# Proposal Writing:
# The Business of Science

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## The NIH System of Review

The NIH has a dual system of review. The first (and most important) level of review is carried out by a designated study section. The second level is carried out by council.

There are about 100 study sections that review applications and make budget recommendations. You may want to become familiar with the interests of the various study sections because so you can request assignment to a particular study section by attaching a brief letter to your application at the time of submission. (If you do not make a specific request, your application will be assigned to a study section based on the title and abstract.)

If you are assigned to a study section that you think is inappropriate, you can ask that the Scientific Review Administrator (SRA) change your assignment prior to the review. The name and address of your SRA will be given to you at the time your application is assigned for review.

Do not simply wait for a negative review by an inappropriate study section because it is usually futile to try to rebut a review.

## New NIH Grant Review Criteria

The grant review criteria used by the NIH have been modified recently. The biggest change is that for the first time, grant proposals will be evaluated on "innovation." The impact of this addition remains to be seen, but it may mean good news for junior investigators (those without a proven track record) as it may promote funding of research with a certain amount of risk. Until now, "bold" research or research whose outcome was uncertain has been more difficult to fund given the tight money climate, which has favored established researchers and research with substantial preliminary data to back it up. But, as the NIH is the first to advise, don't skip the preliminary data section just yet! The trick will be to develop a compromise between new ideas and sufficient grounding to support them (e.g., training, resources, pilot data).

The new evaluation criteria are:

1) Significance (Does the study address an important problem?)

2) Approach (Are the design and methods appropriate to the address the aims?)

3) Innovation (Does the project employ novel concepts, approaches, or methods?)

4) Investigator (Is the investigator appropriately trained to carry out the study?)

5) Environment (Will the scientific environment contribute to the probability of success?)

## The Mission of the NIH

Before you begin writing your proposal, make certain that you understand the mission of the funding agency to which you are applying. The mission of the NIH is to improve the health of the people in the U.S. No matter how scientifically important your work may be, no funding agency will support your proposal if it does not support the agency's mission. For example: You would never dream of applying to the American Heart Association for a proposal to investigate cancer. Thus, do not apply to the NIH if your proposed research does not support its mission. Its mission is not to support the most promising scientific research (although it may very well end up doing that). Its mission is to improve health.

## Components of the NIH Grant Application

The essence of a successful application is the idea underlying it. How can we evaluate whether our idea is a good idea, the definition of a good idea being one with the potential to be funded? Keeping in mind the new review criteria, our scientific idea must be important, that is, it must address a significant problem. The idea must be conceptually sound and doable, that is, capable of being investigated rigorously by the investigator using the resources available at his/her institution. Finally, bearing in mind the new criterion of innovation, the idea must have the potential to contribute to our understanding of disease or the mechanisms underlying human disease. A particularly effective way to present an idea is in the form of a scientific question.

### 1. The Specific Aims

The specific aims state what you want to do in the order in which you want to do it. Think of your aims as experiments designed to test your hypotheses (discussed subsequently). Begin your aims with a brief (two- to three-sentence) summary of the problem/issue addressed in your research. Make certain to refer to the significance of the proposed research in this paragraph. Do not use references in this paragraph or in any part of the specific aims.

Remember that the aims are called specific: make sure they are exactly that - concise and to the point. Since your aims are a "to do" list, it helps to present them in active language, such as "to quantify", "to determine", etc. Avoid vague language that leaves your reviewer uncertain as to exactly what it is you are proposing to do, for example, do not write "to study" (it makes you sound like you are still a graduate student, and the NIH does not fund graduate work!)

A frequent question is how many specific aims should a grant include? Three or four are the norm. Do not try to give the NIH a "scientific bargain" by proposing a laundry list of aims. This makes it appear that you do not understand what is involved in conducting a scientific experiment.

A hypothesis is an educated prediction about the outcome of your study. The most powerful hypotheses are based on pilot studies. Many investigators omit hypotheses as they consider them reminiscent of high school science. Omission of a hypothesis is a major error in that your reviewers can criticize you for conducting a "fishing expedition". This is one of the most common criticisms made by NIH reviewers. But it is one which can be avoided by writing a highly focused grant application developed to test a hypothesis.

