REVIEWS

Demystifying the NIH Grant Application Process

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The process of applying to the National Institutes of Health (NIH) for grant funding can be daunting. The objective of this article is to help investigators successfully navigate the NIH grant application process. We focus on the practical aspects of this process, which are commonly learned through trial and error. Our target audience is generalist faculty and fellows who are applying for NIH funding to support their career development or a clinical research project.

KEY WORDS: clinical research; academic medicine; NIH; funding; grants.
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INTRODUCTION

The National Institutes of Health (NIH), part of the U.S. Department of Health and Human Services, is the primary Federal agency supporting medical research in the United States. A successful research career in academic medicine depends, in large part, on securing NIH grant support, but this goal has never been more challenging.[1–3] The objective of this article is to help investigators understand and successfully navigate the NIH grant application process (Fig. 1). Because several excellent publications focus on selecting a research question[4–6] and writing a scientific proposal,[7] we will not discuss these issues. Instead, we address the practical aspects of the NIH grant application process, including planning the proposal, preparing the final documents, submitting the grant, and following up. These aspects are rarely discussed in the literature, and are instead, commonly learned by trial and error or through informal interactions with experienced investigators.

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THE PLANNING PHASE

Before writing an NIH proposal, investigators must consider several critical questions, including which NIH Institute to target, whether to respond to a particular funding announcement, what grant mechanism to use, and how to leverage both scientific and administrative resources at their home institutions. A wealth of information is available on NIH Web sites, including a glossary of commonly used acronyms (Table 1).

Choosing an NIH Institute

NIH Institutes. The NIH is composed of 20 Institutes and 7 Centers (hereafter Institutes). Applicants must decide which Institute is most appropriate for a given proposal. Understanding the funding priorities of different Institutes and identifying ways to align your proposal with these priorities can assist this decision. Priority areas for research, detailed on NIH Institute Web sites (Table 1), should be carefully reviewed. General Internists may have research interests that cut across content areas. Because the NIH is organized primarily by disease and/or organ system, the Institute best suited to serve as the primary funder may not be obvious. For example, an investigator preparing a proposal to evaluate the effectiveness of screening mammography among older women might target the National Cancer Institute or the National Institute on Aging. Senior investigators (including mentors, Division Chiefs, or coinvestigators) at one's home institution who have received NIH funding, or served on NIH study sections, can often help with these decisions.

When more than one Institute is possible, one strategy is to choose the Institute that has the highest application success rate.[8] Another strategy is to investigate, through conversations with Program Officials (see below), whether two Institutes might co-fund a project.

CRISP. The Computer Retrieval of Information on Scientific Projects (CRISP) is a searchable database of federally funded biomedical research projects that includes abstracts of current and prior projects funded by NIH and several other agencies.[9] CRISP can be searched using several criteria, including investigator name, scientific concepts or key words, grant mechanism, and year. A CRISP search can help identify the

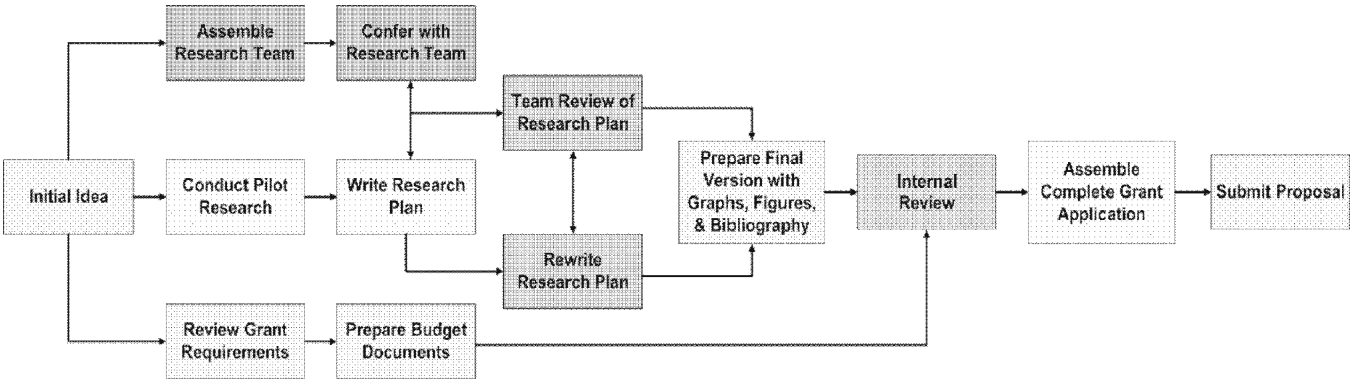

Figure 1. Steps of the NIH grant application process. Steps in preparing and submitting a grant proposal.

most appropriate Institute, funded study designs, and investigators with relevant expertise.

