Preparing Effective Grant Applications

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A successful research career hinges as much on a scientist's ability to secure funding as it does on the scientist's skills at the bench, in the clinic, or in statistical analyses. Much postgraduate training focuses on the later elements and gives short shrift to the earlier ones. This article attempts to fill that gap by discussing a pivotal element of the funding process: preparing effective grant applications. In addition to discussing the fundamental features of the pivotal sections of a standard National Institutes of Health (NIH) R-series application (see "Types of Grant Programs" on the Web site of the NIH Office of Extramural Research for a complete list of NIH-sponsored grant programs[1]), the sections below outline measures preliminary to the actual grant writing process, rhetorical perspectives and tactics useful to grant writers, the NIH grant application review and scoring process, and the importance of revision and resubmission.

Before Setting Pen to Paper

Grant applications (hereafter I often use the common shorthand "grant" to mean "grant application") are, of course, judged not only on the text, tables, and figures reviewed by the funding agency but also on everything that stands behind the document: the ideas, the researchers and their collective experience, and the researchers' host institutions. A successful grant must persuade reviewers that all of these bases have been covered and that the probability of delivering fruitful findings is high. Thus, a necessary preliminary step in planning any research project is to secure the enthusiastic support of department heads, deans, and managers. Demonstrating that the proposed research has institutional support (in the form of researcher time, support staff, physical space, access to necessary equipment, etc) reassures reviewers that the research will be nurtured in a propitious environment. Second, assembling the best team possible to prepare the grant and to accomplish the work is imperative. This is especially important for new investigators who may lack experience and training in some areas necessary for successful completion of the proposed work. Although this step may be difficult for new researchers, engaging senior collaborators can provide valuable initial feedback on how reviewers and the discipline in general may respond to the proposed research.

Of course, securing institutional support and enlisting senior researchers as collaborators will be largely contingent on developing a suitable research question. A good research question should lead toward a testable hypothesis about the mechanisms underlying the disease process under study. A testable hypothesis is one for which a feasible study design will provide necessary and sufficient evidence to support the complementary null hypothesis if true. A feasible study design is one that can guarantee, at a minimum, the following:

- If proposing patient-oriented research, a population of individuals eligible, appropriate, and willing to participate in the study, including a valid comparison group if the design requires one
- If proposing basic research, the availability of tissue or model systems
- Meaningful and measurable experimental interventions or environmental exposures
- Meaningful and measurable states or events that are related to (or suspected to be related to) the exposure or intervention (ie, end points or outcomes)

According to Hulley et al,[2] in addition to being testable, a good hypothesis must also be simultaneously feasible, interesting, novel, ethical, manageable in scope, and relevant. Discussions with colleagues at this stage of planning can help researchers determine whether these formidable criteria have been met. Arguably the most common mistake new investigators make is failing to focus the question so that it is feasible to answer with the research proposed. Alternatively, an equally common mistake is "overambition." When new research is being proposed, oftentimes "less is more"; ie, it is better to limit the scope of the proposed work than to appear overreaching and overambitious. It is best to chisel research questions into shape early with the input of helpful colleagues rather than later with the criticisms of dissatisfied grant reviewers. For a more thorough discussion of the design of research studies, see the works by Hulley et al,[2] Glasser,[3] and Marks.[4]

Finally, the utility of having good models to guide the writing process cannot be overstated. Studying the scope, structure, style, and layout of senior colleagues' successfully funded applications will help to reinforce sound grant writing practices.

Rhetorical Perspectives and Tactics

The 3 rhetorical planks of audience, rationale, and purpose can help guide the development and composition of the grant.

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Audience

Understanding the audience that will be reading and reviewing the grant can be the single most valuable tactic in the writing process. Audiences for grants can be characterized in 2 ways: in terms of the agency to which the application will be targeted and in terms of the actual individuals reading and scoring the applications. Characterizing the former is easier than characterizing the latter. Grant writers should be familiar with the overall mission of the funding agency and spend time reviewing recent research that the agency has supported. Some agencies publish strategic plans that can provide insight to the organization's long-term goals. For example, the National Heart, Lung, and Blood Institute (NHLBI) of the NIH recently completed its strategic planning process; within the plan are the priority areas for the NHLBI that will guide scientific directions for the next 5 to 10 years.[5] Speaking with others who have been successfully funded by the agency and with the program staff at the institute can also be helpful. Finally, becoming well acquainted with the logistical requirements of preparing and submitting a grant well before the submission deadline will enable applicants to deliver exactly what their institutional audience expects.

