishments by which the success of your project is measured.
  o To be assessable, make each specific aim an endpoint rather than a best effort.

• Do not confuse specific aims with your project's long-term goals. Specific aims are what you plan to accomplish by the end of the grant.

• Being too ambitious is a common mistake new PI applicants make. You should probably limit your proposal to three to four specific aims.

• Design your specific aims and experiments so they answer the question posed by the hypothesis. Organize and define your aims so you can relate them directly to your research methods.

• Begin by stating your hypothesis or research objectives.

• You may want to organize this section in outline form: Specific aim 1, Specific aim 2, etc.

• If you are applying for more than one grant, make sure the specific aims differ

Background and Significance

Remember that this is one of the three sections likely to be read by all the reviewers, so you'll write this section in nontechnical terms for the broader audience. Recommended length of this section is two to three pages.

• Convey the significance of your research to 1) increasing scientific knowledge and 2) improving public health.

• Reveal you are aware of opportunities, gaps, and roadblocks in your field.
  o Show reviewers your intimate familiarity with the field and knowledge about research being done, referring to all relevant scientific literature.
  o If you leave out an important work, reviewers will assume you're not aware of it.

• Use this section to show the breadth of your knowledge of your field and highlight why you are uniquely qualified to do the research.
  o Refer to unpublished work, including information learned through personal contacts.
  o Make sure the literature you note here is also in your Bibliography and References Cited section.

• Tie your science to curing, treating, or preventing disease.
  o Tell reviewers how your work suits the NIH mission to improve health through science -- just moving science forward is not enough.
  o Reviewers will judge the likelihood that your research can make an impact on public health.

• Significant also relates to being innovative. That can be tricky; see Be Persuasive, But Be Careful of Being Too Innovative.

Preliminary Studies/Progress Report
By providing preliminary data, you build reviewer confidence you can handle the technologies, understand the methods, and interpret results.

Reviewers use this section together with the biographical sketches to assess the investigator peer review criterion.

Preliminary data help you show that you have the expertise to do the job; here are some pointers:

- Interpret preliminary results critically.
  - Give alternative meanings to the data to show you've thought the problem through and will be able to meet future challenges.
  - If you don't do this, the reviewers will!
- Include enough information to show you know what you're talking about.
  - The more complex the project, the more data needed.
  - Tell them how your early work prepared you for the new project.
- Though you may include publications of others, focus on your own preliminary data or unpublished data from your laboratory.
- When using results from other labs, make sure it's clear which data are yours and which emanated from others.
- Include any previous experience that shows you can direct the proposed research and achieve its aims.
- For tips for new investigators, go to Advice for New Investigators

**Research Design and Methods**

When reviewers judge your application, your Research Design and Methods section has the most weight. It describes the experimental design and procedures -- how you will perform the research. Think carefully about how to organize it.

There is no recommended page length to this section, though you must stay within the 25-page limit of the sections listed on Develop Your Research Plan.

- You may want to organize with:
  - Two sections: 1) a description of your research and your methods first and 2) the methods.
  - A section for each of NIH's five review criteria.
- Create a timetable showing how and when you will accomplish your aims, including any overlap of experiments and alternative paths.
  - Use flow charts and decision trees to show paths of experiments and how they progress, including paths that show alternatives -- what you will do if you get negative results.
  - You can use the same graphics you created to plan the project.
- Spell out in detail what you are going to do, how you are going to do it, and your criteria for success.
- Describe the kinds of results you expect and how they would support continuing your project. Discuss other possible outcomes and contingency plans.
• Define the criteria for evaluating the success or failure of each experiment. If possible include a statistical analysis, which may impress your reviewers.

• Anticipate reviewers’ questions about the feasibility of what you propose, e.g., how you will gain access to reagents, equipment, or study populations.

Research Design and Methods: General

Here are some tips for this section:

• **Give details:** specify animal models, exposure times, reagents and how you will get them, statistical analysis methods, etc.
  - While you may assume reviewers are experts in the field and familiar with current methodology, they will not make the same assumption about you.
  - Details show you understand and can handle the research. It is not sufficient to state:
    
    "We will grow a variety of viruses in cells using standard in vitro tissue culture techniques."

    Reviewers want to know which viruses, cells, and techniques; the rationale for using a system; and exactly how the techniques will be used.

• **Cite references wherever possible.** If a technique is well known, the citation is enough.

• **One caveat: do not give more information than is needed** to state your case. Reviewers will look for flaws and penalize you heavily for them. Don't give them ammunition by including anything in the application you don't plan to do.