Program Officials. Program Officials are professionals with advanced degrees, who oversee a portfolio of funded scientific projects within a specific Institute, and serve as liaisons between the Institutes and study sections (groups of experts that review and score proposals—see below for details). The importance of talking to a Program Official early in the application process cannot be overemphasized. This conversation can help applicants frame their proposal to fit the Institute's priorities. Program Officials may suggest different award types for which the proposal is eligible, or other initiatives at their Institute or other Institutes, and can provide general counsel on preparing the application. Nevertheless, investigators should be aware that Program Officials have a wide range of responsibilities and vary in their experience and knowledge regarding specific topic areas and NIH initiatives. Because their advice may not always coincide with advice from mentors or experienced investigators at your institution, investigators should seek advice from multiple sources.

Identifying NIH Funding Opportunities: RFAs and PAs

Exploring available sources of NIH funding is an excellent place to start. Investigators can receive a weekly e-mail from the NIH listing a variety of funding-related notices, new Requests for Applications (RFAs), and new Program Announcements (PAs; see Table 1 for list serve information). When making funding decisions, Institutes usually consider whether applications are responding to a particular announcement. RFAs and PAs are the two main mechanisms by which Institutes solicit applications on specific topics. While it is not necessary for an application to be submitted under a specific RFA or PA, applications should be related to the interests of the Institute, as described on their Web sites.

RFAs and PAs differ in funding sources and submission timing. Funds for PAs are not "set aside," and funds may not be available even if an application is reviewed favorably. In contrast, RFAs address more narrowly defined areas, so the NIH commits a set amount of money and usually specifies the approximate number of applications that will be funded. PAs have multiple receipt dates for applications (although these dates may vary by Institute) and the announcements are generally active for 3 years, whereas RFAs are usually a one-time competition with a single receipt date.

If your project fits a specific PA or RFA, verify eligibility criteria and identify any "Special Requirements" (e.g., approval from a subcommittee, letters of support, or specific wording to include in the proposal). Those in doubt about the appropriateness of their research project for a given Institute should contact the Program Officials listed at the end of the PA or RFA.

Table 1. General Resources for NIH Grant Applicants

Site	Link	Resources Available
Acronym list	http://grants1.nih.gov/grants/acronym_list.htm	Explanations of NIH acronyms
Center for Scientific Research (CSR)	http://cms.csr.nih.gov/	Study section rosters and meeting dates and additional resources for applicants
NIH Institutes/Centers	http://www.nih.gov/icd/	Contact information for all NIH Institutes and Centers
Office of Extramural Research (OER)	http://grants.nih.gov/grants/oer.htm	General information on NIH grant opportunities
NIH Extramural Nexus	http://grants.nih.gov/grants/nexus.htm	Bimonthly newsletter on grants policy and operations, grants administration, and extramural programs and activities
NIH Guide LISTSERVE	http://grants.nih.gov/grants/guide/listserv.htm	Weekly e-mail listing of funding opportunities
NIH K-kiosk	http://grants2.nih.gov/training/careerdevelopmentawards.htm	Interactive site for selecting career development awards
NIH Regional Seminars on Program Funding and Grants Administration	http://grants2.nih.gov/grants/seminars.htm	Dates, locations, and registration information for regional NIH seminars

Choosing an NIH Grant Mechanism (K- and R-Series)

Several factors influence the choice of grant mechanism, including the applicant (e.g., junior vs senior investigator, M. D. vs Ph.D.), the amount of money needed, the involvement of human subjects, the project duration, available funding (for an RFA), and Institute priorities. Information about selected grant mechanisms is provided in Table 2.