Because grant applicants rarely know exactly who will be reviewing their proposals, characterizing the review team can be difficult. Oftentimes, however, colleagues may know who frequently leads and participates in an agency's application review sections. Applicants can refer to rosters of chartered NIH Study Sections on the Center for Scientific Review Web site,[6] and in their communications to the referral branch with their application, applicants can suggest the appropriate Study Section for their application. Grant writers who familiarize themselves with the work of these individuals are more likely to imbue their own work with features the reviewers both understand and endorse. It is important to appreciate the distinction between catering to an audience's expectations and needs and pandering to reviewers. Gratuitous citation of potential reviewers' work will never hide sloppy thinking or a banal hypothesis. A well-tailored message, however, makes it easier for reviewers to comprehend and appreciate an innovative proposal.

Rationale

Much has been said about the importance of emphasizing the overall rationale for a study, often characterized by the "knowledge gap" that the proposed research intends to fill. Although it is vital that grant writers make this overall rationale for their studies clear (preferably early and often in their application), the concept of rationale must be brought to bear on all elements of the research and all sections of a grant. In other words, applicants must make it clear why they have chosen their particular hypothesis; study design; population; exposure/intervention; end point/outcome; clinical, laboratory, and statistical methods; collaborators; timeline; and so forth. Researchers who fail to explain the motives behind their choices will not create winning proposals.

Purpose

Of course, the overall purpose driving the proposed research is to answer the research question. The overall purpose driving the grant application, however, is quite different: to persuade the reviewers that the proposed research is both valuable and likely to succeed. Grant writers must never lose sight of this important distinction. Maintaining focus on the purpose of a grant (not the purpose of the research project) can be improved by always asking, "What do I want this section (or paragraph or table or figure) to do?" rather than "What do I want this section (or paragraph or table or figure) to say?" For example, a paragraph describing a genotyping method may do the rhetorical work of persuading reviewers that the chosen approach is sufficiently accurate and precise to characterize the exposure variable of the study and that it is also cost-effective. A table describing collaborators' expertise and experience does the work of convincing the reviewers that all elements of the proposed study will be guided by knowledgeable and proficient investigators. Being mindful of audience, rationale, and purpose keeps grant writers focused on reviewer expectations, explaining why particular choices have been made, and how every element of the grant works toward persuading reviewers that the proposed research is both valuable and likely to succeed.

Other Considerations

Many researchers believe such things as spelling errors, poor grammar, oblique organization, and ugly formatting will be ignored in light of the brilliance of the intellectual content of the grant. Nothing could be further from the truth. Sloppy writing suggests that the applicant is unable or unwilling to pay attention to details, which is not a characteristic of a successful scientist. Reviewers who are confused and frustrated by slapdash writing will be unlikely to offer a favorable score.

It is absolutely essential that grants be formatted and packaged in accordance with the criteria of the funding agency. Page count, margin width, header and footer content, font, font size, and other formal elements are often dictated by the funding agency, and any deviation usually results in flat-out rejection of the grant. Within these constraints, however, grant writers have considerable power to shape their documents. In general, prose style should be unadorned, and unnecessary technical language should be avoided. Abbreviations should be used judiciously; they may save space, but overuse can make documents unreadable. Subheadings should be used to guide the reader. Whenever possible, figures should be used to clarify concepts and to visually break up the page. Attractive design elements such as uniform formats for tables and figures can add visual appeal and lend the grant a sense of cohesiveness. It is useful to create "road maps" in the introductory paragraphs of each section that outline the content that follows. For example, the first paragraph in the Background and Significance section (see below) might end with, "In this section, we review (1) the epidemiology of hypertension, (2) the pathophysiology of hypertension, (3) other medical consequences of hypertension, (4) the clinical treatment of hypertension, (5) the genetics of hypertension, and (6) implications for the proposed research." Finally, correct spelling, grammar, and punctuation are obligatory.

The Structure of a Research Grant

For the NIH scientist, the most important sections of a grant include the following:

- Abstract
- Budget for the initial period
- Budget for a 5-year period
- Introduction (for revised or supplemental applications only)
- Research plan
  - — Specific aims
  - — Background and significance
  - — Preliminary studies/progress report
  - — Research design and methods
  - — Use of human subjects
  - — Use of vertebrate animals
  - — Literature cited
  - — Data sharing plan

There are also many administrative forms that must be included from the applicant's institution (eg, face page, checklist), but the sections listed above are the most time intensive to prepare. It is important for the applicant to read the instructions carefully and to check with his or her grants and contracts officer to resolve any administrative issues early in the preparation process. Below, I discuss those sections that will likely have the most persuasive force in the grant application.

