Grant Writing: A Guide to Approval and Funding

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The ability to write a competitive research grant proposal is an important skill for aspiring young surgical investigators. Although the process seems intimidating, understanding some fundamental principles will improve the likelihood of success and make the ordeal easier. This essay describes the grantwriting process from hypothesis development through study section scoring, to revision of a rejected application. A thorough understanding of the process is emphasized. Individuals planning to submit grant applications must think carefully about the problem they wish to study, articulate why and how they plan to investigate this problem, explain how their results will impact medical care or biomedical research, and satisfy the granting agency that they are capable and qualified to perform the studies that they have outlined. The principles outlined, combined with creativity and perseverance, will improve the chances of successful grant funding.

The thought of writing a research grant is intimidating to seasoned investigators and can be terrifying to individuals new to the research arena. However, the economic truth is that money is required to do research. Granting agencies and foundations have money available for research activities, and you need money if you want to perform research. Your task in writing a research grant application is to convince the granting agency that they should fund your research project. Many good ideas and important problems exist. Therefore, you not only need to convince a funding agency that your project is meritorious, you also need to convince the agency that your proposal is more important than all other applications requesting money from the same pot.

Only 10% of applications to the National Institutes of Health (NIH) are funded. Available federal research moneys have remained relatively flat or decreased over the past decade, and increasing numbers compete for these funds. Still, we must remember that funding agencies are not our adversaries. Granting agencies and foundations are in the business of funding research and have a strong self-interest in seeing the most worthy research funded. The challenge in embarking on a research career is to do high quality, important research. The neophyte researcher should avoid falling into an antagonistic mindset for grant submission. Rather than worrying excessively about "grantsmanship," the primary focus should be on doing excellent research.

There is no "right way" to prepare a grant application. Most of what is summarized below is a combination of common sense and limited personal experience. However, there are no guarantees to grant approval and funding. The principles outlined below, combined with creativity and perseverance, will improve your chances of successful grant funding.

THE FUNDING PROCESS

Before the "nuts and bolts" of grant submission are discussed, it is helpful to have an idea of what happens to a grant after it is received by a funding agency. For this, we will focus on the process within the NIH as a model.

Following receipt of a grant application, the first step is assignment to an appropriate institute. Within the NIH there are many individual institutes, such as General Medical Sciences or the Heart, Lung and Blood Institute. The Division of Research Grants (DRG) then makes the assignment based on the title and abstract. (In some cases, your cover letter may assist in assignment to the appropriate study section.) Within each institute there are peer review Research Advisory Groups (RAGs), commonly referred to as study sections. Members of the study section are responsible for assessing the scientific merit of the proposal and assigning a priority score. Correct study section assignment can be extremely important to the success or failure of a grant proposal. Thus it is incumbent on you, the investigator, to be clear both in the title and abstract about what you are studying.

**Study Sections:** The RAG is composed of peer researchers. The individuals on the study section frequently represent a...
cross section of PhDs and MDs. There is a perception (probably correct) that assignment to a study section composed primarily of PhD basic science researchers will result in a more critical examination of the grant. Although this may be true, the overriding principle is that outstanding projects should be funded irrespective of the study section. All members of a study section have been successful in their own research field and all have broad scientific and methodological knowledge. Study section members have seen many different kinds and styles of grants, both good and bad. Remember that study section members may not be intimately familiar with your particular area of research. Modern biomedical research is so specialized that it is unrealistic to expect that two or three members of a study section will be working in the same field as you. The grant should be written with this in mind.

**Reviewer Assignments:** The head of the study section identifies a primary and a secondary reviewer from the members of a study section. Assignments are based on the content of the grant and the members' expertise, with a concerted effort to match grants to the interests and background of the reviewers. Both the primary and secondary reviewers are responsible for submitting a written summary of the grant and a tentative priority score. Grants are scored on a scale of 1 to 5, with 1 being best. Basically, a score of 1 is considered outstanding, 2—excellent, 3—good, 4—fair, and 5—poor. The preliminary score can be made in increments of 0.1. Recently, the cutoff for a high likelihood of funding has been in the range of 1.4 to 1.6, although this varies. One to two additional readers are assigned to review the grant and determine a score, but readers do not submit a written summary.