K-Series Awards. The K-series includes NIH career development grants that support junior faculty to become independent investigators.[10] The NIH "K Kiosk" provides information on career development awards and features an interactive "Career Wizard" that advises applicants based on their professional degrees, prior research training, areas of expertise, and record of independent funding (Table 1). The two most relevant mechanisms for Generalists are the Mentored Patient-Oriented Research Career Development Award (K23) and the Mentored Clinical Scientist Development Award (K08). K23s and K08s are limited to investigators with clinical doctoral degrees. The K23 supports patient-oriented research while the K08 supports non-patient-oriented biomedical research. The K99/R01, or "Pathway to Independence," bridges K awards and R01 awards (see below). The objective of this newer program is to facilitate receipt of an R01 award earlier in an investigator's research career by providing up to 2 years of mentored support followed by up to 3 years of independent support, contingent on securing an independent research position.

R-Series Awards. The "Research Project Grant" (R01) supports large projects and is the oldest grant mechanism used by the NIH. The "Small Grant Program" (R03) supports short-term projects, such as pilot studies or secondary data analyses. The R21 program encourages developmental research by funding feasibility studies or research at the conceptual stage, generally in response to specific PAs. Lastly, the "Clinical Trial Planning Grant Program" (R34) supports the development of Phase III clinical trials (i.e., establishing the research team and developing protocols); it is not designed for collecting preliminary data or conducting pilot studies. Not all Institutes support the R03, R21, and R34 grant mechanisms, so applicants should determine whether specific Institutes accept applications under the desired mechanism.

Key Conversations: Building a Research Team

As grant planning is iterative and collaborative, applicants should initiate key conversations early in the process with members of the research team such as primary and secondary mentors for K awards, coinvestigators for R awards, biostatisticians, and consultants. The strength of the research team is critical for all NIH grant applications. Reviewers evaluate the likelihood of project completion based on the team's expertise, commitment, and resources to complete the proposed research. Each investigator should have a clearly defined role and expertise commensurate with their contribution. Applicants should explicitly address any obvious barriers to completing the research (e.g., physical distance if coinvestigators are at other institutions). Finding coinvestigators and consultants may require local networking or long distance collaborations.

Institutional Colleagues. Institutional colleagues such as a Division Chief or Center Director may be able to provide administrative and intellectual support, procure additional resources (e.g., statistical support), suggest contacts at the NIH, and propose external reviewers who might provide valuable feedback before submission.

Mentorship Teams. Career development awards (e.g., K08, K23, K99/R00) require strong mentorship teams to assure the applicant's career development and completion of the proposed scientific aims. Primary mentors should have a successful record of NIH funding and mentoring junior investigators and expertise in the proposed research area. Reviewers look favorably upon established mentor–trainee relationships (e.g., coauthored publications). Secondary mentors should have relevant content or method expertise and demonstrate a commitment to mentoring junior faculty. The proposal must include a detailed, feasible, and mutually agreed-upon schedule of meetings with each mentor. The mentorship team should provide guidance during the grant preparation and writing stage.

Table 2. Funding Limits and Time Frames of Specific NIH Award Mechanisms

Grant Type	Title	Amount	Duration
K08	Mentored Clinical Scientist Research Career Development Award	Varies by Institute: http://grants.nih.gov/grants/guide/contacts/pa-06-512_contacts.htm	3–5 yrs
K23	Mentored Patient-Oriented Research Career Development Award	Varies by Institute: http://grants.nih.gov/grants/guide/contacts/pa-05-143_contacts.htm	3–5 yrs
K99/ R00	Pathway to Independence	Mentored: $90K/yr Independent: $249K/yr http://grants2.nih.gov/grants/guide/pa-files/PA-06-133.html	<2 yrs <3 yrs
R03*	Small Grants (e.g., pilots, secondary data)	$50K/yr http://grants2.nih.gov/grants/funding/r03.htm	<2 yrs
R21*	Exploratory/ Developmental Research	$275K total (<$200K any one yr) http://grants2.nih.gov/grants/funding/r21.htm	2 yrs
R01	Traditional Research Project	Up to $500K/yr (without approval) http://grants2.nih.gov/grants/funding/r01.htm	<5 yrs
R34*	Clinical Trial Planning	$100K http://grants2.nih.gov/grants/funding/r34.htm	1 yr

Not all Institutes participate in this mechanism
***Funding amount and duration correct as of May 2007*

Coinvestigators. Professional relationships with coinvestigators are based on mutual scientific interests, complementary expertise, or convergent agendas, and can take time to develop. Former mentors on K awards often become coinvestigators on a trainee's first R01. While mentors on K awards are unpaid, the relationship between the PI and coinvestigators of an R01 assumes a business aspect. This distinction requires up-front communication about responsibilities, authorship, and salary support. Of note, all Federal research agencies are currently implementing policies to allow more than one PI on individual proposals.[11]

Biostatisticians. Most NIH applications include biostatisticians as key personnel who are allocated some salary support. Whenever possible, the biostatistician should write a significant portion of the statistical analysis section of the proposal. However, to ensure that the analytic plan is understandable and well integrated, applicants may want to edit this section. The analytic plan must be comprehensible to a general reader, but sophisticated and detailed enough to withstand careful scrutiny by statisticians and other methodologists in the study section.