• **If your proposal is highly innovative,** you'll need to make a very strong case for why you are challenging the existing paradigm and have data to support your innovative approach. Also read Be Persuasive, But Be Careful of Being Too Innovative.

• **If you gather additional data** between the time you send in the application and the date of the review, you may be able to send it to the scientific review administrator of the study section reviewing your application.
  - Call the SRA to find out whether this is possible and the deadline.
  - Policies vary among study sections. See If I forget something, may I send it after the due date?

Research Design and Methods: Approach

After you give an overview of the type of research you propose, do the following:

• **Defend your choice of study design.** Be sure to state the expected outcome of your research.

• **List each set of experiments in the same order as your aims.** Link your experiments to the specific aims, so reviewers can see how you will achieve them.

• **Put experiments in a logical sequence.** They should flow from one to the next with clear starting and finishing points.
  - Propose a realistic level of work for the allotted time.
  - Estimate how much you expect to accomplish each year of the grant and state any delays you can anticipate.
• **Convince reviewers you chose the right methods.**
  o Ask yourself: Are my procedures feasible and within my competence?
  o If your methods are innovative, state why you chose them and how you will avoid technical problems.
  o Explain a method in more detail if you have little published experience with it.

• **Discuss your methods for gathering and interpreting data in detail.** Make sure your experiment can yield statistically significant results.

• **Rely on consultants to fill in expertise.**
  o State how collaborators or consultants will fit into the work.
  o List them as key personnel, and provide biosketches. See next bullet.

• **Describe sources for key reagents and equipment.** If collaborators will provide them, include Letters of Support attachments to the PHS 398 Research Plan describing their agreements with you, including their role on the project.

• **Animals or human subjects.** Give details if using.

• **Hazardous materials.** If working with hazardous materials, state the special facilities you can access for protecting the environment and staff.
  o Describe the precautions you will take in handling the materials.
  o Describe the training people involved have had in safe practices.

**Explore Alternatives, Thoroughly Reference**

**Explore Alternatives**

• **Discuss the limitations** of each approach you are proposing and how they may affect your results and data.
  o Call attention to potential difficulties.
  o Propose alternatives.

• **State what you’ll do if results are negative**, how negative findings will also advance the field, and what you’ll do next.

**Thoroughly Reference**

• **Reference all the methods and concepts** you've used and include a list of the citations in the Bibliography and References Cited attachment of the Research and Related Other Project Information form. For a paper application, use the Literature Cited section of the Research Plan in the PHS 398.

• **Include well-designed tables and figures that have accurate and informative titles.** Reviewers expect to see supporting data.
  o Label the axes and include legends. Reviewers will look for discrepancies between your data and text.
  o Check and double check to avoid glitches.

• **Put publications in the appendix,** if you or your collaborators have publications showing your use of the proposed methods.
  o Include in the appendix only published manuscripts or those accepted for publication.
For more information, see Do You Need an Appendix?

How Will You Deal With Results?

To succeed, your application must convince reviewers you'll be able to interpret your results. Do this by revealing your understanding of the complexities of the subject and breadth of knowledge of your field.

- **Show you are aware of the limits to -- and value of -- the kinds of results you can expect** based on current knowledge.
  - State the conditions under which your experimental data would support or contradict your hypothesis and the limits you will observe in interpreting results.
  - Define the criteria for evaluating the success or failure of a test.

- **Describe your statistical methods** for analyzing the data you plan to collect.
  - When evaluating your approach, peer reviewers will want to assess your methods of data analysis and power calculations as well as your justification for your proposed sample size.
  - Well-designed statistical methods will impress reviewers favorably.
  - Consider getting a statistician involved early to advise you on sample sizes and the amount of data you'll need to collect.

Bibliography and References Cited

List all the publications you've cited in your Research Plan and other parts of your application.

- In the Research Plan, cite the scientific literature thoroughly but not excessively.
  - Include only current citations relevant to the project.
  - Include all publications supporting your hypothesis and methods.
  - Your list should probably have fewer than 100 citations.
  - There is no page limit.

- Each citation must have the names of all authors (do not use "et al.") in the order listed in the original publication, name of the book or journal, volume number, page number range, and year of publication.

- Citations show reviewers your breadth of knowledge of your field.
  - Research proposals do not fare well when PI applicants fail to reference relevant published research.
  - This is particularly true if the proposed approach has already been attempted or the methods were found to be inappropriate for answering the questions posed.
  - Check the list of your reviewers. Be sure to include any publications of theirs that are relevant to your project.