**Reviewer Workload:** NIH study sections meet three times a year, usually for 2 or 3 days at a time. At each meeting the study section is responsible for scoring 100 to 150 grants. Typically, each member of the study section is assigned 10 to 15 grants as primary or secondary reviewer or as reader. Most study section members are primary reviewers on 3 to 4 grants, and secondary reviewers for a similar number. All members of the study section have the opportunity to review all 100 to 150 grants to be discussed. This fact is mentioned so that applicant investigators can get a flavor for the conditions under which their grant is evaluated. All members of the study section are very committed to a fair and thorough evaluation of all grant applications. Nonetheless, study section members are human, and they face a daunting task every 4 months. Organization and clear writing of the proposal make it easier for the reviewer to read and assess fairly the merits of the proposal to the investigator's benefit.

**Study Section Meeting:** When the study section meets, a list of the tentative priority scores from the primary and secondary reviewers is examined. Considering the current fiscal realities and the need to streamline the evaluation process, the NIH has adopted a policy known as *triage*. If two or more reviewers deem that a grant falls in the lower half of grants being considered (tentative score ≥ 2.5), the proposal is deemed provisionally unfundable. The entire study section votes on whether to accept the unfundable recommendation of the reviewers; if accepted, there is no further discussion of that proposal. If any of the reviewers or members of the study section wish to discuss the grant, it is discussed fully by the entire study section. Investigators submitting grants deemed unfundable receive the written comments of the reviewers and can begin the resubmission process immediately.

**Study Section Scores:** Ten to 15 minutes are allowed for discussion of each grant proposal. Any member of the study section who might have a conflict of interest with the proposal under discussion must excuse himself or herself during the discussion of that proposal. The primary reviewer is responsible for succinctly summarizing the merits of the proposal to the entire committee, and the secondary reviewer provides additional comments (Table 1). A general discussion concerning the merits and/or shortcomings of the proposal follows. At the completion of this discussion, study section members assign their own priority score. The score received by the grant is based on a numeric average of all study section members and converted from a 1 to 5 scale to 100 to 500 scale.

**From Priority Score to Funding:** After this meeting, the scores are forwarded to the Director of the institute. The Director then makes a determination regarding program relevance and sends a recommendation to the NIH Advisory Council. The Advisory Council is responsible for making the final funding recommendations. The NIH Director must approve the Council action within budgetary constraints. Finally, funds are allocated. In most cases, the time between grant submission and availability of funds through the NIH is 10 to 11 months.

**Preparing a Grant Submission**

**What are you going to study?** A lot of thought and consultation is involved in a proposal. The first and most important thing to think about is what you want to study and why. You must have a clear idea of what you want to investigate before you can describe it to anyone else. In this era of diminished fund availability, it is crucial to pick important problems or questions to study. Discuss the problems or questions that interest you with friends or colleagues to assess how important they are. Do not limit these discussions to surgeons or even physicians.

**Where do you apply?** The next step is to identify the most appropriate funding agency. We tend to think primarily about grant submission to the NIH; however, there are

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<th>Table 1 Questions reviewers ask</th>
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<td>1) Does the proposal show sufficient understanding of agency priorities and guidelines?</td>
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<td>2) Can the proposal's approach meet its objective?</td>
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<td>3) Why is this proposal's approach a good one?</td>
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<td>4) Are there elements that could result in delay or expansion of the project?</td>
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<td>5) Does the proposal have an efficient time schedule?</td>
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<td>6) Does the proposal specify personnel assignments?</td>
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<td>7) Are the personnel qualified for their assigned tasks?</td>
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<td>8) How will consultants be used?</td>
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<td>9) Has the proposal specified the necessary resources and equipment?</td>
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<td>10) Is the budget realistic?</td>
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<td>11) What is the organization's track record in this field?</td>
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Table 2 Characteristics of fundable research ideas

1) The idea is new, innovative, or responsive to a current scientific or societal issue.
2) The idea is timely.
3) There is a clear, documented need for the project.
4) The project has the potential to be cost-effective.
5) Local funds will be available to support (match) the project.
6) The idea has long-term or far-reaching implications.

many other agencies and foundations. Target your proposal to the agency to which you are applying. Write down the questions or problems you propose to study. Review and revise these questions. Writing a grant is not something you can do over the weekend. Ask yourself and your colleagues, are the questions that you have outlined reasonably amenable to research? Some very worthy questions may be too difficult to test, for example, "Why are we here?" Table 2 outlines some important characteristics of "fundable" research.