Consultants. Consultants are collaborators, usually based at external institutions, who fill a specific gap in expertise. Their compensation is usually budgeted at $500–750 per day. Although their level of effort is not as high as a coinvestigator's, they can be critical members of the research team.

Letters of Support and Biosketches. A typical NIH grant application includes letters of support from all consultants and mentors and sometimes from other key institutional leaders or collaborators (e.g., the director of a clinical recruitment site). For example, a K23 application includes letters of support from the applicant's Department Chair, primary mentor, secondary mentors, three additional letters written by professional colleagues who know the applicant well but are not involved with the proposed research, and consultants if they are listed in the research plan and budget. Biosketches in NIH format are also required for all investigators. Therefore, for any grant, substantial time is required to obtain letters updated biosketches. To facilitate the timely return of letters of support, applicants commonly offer to write a draft for the recommender. If this is the case, applicants should craft a very strong letter that targets the preparation, skills, and potential for future independence, which are review criteria for that specific type of proposal (see Gill et al. for details [10]). Allow at least 2 months for these tasks and plan to send regular friendly reminders, follow-up thank you notes, and updates on submission and funding status.

PREPARING THE PROPOSAL

In this section, we discuss practical tips that can make preparation more efficient, and review the main components of an NIH research plan. Our goal is not to explain how to craft a high-quality scientific proposal but to detail the preparation process, in which writing is a key component. Because grant writing is a critical skill to develop, we refer readers to relevant articles.[7,12,13]

Reviewing Successful Applications

Reviewing examples of successful applications can be extraordinarily helpful, particularly if they share the same grant mechanism, research design, or content area. Colleagues and mentors can help identify and procure such proposals. If such examples cannot be obtained from one's home institution, external investigators should be solicited. CRISP can identify relevant projects and researchers who may be willing to share their proposals, discuss their results, or collaborate. A CRISP query can also supplement a standard literature search by identifying funded studies that are under way but not yet published. Funded NIH applications identified by CRISP can also be requested through the Freedom of Information Act. However, these requests may require 8 weeks or more to allow investigators to redact sensitive information, such as salaries, and the principal investigator of the funded application is given the name of the requestor. Therefore, it is often more efficient, and probably more collaborative, to contact the investigator directly.

Following NIH Instructions

All NIH grant applications are divided into numerous sections, each of which must comply with detailed instructions. Institutes will administratively reject, without review, any applications that are incorrectly prepared. Fortunately, the NIH provides online guidelines for both paper[14] and electronic[15] submissions. Despite their length, every first-time applicant should assiduously review the appropriate guidelines because they contain answers to most questions on preparing a proposal.

Formerly, applicants prepared NIH applications using a series of pages known as Public Health Service (PHS) 398. After collating individual grant components, such as the face page, budget pages, letters of support, biosketches, research plan, and appendices, applicants mailed the original and five copies to the NIH.

In August 2005, the NIH transitioned from paper to electronic applications and from the PHS 398 format to the Standard Form 424 (Research & Related), or SF 424 (R&R). To support these changes, the Federal government created a new electronic portal, http://Grants.gov, which provides information on all Federal grant programs, including those offered by the NIH. The transition is being phased in gradually, with different target dates for different grant mechanisms. Program Project Grants (R01s), Small Grant Programs (R03s), and Exploratory/Developmental Research Grants (R21s) have already completed their transition to electronic submission, and the date for transition of the K series has not yet been announced.[16,17]

The Electronic Research Administration or eRA Commons[18] is the platform for transactions related to the receipt, review, and administration of NIH grant applications. Applicants intending to submit a proposal must register with the eRA Commons database through their home institution's grants administration office. Applicant organizations (but not investigators) must register at http://Grants.gov as well as eRA Commons, as access to each is required for electronic submission of all NIH grant applications.