Abstract

The abstract and specific aims (described below) sections, two of the most important components of any grant application, must provide a cohesive framework for the application. The abstract provides an outline of the proposed research for the funding agency and the reviewers. Despite the fact that the abstract comes before the research plan in the physical document and is probably read before the other parts of the grant, it is usually written after the research plan is completed. The reason for this should be obvious: It is easier to create an accurate miniature version of the research plan after the hard work of developing the plan and committing it to words is finished. The abstract should include a rationale statement (ie, the "knowledge gap" the research intends to fill), the research question, the overall hypotheses to be tested, a description of the study population and methods (recruitment, clinical, laboratory, statistical, etc), and a summary of the specific aims. The final statement in the abstract should indicate how the proposed research will advance knowledge and practice in the discipline. In addition to providing a summary of the grant for reviewers, the abstract will be used by the funding agency to decide which group of reviewers is best suited to assess the grant. NIH grant abstracts are also uploaded into Computer Retrieval of Information on Scientific Projects, a searchable database that provides scientists the ability to search for scientific concepts and emerging methods or to identify specific grants and/or principal investigators.

Research Plan

Specific Aims

In an NIH grant, the specific aims are the practical extensions of the research question and hypotheses; they break the work necessary to test the hypotheses into conceptual, goal-oriented chunks. The entire specific aims section should generally be no more than 1 page and should begin with (1) a brief introduction that underscores the importance of the proposed research (ie, the overall rationale), (2) a brief summary of recent findings and the current research front, and (3) the problem that the proposed research will address. For example, a grant that proposes to identify the genetic determinants of left ventricular hypertrophy might begin with the following elements: "(1) Left ventricular hypertrophy is a common condition associated with cardiovascular morbidity and mortality . . ., (2) we and others have shown that left ventricular hypertrophy is, in part, genetically determined, and (3) we anticipate that our research will identify genetic variants that play clinically significant roles in left ventricular hypertrophy. Such knowledge may suggest novel pathways to be explored as targets for preventive or therapeutic interventions."

This should be followed with a statement of the aims themselves. Specific aims can build on a variety of models. For example, each aim might present a different approach to test the central hypothesis. Another model may be to have each aim develop or define the next logical step in a disease process. Avoid models in which one aim is dependent on the successful completion of an earlier aim. Such "contingent aims" reduce the merit of a grant because reviewers cannot easily assess the overall probability of success.

Regardless of how the aims are structured, they should be comprehensive in terms of the proposed research but also brief, simple, focused, and limited in number. Most important, the aims should be kept simple, at the appropriate level of the research team's expertise, and supportable by available preliminary data. The aims should represent the team's capacity to complete the work proposed within the budget and the time requested. It is useful to build aims around action verbs such as "characterize," "create," "determine," "establish," "delineate," "analyze," or "identify."

Background and Significance

The 2- to 3-page background and significance section provides an opportunity to present the overall rationale of project in detail and the rationale behind specific study design decisions. This section also allows applicants to review the relevant literature, thereby furnishing a context in which the remainder of the grant can be understood. Most important, the background and significance section of the grant must generate enthusiasm; it must leave no doubt in the reviewers' minds that the work is fascinating, exciting, important, and worthwhile.

There are no strict rules as to how the background and significance section should be arranged, but the section should answer at least the following questions:

- What is the current state of knowledge in the field (generally) and surrounding the research question (specifically)? That is, what does the literature tell us about the research front?
- How might the specific work proposed in the grant advance the overall research goals of the discipline? That is, what is the knowledge gap with respect to research?
- How might the proposed work benefit clinical practice, individual health, and public health? That is, what is the knowledge gap with respect to clinical practice?
- How are specific elements of the study design suited to achieving the specific aims?

- How do specific research methods make use of or advance the state of the art?

Whatever arrangement scheme is used to answer these questions, the final paragraph in this section should contain a strong reaffirmation that the grant proposes work in response to a recognized knowledge gap, that the study and its team are uniquely qualified to successfully fill the gap, and that the research will advance both knowledge and practice in the field.