Consult the Agency Program Director: Another potentially important but often overlooked aspect of this early pregnant writing phase is to consult with the administrator or program officer of the agency to which you are applying. Explain the needs of your program of study, ask about the agency's programmatic priorities for the next year, and inquire about the availability of special programs for new investigators (Table 3). Other important questions to ask: What is the average dollar amount of an award? What is the average length of submitted proposals? Do they allow duplicate submissions? Are there budgetary restrictions? In many cases these individuals are extremely helpful about how to go about submitting an application and whether you are contemplating submission to the correct agency to fund your research. In addition, agencies often put out a Request For Application (RFA), looking for grant proposals to study particular problems.

Literature Review: Once you identify the field you want to investigate and have a rough idea of the questions you want to consider, review the literature, using your preliminary study questions as a guide. Ask yourself, "Has the problem been studied? Are there unanswered questions? What methods have been used and what methods have been rejected?" Continue to ask yourself, "Why is this problem important?"

Table 3 Funding prospect checklist

1) Are the funding agency's priorities compatible with what you want to accomplish?
2) Do you have the resources to do the job?
3) Are you eligible for the funds?
4) Can you meet the sponsor's deadlines?
5) Have you gotten positive feedback from preliminary contact with the sponsor?
6) Is your organization committed to your project?
7) Has the sponsor funded proposals in your geographic area before?
8) Has the sponsor funded similar projects?
9) Is your proposal in the dollar range of the sponsor's past grants?

What questions have been answered in the field and what questions remain unanswered? What needs to be done?" The extent to which an investigator has reviewed the literature is crucial to successful funding. One question that is often intimidating to new investigators is, "How can I compete with these experts?" Your goal in reviewing the literature is to become an expert in this field. Consider writing a review article about the area that you plan to investigate. Writing and publishing a review article establish you as an "expert" in this area and ensure that you have a deep knowledge of the field.

Research Strategy: Next, choose a basic research strategy. In terms of answering the question that you want to propose, what is the best experimental methodology to study this problem? For example, in the area of basic research, do you want to use an in vitro or an in vivo model system? Will your studies use cell culture or whole animals? For clinical studies, think about what kind of study you want to do. The gold standard clinical study is a prospective randomized trial. However, such trials can be very expensive, time-consuming, and may be unnecessary. On the other hand, funding agencies take a dim view of retrospective studies that can often be performed without extramural funds.

Preliminary Data: Your application will be much stronger and your likelihood of success will be much greater if you have preliminary data to support your hypothesis. You will usually need to perform pilot studies or have access to preliminary data from a mentor, collaborator, or from the literature. Having preliminary data is extremely important. Because there are limited funds to disperse, granting agencies do not tend to award impractical ideas. They want assurance that useful information will arise from their endorsement. Furthermore, they want assurance that you can perform the studies! Performing preliminary studies will give you a much better idea of the problem, allow you to work out model system bugs, and will make you write a much more focused grant application.

WRITING THE GRANT

General Suggestion: Before you begin to write the grant, sit down and read the instructions from the funding agency and then reread the instructions! Follow the instructions to organize your application, paying particular attention to page limitations or special instructions. Use a logical organization to your application as well as the format preferred by the agency. Help the reviewers and subdivide your grant application into sections, making liberal use of headings and subheadings. Leave some white space within the application, too. Do everything you can in terms of layout to help the reviewer complete your proposal and understand what it is you wish to study and how you want to study it. Do not impair the reviewer's ability to assess your grant by poor layout or organization.