With the transition to electronic applications, PIs are no longer responsible for the final submission of their completed proposals. Each institution must designate an "Authorized

Organizational Representative" (AOR) with the authority to fulfill the requirements of the application process on behalf of the institution.[19] The change to electronic submission may therefore be more challenging for senior investigators who are comfortable with the paper application process. Close and early communication with local grants administration staff who understand the new system can minimize misunderstanding and avoid missed deadlines.

Another major change is that electronic submission requires investigators to modify their timelines. Formerly, if a paper application was prepared incorrectly, it was administratively rejected and returned by mail, and the applicant could not resubmit until the next submission cycle. Electronic applications, however, involve an initial submission during which the NIH reviews proposals for administrative errors. Common errors and how to avoid them are detailed at http://Grants.gov.[20] If errors are found, the applicant and AOR have one week to correct the errors and resubmit the application to the NIH. Institutional grants administration offices generally require the complete application package 2–6 weeks before the official deadline to ensure a timely final submission.

Complying with Institutional Policies for Internal Review

Every academic institution requires submission of documents for internal review before a grant can be sent to the NIH. These documents commonly include information about the budget and human subjects. The review process varies across academic institutions, so it is necessary to become familiar with local forms and deadlines. Local grants administration office should be able to supply details.

Preparing a Budget

Applicants must carefully prepare budget pages and obtain internal approval before submission to NIH. Academic institutions provide varying levels of administrative support for budget preparation. However, even at institutions where an administrator prepares the budget, the applicant must have a solid understanding of the budgetary components and be in frequent communication with the administrator, particularly to discuss any changes to the project during preparation.

A key budgetary concept is the distinction between direct and indirect costs. Direct costs include salary support (plus fringe benefits), consultant fees, subcontracts, and supplies. Fringe benefits are a percentage of salary support, determined by each institution, that change frequently. Consultant fees are individually negotiated. A subcontract is the financial mechanism through which PIs interact with collaborators from other institutions. For projects with annual direct costs less than $250,000, a simplified or modular budget form is used. The NIH then requests more detailed budget information if funding is approved ("just in time" or JIT submissions). For projects with annual direct costs between $250,000 and $500,000, an itemized budget form is submitted with the application. For projects with annual direct costs greater than $500,000, PIs must obtain written approval from the appropriate Institute before submission. All budgets are accompanied by a written budget justification.

Indirect costs, also called facilities and administrative (F&A) costs, represent institutional overhead such as heat and electricity. Indirect costs are calculated as a percentage of direct costs, and their calculation can be challenging because they are established by individual institutions and change yearly. Thus, an application may need to be updated between the time of submission and the time of funding. Of note, a subcontract's indirect costs are not included in a project's direct costs.

Understanding NIH Review Criteria

Investigators should fully understand the principal NIH grant review criteria: significance, approach, innovation, investigators, and environment. These were most recently updated in 2004.[21] Additional review criteria for career development awards include quality of the candidate, mentorship team, institutional support, and training plan. Reviewers are also required to comment on the adequacy of the plan for protection of human subjects; inclusion of women, minorities, and children; and care and use of vertebrate animals.

Investigators who have never been PIs on an NIH grant—*other than* a K award, an R03, or an R21—qualify as "new investigators".[22] If eligible, applicants should indicate this on the application face page, as reviewers' evaluations and scores should reflect the more limited experience of new investigators in terms of research accomplishments, preliminary results, and general grantsmanship. In addition, some Institutes, such as the National Heart, Lung, and Blood Institute and the National Cancer Institute, maintain a higher funding percentile (see below) for new compared to established investigators.[23,24]

Structuring the Proposal

The research plan of every NIH grant application consists of the following sections: A. Specific Aims; B. Background and Significance; C. Preliminary Work; D. Research Design and Methods; and E. Human Subjects Research. Valuable resources for preparing the research plan are provided in Table 3. Because reviewers read numerous grants, they expect to see certain things in certain places. Thus, it is essential that applicants adhere to established formats, which they can learn by reviewing funded proposals. The only criterion that changes according to grant mechanism is the number of pages allotted for sections A–D. R03s are limited to 10 pages; R21s have 15 pages; and R01s have 25 pages. For K08s and K23s, the 25-page limit includes sections A-D and a candidate section and a detailed career development plan.