Preliminary Studies

According to NIH guidelines, the preliminary studies section should provide an account of the applicant's previous studies that are relevant to the proposed work and any other information that will help establish the research team's ability to successfully complete the proposed project. Six to 8 pages are recommended for this section. Content should include findings from published and unpublished previous research that set the stage for the remainder of the proposal and build a foundation for the study. Pilot study data should be summarized in tables and figures. Interpretation of these data is critically important because it allows the applicant to demonstrate an ability to accurately articulate the relevance of the pilot data and to correctly state the implications of the work. This section also uses the previous results to demonstrate the feasibility of the proposed project. Note that pilot studies are required for many (but not all) R-series grants. The preliminary studies section is particularly important for junior investigators who may lack adequate experience or training for the proposed research and have a limited publication record. By offering pilot study data and providing detailed descriptions of collaborators' previous work, new investigators can make a convincing argument that they are prepared to succeed.

Research Design and Methods

This section describes all the materials and methods needed to complete the proposed research. Grant writers must allocate adequate time to prepare and sufficient space to present this section. Because this is the section where many reviewers begin to read an application (despite the physical ordering of sections), it is useful to summarize each specific aim in the opening paragraph of this section.

Applicants must be clear, concise, and detailed in their descriptions of how data will be collected, analyzed, and interpreted. It is often effective to organize this section according to specific aims, with each aim serving as a major subheading. Not only is it important to describe what design; study population; intervention; outcome; and clinical, laboratory, and statistical methods have been chosen and how they will be used, but it is also useful to briefly reiterate why a particular design, study population, or method has been chosen. Applicants should provide descriptions of the important techniques to be used in the research. For long-established or commercially available methods, only a brief description or reference is necessary. However, for novel methods crucial to completing the study, a more detailed description and thorough documentation pointing to recent literature are essential.

For many studies, recruiting a sufficient study population poses a significant challenge. Effective grant writers recognize this and devote considerable attention to describing the sample and reassuring reviewers that recruitment will be successful. For research involving human subjects, applicants should discuss from where the population will be recruited, how potential participants will be contacted and encouraged to participate, and what the population characteristics will be (eg, gender, age, and inclusion and exclusion criteria). Reviewers should be convinced that the applicant is cognizant of and responsive to special issues related to ascertainment such as sample sex ratios, participation of minorities and children, and participant burden.

Finally, good design and methods sections also discuss contingency plans that can be put into action in the event that recruitment efforts or preliminary findings vary substantially from what was anticipated or if proposed laboratory or data analytical methods should fail. Carefully contemplated alternatives demonstrate to reviewers that the applicant is not glib and is prepared to maneuver when he or she encounters the inevitable surprises that characterize all cutting-edge research. The design and methods section should conclude with a project timeline that delineates when project milestones in recruitment, data collection, data analysis, and publication will occur.

Submitting the Grant Application

Grant applications should be prepared far enough in advance of the submission deadline to allow mentors, peers, and collaborators time to carefully review the document and to allow the applicant time to consider the critiques and to rework the grant accordingly. Only when a grant has been carefully revised and edited and is above any level of embarrassment should it be submitted.

While waiting for a grant to be reviewed and scored, it is important for applicants to remain confident that the proposed work is both valuable and fundable; however, it is also important to remember that most grants are not funded. This harsh fact must serve to motivate rather than immobilize researchers; researchers must begin planning the next grant while one is under review.

NIH Research Grant Application Review and Scoring

Applications submitted to the NIH undergo a uniform process of peer review. The Center for Scientific Review is the central point for receipt of applications to the NIH and many other federal agencies; the Center for Scientific Review is also responsible for initiating the review process. Each application is assigned to an appropriate place for each of the 2 phases of peer review: review by a scientific review group (called Study Sections by the Center for Scientific Review) for scientific and technical merit and review by an institute/center National Advisory Council,[7] which makes recommendations regarding support. National Advisory Councils and chartered Study Sections regularly meet 3 times per year.