Remember that hypotheses must be testable. Do not simply rewrite the objective of your application as a hypothesis, e.g., "We propose to use such and such method to determine whether such and such substance is present in such and such part of the anatomy. Our

hypothesis is that by using such and such method we can detect such and such substance in such and such part of the anatomy." This type of simplistic restatement of work is not a hypothesis in the scientific sense of the word. The point of your research proposal should be to develop experiments designed to test your hypothesis. Make sure it's testable!

The question often arises as to how many hypotheses are appropriate. One strong hypothesis is fine. Some investigators have a hypothesis underlying each aim. That is also fine. The question of how many hypotheses to include should be driven by the nature of the questions you seek to answer.

The overall goal (sometimes called a long-term goal) is the final component to include in the specific aims. The overall goal should provide the reviewer with a sense of not only what you wish to accomplish in the proposed research, but how this piece fits into your future plans. It is particularly important for a young scientist to provide the reviewer with a sense of future direction in this statement. This is because when the NIH commits to funding the proposal of a young scientist, they are also investing in that person's career. Therefore give them a sense of where you're headed and how this proposal will move you in that direction.

Finally, your aims should be the first piece you write. In fact, it can be very helpful to draft the aims, then circulate them to your grant team for review. This is important, because your aims are the basis for your application; if you draft a proposal based on weak aims, you will have wasted a lot of time and effort. Therefore, begin work on your proposal early and plan to draft the aims first, circulate them to your team or to a mentor, incorporate their feedback, then draft the proposal.

2. The Background and Significance

The background and significance section serves several purposes, which are often misunderstood. It is not a literature review, as is commonly believed. By definition, a literature review is exhaustive, whereas the recommended length of this part of the application is two to three pages. The first purpose of this section is to demonstrate your understanding of your field by critically analyzing the pertinent work of other investigators leading up to your proposed work. "Critical" does not mean negative, however; critical means that you are able to appreciate the salient contributions of other scientists upon whose work your work builds. Do not disparage the work of others in this section (or anywhere in your application). You never know who may end up reviewing you. Besides, it looks like poor sportsmanship.

Once you have identified the pivotal work leading up to yours, state explicitly what scientific questions other scientists have not yet answered about your field. This is what is meant by the NIH instructions to identify the "gaps in our understanding". Next suggest how your work will be structured to address these important questions.

Finally, make certain that the significance of your proposed work is clearly shown. This is not the same as showing that the health issue/disease to which your research relates is significant. A lot of investigators become confused about this distinction. For example, junior researchers often argue that the disease to which their research relates is significant. But this is a waste of precious space in that the reviewers rarely question the significance of the disease. Rather, what the reviewers are looking for is the impact of your research on the disease or health issue in question. Similarly, you do not need to justify your research by quoting statistics about the prevalence of a disease if it is well known (e.g., the prevalence of heart disease and cancer are widely appreciated). Rather, use this space to convince your reviewers that your proposed research addresses an important clearly defined question

pertaining to health/mechanisms of disease. Stick to the research issue and do not digress. (Remember the advice of Joe Friday from the TV series Dragnet: "Just the facts, Ma'am.")

3. Preliminary Studies

The preliminary studies section is the place to establish the ability of you and your research team to carry out the proposed studies. In science, the time-honored way to demonstrate competence, of course, is by publications. Often, however, junior investigators are at a disadvantage in terms of the number of their publications.

Remember that there are other ways to demonstrate competence, including pertinent prior work or training. Also remember that it is appropriate to discuss previous related work by your collaborators. By far the most persuasive prior work by collaborators, however, is work that was undertaken by you and your collaborators as a team. If you and your collaborators have not yet had the opportunity to publish together, it can be helpful to try to develop a publication before your application is reviewed. You can then send in a supplement. A supplement is additional information submitted after the application has been submitted, but before it has been reviewed.

Contact your SRA to receive specific information about what type and how much information he/she would be willing to receive as well as the deadline for submitting it, as this varies. As a general rule, however, remember to be considerate and keep supplements to an absolute minimum as your reviewers will be receiving it later in the review process. In fact, sometimes supplements don't reach reviewers until the actual study section meeting. In keeping with this, remember the KISS rule and Keep it Short and Simple!

A widespread misconception about the preliminary studies section is that it serves to demonstrate that you have completed some percentage of the proposed work and that you are now seeking funds to finish the study. This way of thinking misconstrues the purpose of the preliminary studies: grant funding is not a "reward" for a partially completed study. Rather, the point is to demonstrate that you can do what you propose to do. After all, if you've already performed one-third or half of the study, the reviewers might well conclude that you can come up with the funds to finish it.