The candidate section of career development awards begins with a narrative detailing the candidate's background, training, career goals, and scientific accomplishments. The career development plan highlights gaps in the candidate's training and strategies for filling them during the funding period. This section should therefore include a detailed schedule of mentorship meetings, relevant coursework, and concrete skill development. Reviewers critique career development plans as rigorously as they critique research plans, and proposals may suffer under review if this section is not well crafted.

Table 3. Additional Resources for Preparing the Research Plan of an NIH Grant

Site	Link	Resources Available
Research and Training Opportunities at the NIH	http://www.training.nih.gov/careers/careercenter/grants.html	Links to information and courses about writing grant proposals
National Institute of Allergy and Infectious Diseases (NAIAD) "All About Grants Tutorial"	http://www.niaid.nih.gov/ncn/grants/default.htm	General tutorials on planning and writing a grant proposal as well as specific tutorials (e.g., career development grants, electronic submission)
NIH Grant Writing Tips Sheet	http://grants2.nih.gov/grants/grant_tips.htm	Suggestions for grant writing from different Institutes
National Network of Libraries of Medicine	http://nnlm.gov/funding/	Links to grant writing resources
An evidence-based guide to writing grant proposals for clinical research	Inouye SK and Fiellin DA. Ann Intern Med 2005;142:274–282.	Key recommendations regarding the grant-writing process and discussion of sections frequently scrutinized and critiqued.
National Heart Lung and Blood Institute Clinical Research Guide	http://www.nhlbi.nih.gov/crg/index.php	Suggestions for Preparing, submitting and managing a clinical research award.

Human subjects. Section E of the research plan addresses issues related to human subjects research. As with other sections, detailed instructions describe the required elements, including risks to subjects; adequacy of protection against risks; potential benefits of the proposed research to subjects and others; importance of the knowledge to be gained; plan for data and safety monitoring; and inclusion of women, minorities, and children.[25] Section E is not included in the page limits and can be any length required. Further information on issues of human subjects research is provided by the Office for Human Research Protections.[26]

SUBMISSION AND FOLLOW-UP

Key elements of the submission and NIH review include study section assignment and review process. In this section, we explain why the applicant should remain actively involved with the project after submission by learning which study section will review the application, when it will meet, and when the results will be announced. Steps taken by the applicant after review may vary, but are always extremely important, as it is uncommon for proposals to receive funding on their first submission.

Center for Scientific Review

The Center for Scientific Review (CSR) organizes the study sections that evaluate the scientific merit of most (70%) of the research grant applications submitted to the NIH. The CSR is divided into three major scientific divisions: Cell and Molecular, Physiological Systems, and Clinical and Population Based Studies. Review activities of the major divisions are further organized into Integrated Review Groups (IRGs). Each IRG represents a cluster of 10 to 15 study sections around a general scientific area. Research grants are usually assigned first to an IRG, and then to a specific study section within that IRG. This is in contrast to career development grants, which are usually reviewed by study sections within individual Institutes. The CSR home page (Table 1) provides information about peer review guidelines, selection of reviewers, and study section meeting dates. This site also includes links to resources for applicants and relevant updates, for example, revised submission deadlines that took effect in January 2007.[27]

Cover Letter

Applicants can increase their likelihood of an appropriate review by including a cover letter addressed to the CSR staff. This letter should express the critical research idea in a few sentences and suggest which study section should review the application and which Institute should be the primary funder. The following generic example denotes the key elements: "My project focuses on these areas... Therefore, experts in the areas of A, B, and C are appropriate for reviewing it." The cover letter may also suggest that a particular study-section member should not review the application because of a conflict of interest or other valid reason. While the final decision for assignment to a specific study section is made by CSR staff, reasonable requests are usually honored. In the absence of a cover letter, decisions are most often made after reading only the project title and/or abstract.

Identifying the "Right" Study Section

In addition to talking with senior colleagues, several other strategies can be used to identify the study section that is best suited to review a grant application. Check the rosters and review the specific content areas that are covered by the standing (or chartered) study sections. For R-series applications, this information is available on the CSR website.[28] For K-series applications, it is available at the eRA commons site.[29] Once your search has been narrowed to a few potential study sections, contact the scientific review administrator (SRA) for each study section under consideration and/or the designated Program Official if you are responding to a PA. Sending an email message with your research question and specific aims, followed by a phone call, is often an effective communication strategy. Note that applications submitted in response to an RFA are typically reviewed by "Special Emphasis" panels, which are formed ad hoc, so there is no opportunity to request a specific study section.