Applications either are unscored or are scored on a scale from 1.0 (exceptional) to 9.0 (poor). Applications are voted by Study Section members in whole numbers (1, 2, 3, etc);

their scores are averaged, and the result is multiplied by 10 to determine the final impact or "priority score" (see "Scoring System and Procedure" on the Web site of the NIH Office of Extramural Research[8]). This priority score is then transformed into a percentile rank based on 3 application rounds. The standard criteria for scoring are significance, approach, innovation, investigators, and environment, each weighed by the judgment of reviewers, with significance being most important. Unscored applications are at or above the 50th percentile and are not discussed by the Study Section. However, written critiques from ≥3 reviewers are provided in the summary statement (ie, the compilation of the critiques from the reviewers) sent to the institute and the applicants (accessed through an NIH commons account) for all applications. Scored applications have additional portions in the summary statement written by the Scientific Review Officer (ie, the NIH staff person in charge of the Study Section).

After the scientific review, each institute or center (eg, NHLBI) that has accepted an application will consider it and make recommendations for funding for those applications that show promise of making valuable contributions to knowledge at the meeting of their National Advisory Council (ie, an advisory group of senior leaders in the field that considers applications for research). These meetings occur ≈3 to 4 months after the Study Section meeting. Because different institutes and centers have different budgets and commitments, they often have different "paylines" (ie, the percentile rank up to which they generally support applications). To increase the probability of funding, it is important to propose research that is relevant to the mission of >1 institute or center.

Although priority scores representing the assessment of scientific merit are an important factor in the recommendations made by National Advisory Councils, they are not the only factor. Other important considerations include priorities related to the missions of the institute or center, new investigator status (in an effort to recognize the need to help establish new investigators), portfolio balance in different scientific areas, ongoing studies, public health and clinical relevance, congressional interest, and particular emergent areas. Funding decisions are ultimately made by the institute or center directors, usually on the basis of the combined assessments of the 2 stages of peer review (Study Section and National Advisory Council). Each institute director also has numerous ongoing commitments and new initiatives to consider when making award decisions. For specific information regarding the paylines for NHBLI, see "FY 2010 Funding and Operating Guidelines."[9] Although the paylines for any given cycle are low (as of September 2, 2009, the R-type grant payline of the NHBLI is the 12th percentile), the overall success rate is higher. For example, for 2008, NHBLI reviewed 4492 applications and awarded 999, which translates to a success rate of 22.2% (see "Research Project Success Rates by NIH Institute for 2008"[10]).

Revising and Resubmitting

It has been said (only semifacetiously) that the "3 Rs" of grant writing are revising, resubmitting, and resubmitting. Grants with merit that are denied funding must be reassessed, rewritten, and resubmitted. Thoughtful, responsive revisions result in much stronger proposals. It is essential that applicants take reviewers' critiques seriously and respond to all comments in their revisions. In some cases, a response to a reviewer might consist of a simple clarification of a misunderstood point; in other cases, a response may involve major changes to the study design. In either case, the introduction section of a revised grant should briefly explain how the applicant has addressed every substantive critique made by every reviewer.

Submitting to Multiple Organizations

The focus of this discussion has been NIH grants because these grants are very important to institutions. NIH grants are important because they cover indirect costs (ie, costs that are not specifically attributed to an individual project) to pay for many of the facility and personnel costs needed to conduct the research such as research administrators, utilities for buildings that house the research, telephone services, postage, and office supplies, to name just a few. Given the overall success rates for grants, applicants must be prepared to submit an application to foundations or other health organizations that fund research, even though these groups typically cover fewer indirect costs relative to the NIH. For example, the American Heart Association funds about $140 million dollars in research per year and emphasizes early career investigator programs (see "National Program Funding Opportunities" on the American Heart Association Web site[11] for programs offered by the national program). New investigators should be aware of the special opportunities available to researchers in the early stages of their career.[12]

Conclusions

Good grant writers spend a large amount of time planning their research, discussing ideas with colleagues, and assembling a research team. They anticipate the expectations and needs of their audience. They keep in mind that their primary purpose is to persuade reviewers that the proposed research is both valuable and likely to succeed. They always remember to explain why they have made the choices they have made. They create a set of specific aims that can serve to organize both the grant and the research effort itself. They provide a context in which the proposed work can be understood. They bolster reviewer confidence by describing their relevant past work and discussing pilot data. They detail a study design and methods that are perfectly tailored to successfully accomplishing their aims. They create cleanly formatted and meticulously proofread documents that fulfill the submission criteria of the funding agency. They confidently await review and gracefully revise and resubmit when necessary. Finally, good grant writers write grants; like any skill, grant writing prowess can be developed only by doing it repeatedly. One can read all about the physics of hitting a baseball, but the only way to really learn is to step up to the plate and swing. Repeatedly.

Disclosures

None.

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