4. Research Design and Methods

The research design and methods section comprises by far the longest section of the research plan; approximately half of the pages in the research plan are devoted to it. This fact underscores the importance of this component to your application. The purpose of the research design and methods section is to explain how you will carry out your specific aims. Therefore, a particularly effective way of organizing this section is by aim; that is, begin this section with a brief description of your overall approach, then describe the experiments to be conducted to achieve each aim in consecutive fashion.

As you begin to write this section, keep in mind its title: that is, it is called, research design and methods, not simply methods. This is not just an issue of semantics, as shown by the fact that the NIH went to the trouble of changing the name of this section some years ago to include the word design.

Beginning scientists are often confused about the distinction between design and methods, leading them to lump the two together. Discuss them separately: The design is the way in which you conceptualize your experiments, whereas the methods are a detailed discussion of exactly what you will do to carry them out. The design is often given under a subhead called

the rationale. The design section is relatively brief, particularly when compared to the methods, but it is inherently interesting in that it shows your reviewers how you think about your work. It tends to be creative; e.g., you could have designed your project in any number of ways, but you chose this one. Why?

The methods, by contrast, are straightforward, but critical, as reflected by the number of pages allocated to them. Make sure you provide your reviewers with sufficient detail to evaluate your work. This is particularly important if you are proposing to develop a new methodology or a new technique.

The research design and methods should include a data analysis section. This section should not simply consist of the names of the statistical tests to be performed, but should convey what types of data will be recorded, how they will be analyzed, and what they will mean in terms of your hypotheses. The absence of a detailed data analysis section is one of the most frequent criticisms made NIH reviewers. If your analysis is complex, you may wish to include a statistician among your investigators. If so, have the statistician help you design the project, not simply "crunch numbers" upon its conclusion. Another very important part of this section is a discussion of the potential limitations of your proposed work as well as your plans for dealing with them. This section often focuses on problems of interpretation; the point needs no elaboration that you do not wish to discuss problems for which you have no potential solutions. Rather, you want to discuss any technical problems that may arise and what alternate plans you may implement. This is a sophisticated part of the proposal, which should be reviewed carefully with a mentor.

End the research design and methods section with a timeline. It is important to convey that your experiments are doable in the proposed time and that you have developed a logical plan for carrying them out.

5. The Abstract

The abstract appears at the beginning of the research plan, but it is presented last here because it really should be written after you have finished the rest of the research plan. This is because an abstract should reflect the contents of the entire application and it should present them in the order in which they appear within the application. The abstract should serve as a "stand alone" piece, because it may be the only part of the application that some reviewers read. Consequently, it should be revised until it is a well-written, accurate summary of the entire proposal.

The abstract is similar to the specific aims, which causes some confusion. Beginning investigators are sometimes reluctant to include the aims in their abstract since they appear shortly after in the specific aims. But it is important to include them in both sections and to use exactly the same wording. The abstract should also include an overview of the methodology, whereas this is not necessary in the aims. Finally, the abstract must reflect the health-relatedness of the research (remember the mission of the NIH) and a significance statement.

**Some Concluding Thoughts**

Even if you are able to incorporate all of the suggestions made here, the reality is that there are no guarantees of securing funding in today's very competitive grants climate. If your application does not receive a fundable priority score, it is understandable to be disappointed, but do not become unduly discouraged. The fact is that many investigators need to revise their applications prior to receiving funding. This is equally true of full professors as well as

those just starting out. The "trick" to getting funded on a revised application is be responsive to the criticisms made by the reviewers. This is not to say that you must necessarily incorporate every one into your proposal, but you will probably need to incorporate the majority to receive funding. It is essential to address every criticism, no matter how seemingly small.

Demonstrate that you have considered the criticism made, and if you cannot incorporate the suggestion, explain your reasons. But do not ignore what you consider to be a trivial criticism as your reviewer obviously considered it important enough to mention.

The tone of your response should be objective, neither angry nor obsequious. It is also very helpful to demonstrate continued progress in a revised application. In other words, show your reviewers that you are sufficiently committed to the project that you continued to work on it, even without outside funding.

While it is frustrating to have to revise an application, many revised applications are successful. Keep at it, and odds are that you will succeed, too.

Good luck!