Steering a proposal to the appropriate study section will allow the applicant to anticipate who may review it. Knowing one's audience is an advantage in determining the proper balance between breadth and specificity when crafting a proposal. If possible, cite relevant work of potential reviewers. Of course, applicants may not receive the study section they request, and reviewer assignments are not disclosed. In

addition, if sufficient expertise is not already available in the study section, the SRA may recruit ad hoc reviewers who are not listed on the available rosters.

Timeline After Submission

Within 6 weeks of submission, eRA Commons will display information on study section assignment, funding Institute, review dates, and names and contact information for assigned SRA and Program Officials. The actual review usually occurs 5 to 6 months after submission. The summary statement is usually available 1 month after the review and includes written critiques by the assigned reviewers, a summary of the study section's discussion, and a priority score and percentile. If approved by the Institute's Council (an advisory committee of senior scientists), funding for an NIH application usually begins no sooner than 10 months after submission, although a final funding decision for an application that is close to the cut off for funding may not be available for several additional months (see below). Currently, an unsuccessful application can be resubmitted no sooner than about 9 months after the initial submission. AIDS-related applications have different submission dates (May 7, September 7, January 7) and are subject to "expedited review," which means that they are required by law to be processed and reviewed within 6 months from receipt deadline to funding decision, as opposed to the standard 9 months for non-AIDS-related grants.

Recognizing that the review and resubmission cycle is currently too long, the NIH launched a pilot program in February 2006 to reduce the current schedule by up to 4 months for new investigators. Key features of this program include a shortened time for reviewers to consider applications, earlier study section meetings, accelerated production of summary statements, and a delayed submission date for amended applications. For example, study sections that meet in February will be required to produce summary statements by March 1, and new investigators will have until March 20th (instead of March 5th) to resubmit, which allows re-review by study sections that meet in June. This pilot was recently expanded, and by November 2007, all new investigators applying for an R01 grant will have the opportunity to submit an amended application for the next receipt deadline, about 4 months after the original application.[30]

Between Submission and Study Section Review

Investigators may send additional supporting information after their application has been submitted. Including additional pilot data, manuscripts newly accepted for publication, and other major accomplishments can often strengthen an application. The supporting information should be sent to the SRA with a brief message similar to this example: "I am writing to respectfully request that the following information be made available to the members of the study section that will be reviewing my grant application." While the SRA is under no obligation, these requests are usually honored. If submitted far enough in advance (e.g., 6 weeks before the study section meets), this information may be provided to reviewers along with their grant assignments. Otherwise, it will be provided at the meeting.

Because the summary statement will usually not be available for several weeks after the study section meets, the presence of the assigned Program Official during the review can be helpful (see below). Send the Program Official the dates scheduled for your proposal's review and ask whether he or she may be able to attend. If the Program Official is unavailable, ask whether a colleague of theirs will be present; this individual can serve as a resource for information after the review.

The Study Section Review Process

Each application is commonly assigned by the SRA to three reviewers (primary, secondary, and discussant), who often have complementary areas of expertise. About 1 week before the study section meeting, reviewers are asked to identify applications deemed to be "noncompetitive." These applications are judged to be in the lower half, qualitatively, of applications normally reviewed by that study section. If there is unanimous agreement, these applications are "streamlined" or "triaged", meaning that they are not discussed at the meeting and do not receive a priority score (i.e., are "unscored"). For each application that is not streamlined, about 15 to 20 minutes are usually allotted for discussion. Reviewers provide their preliminary scores, ranging from 1.0 to 5.0 and verbally present their assessments of the application. A vigorous discussion ensues among the section members, who have also received the grant for inspection (but may have read only the abstract or skimmed the proposal). Subsequently, the reviewers provide their final scores, which usually establish a range for other section members, who score the grant anonymously. Scores between 1.0 and 1.5 reflect an "outstanding" application. Applications that receive a score between 1.6 and 2.0 are considered "excellent"; between 2.1 and 2.5 are "very good"; between 2.6 and 3.5 are "good"; and between 3.6 and 5.0 are considered "acceptable". To provide an inside look at the scientific review process for NIH proposals, CSR has produced a video of a mock study section meeting, which shows how reviewers assess applications and how study section meetings are conducted to ensure fairness.[31]

After the Review

After the meeting adjourns, the section members' scores for each application are averaged and multiplied by 100 to obtain the priority score, which is usually available to applicants within 2 to 3 business days through eRA Commons. Because the summary statement is generally not available for at least 4 weeks, applicants may want to contact their Program Official to hear their impressions. For example, the Program Official might be able to highlight salient issues that emerged during the discussion, including some that may not be reflected in the summary statement, and might offer some preliminary feedback on the likelihood of funding. Applicants are not permitted to discuss their applications with the SRA after the review has been completed.