Consider whether you will need any required institutional approvals such as animal care, human subjects, radiation safety, etc. In many cases such approval can take several months; therefore, it is important that you initiate these processes early. Prior approval on the final grant submission is preferable to an indication that such mandatory requirements are "pending." Remember that your institution is also a partner in the process of obtaining research funds.
Where do I begin? You may experience difficulty in deciding where to begin in writing a grant, an article, or even an abstract. Personally, I find that the best place to start is with the page entitled, "Introduction and Aims." The NIH grant submission guidelines suggest that this section be limited to one page. This is your opportunity to summarize succinctly the problem you plan to investigate and the manner in which it will be investigated. Most importantly, you need to delineate several "specific aims" that the investigation will address. Most people feel that the specific aims should be limited to two or three; this helps to sharpen the focus of the application. Keep in mind that the "Introduction and Aims" page serves as a reference point for constructing the remainder of the grant. Furthermore, reviewers may find it useful to refer back to the introduction page to remind themselves of what you are studying. Investigators preparing a grant application should spend a significant amount of time on this page. Get expert consultation or feedback regarding the general strategy of the grant, the background, the objectives of the study, and whether the introduction is readable. Your goal as an applicant is to get the reviewer interested in the application right from the beginning. You may lose the race before you start if the introduction is confusing or makes a weak statement of the aims or objectives. An abstract is also required, but do not write this yet (see "Abstract" below).

Title of Grant Application: An often neglected strategy is the selection of the title. For NIH submissions, the title cannot exceed 50 characters, including the spaces between words and punctuation, so choosing a specific and descriptive title is vitally important. The title of the application may have an important impact on institute and study section assignment. If appropriate, include the word surgery in the title. This increases the likelihood that the application will be assigned to the General Medical Sciences Institute and specifically to the Surgery, Anesthesiology, Trauma study section. Many surgical investigators feel that this study section is the most appropriate "peer" committee assignment for surgeons investigating problems applicable to clinical surgery.

After the introduction and aims are completed, it is useful to lay out a very rough proposed experimental design that answers your specific aims, questions, or problems. Think about the hypothesis or hypotheses that you want to test. This exercise, along with your previous review of the literature, will lay the ground work for a more detailed background review of the problem. Knowing where you are going allows you to make the best argument about the direction of your proposal.

Background and Significance: After the Specific Aims page, the next section of an NIH grant application is entitled, "Background and Significance." This is your opportunity to sketch the background information pertinent to the present application, using your "review" of the literature. Use this section to make a strong case for the importance of your proposed aims and to delineate the gaps in current medical knowledge. Note that you will have ample opportunity in the remainder of the application to address how you will fill those gaps. Your main goal here is to pique the interest of the reviewers in the importance of your questions. Emphasize the clinical importance of the problem under study, but be realistic in your descriptions. Exaggerating the clinical significance of a research problem undermines your credibility.

More about preliminary data: After the "Background and Significance" section, new applications contain a "Preliminary Data" section. As discussed above, this section is extremely important, because it is the link between the questions identified in the background section and the proposed experiments. Use this section to show that you are capable of performing the studies. Assure the reviewers that you possess the skills, are familiar with the model system, have access to the needed facilities, and have your own data related to these problems. This information will assure the study section that your model system works and that you can obtain and interpret data reliably. Compare and contrast your results with other results in the literature. If there are areas of controversy, do not avoid them, rather address them in a forthright, direct fashion. For NIH applications, this section should occupy 6 to 8 pages. There are no restrictions on use of figures or tables, and to the extent that they help to make your point, they should be used liberally. Figures and tables do take away from the amount of text that can be included, but you should be able to make your point within the 6 to 8 pages despite the use of graphic data.

Throughout this time of writing the "Background" and "Preliminary Data" sections, continue to recheck the "Aims and Introduction" page to be certain that your goals or methods have not changed. If your goals have changed, revise that page to reflect your current working hypothesis.

Writing the Experimental Design Section: You are now ready to write a detailed experimental design. You already have a preliminary sketch and layout of the proposed design and you can now expand and amplify on this. Organize your experimental design around the specific aims or study questions. Again, let me emphasize that you want to make the reading process easy for the reviewers. Do not force them to look back at the "Aims" page to recall your specific aims; rather, use headings for each experiment, identify the questions being studied, and explicitly state the hypothesis under investigation.

In terms of delineating the methodology, be specific but not exhaustive. Many investigators find it useful to follow the experimental design sketch with one or two pages of specific Materials and Methods. To detail the experimental design is appropriate if there are specific experimental conditions or reagents crucial to that experiment. Organize your experimental description in a logical, easy-to-read format. In the course of describing each experiment, or after the experimental description, critique your proposed experiment. This gives you the opportunity to explain your reaction to unexpected results. Unexpected results are the norm rather than the exception in experimental research. Let the reviewers know that you have thought critically about the experiments. Show them that you are not naïve enough to think that your experiments (particularly in the absence of preliminary data) will turn out precisely as you plan.

After completing the description of the experiments, you should compose a timetable that realistically reflects when you will be performing the experiments. That is, "Experiments 1 and 2 will be performed in the first year. The second year will be used to perform Experiments 3, 4 and 5." Provide a table or timeline, but also provide a narrative description of the temporal conduct of the research plan. Finally, recheck your "Introduction and Aims" in light of...
your detailed experimental design to be certain that nothing has changed.

**SWEATING THE DETAILS**

At this point you might think that the grant is almost finished. You worked hard, you reviewed the literature, and you clearly stated your preliminary data and put forth a brilliant experimental design to address your specific aims. Unfortunately, the reality is that you are probably only 75% to 80% done with the grant. Often problems with grants arise from lack of attention to details. Remember that this is your application. You should not rely on clerical or secretarial support to make certain that all aspects of the application are complete, inclusive, and consistent. Grant application deficiencies will hurt you; therefore, you have to be responsible for making sure that the application is complete.

**Budget:** Another critical aspect that is often neglected is preparation of a realistic and appropriate budget. Use local experts, mentors, or collaborators to get a realistic idea about the costs involved. Be certain that all of the figures add up (percentage effort, percentage fringes, and animal per diem calculations). Explored whether any matching opportunities exist within your institution for budgetary items. Make sure that all budgetary items are completely justified, describing who, what, why, where, or when this person, reagent, animal, or supply will be needed. Use continuation pages if needed. There is no page limit on the budget justification (although be reasonable).

**Resources and Environment:** Describe the resources and environment in detail, including in this description a listing of all the major equipment available to the principal investigator. Be particularly mindful of informing the agency that you have the equipment that you need to perform the study. For example, your application will raise concern in the study section if you will be using 100,000 x g cell cytoplasmic for your experimental studies, but the resources and environment do not confirm that you have access to an ultracentrifuge. The reviewers will also immediately discount your request for a peristaltic infusion pump if your description of resources indicates that you have access to four such pumps. Reviewers in study sections are particularly hesitant to use valuable research dollars for acquisition of new capital equipment. Any request for capital equipment merits a detailed justification about why this equipment is critical to the research proposal and not otherwise available.

**Collaborators:** Using research collaborators, from within your institution or without, will benefit the grant and assist your personal career development. Applicants would be strongly encouraged to use research collaborations wisely in their application. Such arrangements should be explained in a letter of collaboration that must be included with the grant application. In a similar vein, letters from a department chairperson or your division head regarding administrative details (protected time, access to laboratory space) should be included.

**Human or Animal Subjects:** A detailed description and justification of the use of experimental animals or human subjects must also be included with the application. When human subjects are involved, a copy of the informed consent agreement might be included as an appendix to the application. For studies involving human subjects, pay particular attention to issues of gender and minority balance in the proposal. Describe in detail your reasons for using experimental vertebrate animals as well as the specific protocols to be used for the animals. Pay particular attention to procedures that cause animals discomfort and the measures you will take to minimize or eliminate this discomfort.

**Biosketches:** Applications require a "biosketch" of all "key" personnel. Essentially, this is similar to a miniature CV. The usual format is limited to two pages and states the academic training of the individual, membership and professional societies, and key publications. Biosketches of collaborators are also usually included. Therefore, it is important to plan early so that you do not find yourself scrambling to obtain biosketches the day before the application deadline.

**Appendices:** An appendix can be added to the application to expand on important points made within the application or to clear up confusion. Appendices should be used judiciously, but are important to use. Reprints of key preliminary data, particularly if they arose from your laboratory or the laboratory of your mentor, may be helpful in describing your model and/or questions. Other information that directly supports the application could be included (e.g., letters of support, documentation of related research).