Summary Statements

Summary statements or "pink sheets" are posted on eRA Commons within 4-6 weeks of the study section meeting. All summary statements include the unedited critiques of the assigned reviewers and a complete listing of the section members. For applications that were not streamlined, the summary statement also includes a "Resume and Summary of Discussion," which highlights the most important issues, the priority score, and a percentile, which reflects the application's rank in

the current meeting plus the two previous meetings of the same study section. The percentile ranking applies to R-series grants and is designed to smooth out the differences in scoring behavior between study sections and between meetings of the same study section. Depending on the Institute, the percentile rank for receiving funding (or "payline") currently ranges from about the 8th to the 16th percentile.

Next Steps

If a proposal is not funded, applicants must decide whether to submit an amended version. Note that deadlines for submission of amended applications are 1 month later than those for initial submissions. It can be helpful to read the summary statement, put it away for a few days, and then review it more dispassionately. A careful rereading of the critiques should focus on the summary of the discussion, which addresses the issues on which the priority score was based. One approach is to categorize these issues into the types of action necessary to improve the proposal. These may include revising the rationale for the proposed research, including preliminary data, reconfiguring or jettisoning a specific aim, or revising the research design, the statistical analysis, or the investigative team.

Note critiques, possible responses, and "fatal" flaws that might preclude an amended application, and then seek advice about improving the application from the Program Official. Applications that were not discussed (i.e., "streamlined" or "triaged") may not have a fatal flaw and often fare well if revised. Finally, discuss critiques with mentors, coinvestigators, and senior colleagues; listen carefully and seek frank appraisals.

If the final score is near the payline, applicants must decide whether to resubmit before a final funding decision is available. Applicants who are risk averse may want to proceed with an amended application. NIH applications remain "active", or eligible for funding, for the duration of the fiscal year, which runs from October 1st to September 30th. Should the initial application subsequently get funded, the amended application can be withdrawn. Because NIH Institutes are often more conservative in their funding decisions early in the fiscal year, unfunded applications that are near the payline may get funded later in the year. Discussions with Program Officials are essential to making an informed decision.

In general, reassignment to a new study section is uncommon, and CSR considers this a burden. However, if the initial application did not receive a fair review, ask the Program Official about having the amended application reviewed by a different study section and be prepared to justify why.

Amended Applications

To respond to the reviewers' critiques, applicants are allowed three additional pages, referred to as the "Introduction to Revised Application". Craft this introduction carefully by reviewing successful revisions and getting feedback on structure, tone, and content. The revised grant may be assigned a new reviewer (or many months may have passed since the original reviewer read the initial submission), so the introduction should not assume reviewer familiarity with the content of the grant. One approach is to individually respond to each of the concerns raised. Another approach is to synthesize reviewer's comments and organize revisions by topic area, making sure to include all critiques. Indicate how and where the application was revised, using special markings (e.g., bold, italics, or borders). Be professional and concise and clearly justify each decision and the resulting changes (or lack thereof).

As nearly a year will have passed since the initial submission, include additional preliminary data or new accomplishments as appropriate. Finally, re-read the entire proposal and strengthen other aspects that were weak. Even if the reviewers did not identify these weaknesses, reviewers regularly rotate on and off study section panels, and there is no guarantee that the same reviewers will be assigned to the amended application. Furthermore, reviewers are not obligated to limit their comments to issues that were raised in the initial review.

Skipping a Cycle

As noted earlier, the soonest an amended application can usually be submitted is 2 or 3 months after receipt of the summary statement. While this time is often sufficient, applicants can skip a cycle when the application requires extensive revisions (thereby gaining 4 months). The resulting delay in potential funding should be weighed against the NIH policy that no more than two amended applications can be submitted. Of note, there is no time limit for resubmission of an amended application.

SUMMARY

For academic researchers, securing extramural funding is essential for a successful career. We have attempted to demystify the NIH application process, which is rarely explicitly discussed. By understanding how to plan a proposal, prepare an application, and optimize submission (and resubmission) of a grant, applicants will be better equipped to successfully compete for NIH funding.

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