**Abstract:** An abstract is also required for the application. The abstract is typically limited to 300 words and should summarize your entire proposal, including a brief description of the problem, the aims, the background, and your methods. Many people begin a grant by trying to write the abstract. I would advise against this. The abstract is the only part of the grant (along with the title) that is ever seen by many individuals interested in your project (e.g., many study section members or the agency's program director). Because you are limited in space and this is important, I implore you to save it for last. Write the abstract now that you have finished the grant and know exactly what you want to say.

**Final Preparations:** Prepare a cover letter to accompany the application. In the cover letter you can request an institution in which you think the proposal should be reviewed, although the director of the Division of Research Grants may not honor your suggestion. Organize all components of the application and make sure that you stayed within page restrictions (including restrictions on margins, font, type size, and spacing). Check the page numbering and any cross references within the application. After you have checked them, recheck them! Be certain that the grant is appropriately signed by administrative personnel at your institution. Personally see to it that it is shipped in a manner that will get it to the funding agency in time. Also remember that there is always more to do at the end than you think there will be. Therefore, do not wait until the last minute, especially for a first grant.

**WAITING**

As discussed above, 10 to 11 months may pass from the time you submit your grant application to the receipt of funding for a successful application to the NIH. Within a few weeks after receipt of the application you will receive notice of study section assignment. The study section will meet approximately 4 months after the submission dead-
Table 4 "Kiss of death" statements by reviewers

- "The preliminary data are unclear."
- "Proposed project is largely empirical."
- "Proposed project is large undertaking that does not get at the mechanism of the PI's observation."
- "Proposed experiments are not particularly novel and unlikely to advance this area of research."
- "Enthusiasm was diminished by lack of evidence that results from this paradigm are fundamentally different than other situations."
- "Research goals are too diffuse."
- "A number of problems exist regarding _______ (fill in blank)."
- "The experimental design is not sufficiently described."
- "Nothing original in this proposal."

line. A week or 2 after the study section meets, you'll receive a postcard indicating the priority score. Several weeks later a "pink sheet" will be sent to you providing a detailed critique of the proposal as well as a summary of the discussion that occurred within the study section. Included with the priority score is a percentile ranking of your grant compared to other grants reviewed in the same cycle. As a general rule, percentile scores under 10% have a high likelihood of being funded and percentile scores greater than 20% are unlikely to be funded. The actual final notice of award awaits NIH Council action and takes an additional 4 to 6 weeks.

In the event that you are funded, congratulations! In reality, the more likely outcome, particularly with your first application, will be that you will not be funded. If the score is greater than 250 (percentage > 50%), it suggests that there were serious problems or deficiencies with the proposal (Table 4). Rethink the proposal and take seriously the comments and criticisms of the study section contained within the "pink sheet" to prepare a revised or new application. If the priority score is less than 250, it suggests that the study section felt that the grant had real merit and was potentially fundable (Table 5).

Critically assess the comments of the study section. The study section is not the enemy. The reviewers are trying to help you get funded. You are strongly advised to resubmit the proposal addressing the points raised on the pink sheet. There is a very good chance that resubmission will result in a better score. A better score is almost guaranteed if you address the concerns raised on the pink sheet. Depending on how well you address those criticisms and what the initial score was, this significantly improves your chances of successful funding. Alternatively, depending on the suggestions, you may wish to consider other funding agencies or foundations.

CONCLUSION

Although preparing a research application is a difficult and intimidating task, it can also be an illuminating academic exercise. The process of writing an application will make you a better researcher, helping you to focus your hypotheses, goals, and methodology more clearly. If you do not win the award, you will still have organized your project. Success cannot be guaranteed in biomedical research, but these principles and tips should substantially improve your likelihood of successful grant approval and funding.

APPENDIX

The following resources may assist you in submitting a grant, particularly to Federal Agencies:

**NIH Home page**: A good source of information about the NIH, policies, procedures, programs, etc.
http://web.fie.com/fedix/nih.html/offices

**NIH Grants Database**: Federal grant information (PI, amount, and abstract). Search function to cross-reference federal grants by “keywords.”

**NIH Grant Template Forms**: Wordprocessor version of NIH grant application forms. PC: http://tram.nie.edu/TRAM/forms/phs.pc.html
Mac: http://tram.nie.edu/TRAM/forms/phs.mac.html