INTRODUCTION

The process of transforming a research idea into a grant requires careful thought and planning. This article describes some of the steps necessary to write a successful grant application for clinical research. An additional excellent resource can be found in the recently published guide from Inouye and Fiellin.1

PREPARATION AND PLANNING

Once one has an idea for a potential research project, the next step is to develop a research hypothesis. This should not be done in a vacuum but is best done as a “brainstorming” exercise with colleagues with a similar research or clinical interest. A research mentor is vital to this process for the novice investigator. This process serves several purposes. First, it will allow one to clearly focus the research question. Second, it is a good form of reality testing. By bouncing the idea off others, especially experienced investigators, one can determine the feasibility of the project. Specifically, one will need to determine whether the training, time, resources, and environment are available for answering the research question. This process will also allow one to determine the institutional resources needed to conduct research in terms of mentors, collaborators, space, equipment, and time.

The second phase of preparing to submit a grant is to determine what funding source is sought. Sources of funding may originate from the government (NIH, VA, CDC, and AHRQ), professional societies (ASGE, ACG, AGA, American Cancer Society), private nonprofit foundations (Crohn’s and Colitis Foundation), industry, or intramurally (institutional research funds). It is necessary to match the idea to the funding source by determining which funding source has the most interest in the research project. If one is in doubt, it is perfectly reasonable to contact the program administrator or grants officer of the funding organization for insight into this question. Doing so early in the process is critical in order to see if the idea and the funding organization’s priorities are in alignment.

Once the funding source is identified, the application instructions must be reviewed to determine the grant requirements, format, and most importantly, the deadline. The importance of this last point cannot be overstated. It is essential to allow adequate time to prepare a grant application and fine-tune it rather than waiting until the last minute. Typically 3 to 6 months should be allocated for planning, writing, and submitting a competitive research grant. Thus, it is important to start the preparation of the grant early, not only to allow time to write the grant, but also to allow for adequate time for review by collaborators. It is also a good idea to find a senior colleague not involved in the study to review the grant, but it is important to give this individual adequate time to do so. Other considerations in the grant preparation process include allocation of sufficient time to conclude preliminary studies, typically at least 8 weeks before the grant deadline, and adequate time to deal with layers of institutional approval such as the Institutional Review Board (IRB). Finally, it is a good idea to put the grant aside for at least 1 week prior to finalizing it in order to provide an opportunity for additional review with a fresh set of eyes.

Other logistics that need to be considered include preparation of figures, biosketches, budgets, and letters of support from collaborators. In addition, it is critical to allocate sufficient time to complete and submit pertinent manuscripts before grant submission. A complete literature review relevant to the topic is warranted, and familiarizing oneself with a reference management system to organize the citations is a good up-front investment of time.

Last, it would be wise to seek out a model of funded grants in the category either from a senior colleague or from the website of the funding agency prior to commencing the grant writing process. This is an invaluable resource for putting together the grant application.

SPECIFIC AIMS AND HYPOTHESIS

The specific aims and hypothesis section may be viewed as perhaps the most critical component of a grant submission. It should start with an introductory paragraph to provide a context for the specific aims. This should be followed by a concise synopsis of the work proposed in terms of study design and primary outcome measures in order for reviewers to understand what is actually going to be done in the study. The specific aims should then follow, with a clear description of the goals of the study. It is a good idea to limit this section to no more than 2 or 3 specific aims. This should be followed by a clearly stated research hypothesis.

BACKGROUND AND SIGNIFICANCE

This section of the grant should be a concise synthesis of the current state of knowledge in the area to be studied. It should summarize and synthesize all relevant studies done to date, while clearly identifying knowledge gaps that remain. Thus, this section should be viewed as building a case for the research proposal. It is a good idea to provide
a final paragraph in this section that frames the status of work in the field under study and explains how the proposed project will contribute to the field. It is essential that this section act to justify the specific aims of the proposed study.

**METHODS**

The methods section should be viewed as the operations manual of the study and should be closely linked to each specific aim. It should begin with a brief overview of the study followed by a clear description of several components.

- **Study design:** The design should be described in detail. It should be clearly stated if this is a clinical trial or an observational study.
- **Study setting:** The setting needs to be defined in order to describe the patient population being sampled and the methods of identification, recruitment, and enrollment of subjects.
- **Study subjects:** The inclusion and exclusion criteria for study subjects should be explicitly stated and justified. Any potential biases in subject selection should be addressed here. This section will need to address inclusion of women, minorities, and children. It is important to demonstrate in this section that a realistic pool of patients is available to complete the proposed study and to provide pilot data if need be to support this.
- **Data collection:** This section should describe all study variables, outcome measures, measurement tools including their performance characteristics and validation, and data entry including who will collect and enter data as well as the training required to do so. Quality control measures for data entry and handling of missing data should be specified here as well.
- **Data analysis and sample size calculations:** To write this section correctly, early involvement by a collaborating statistician is crucial. In this section, it will be necessary to describe the primary and secondary outcomes and the sample size calculations relevant to the primary outcomes. The analysis section needs to provide a detailed description of the statistical methods used for hypothesis testing for each endpoint and provide an analytic approach as appropriate for each of the questions asked.
- **Advantages and limitations:** The last component of the methods section is a summary of the strengths and weaknesses of the project with a clear plan for pitfalls and contingencies. The nature of scientific research is that things do not always go according to plan. Thus, well-thought-out contingency plans for these possibilities need to be incorporated into the methods section of the grant.

**PRELIMINARY DATA**

There is no better way of demonstrating that one is the right person to be awarded extramural money than by demonstrating that he or she is capable of performing the studies suggested. Preliminary data establish the feasibility of successfully completing the study envisioned—by demonstrating that the study methods can be performed at the suggested site and that subjects are in fact available and the collaborative team is in place to perform the study. Publications relevant to these studies are yet another measure of demonstrating a record of accomplishment of productivity in the field.

**RESOURCES AND ENVIRONMENT**

This section of the grant allows one to tell the reviewers that all the right assets are in place to conduct the research. These include (a) the institutional assets; (b) the expertise, experience, and prior work of the research team; and (c) the space and equipment available to perform the project. Furthermore, it is helpful to have the division and department chairs describe how they will support the work environment.

**LETTERS OF COLLABORATION**

Collaborators, both intramurally and extramurally, need to provide a letter of support indicating that they are willing and able to perform the work described in the grant application. It would be best not to draft a letter that looks the same for each collaborator!

**APPENDICES**

Grant appendices might not be read. As such, vital information should not be placed in this section, and the appendices should not be viewed as a way to circumvent page limits of the grant. Rather, appendices should be used to provide supporting materials only, such as data-collection forms and pertinent publications relevant to the project.

**WRITING FOR REVIEWERS**

In writing a grant, it is important to know the review criteria. The **significance** of the grant should clearly point out why the problem addressed is important and how scientific knowledge will be advanced by the proposed study. The **approach** should include logical specific aims, appropriate study design, and methodology, feasibility, and clear acknowledgement of pitfalls and contingencies. **Innovation** should be demonstrated by new and innovative aims and approaches that challenge existing paradigms. **Investigators** need to be properly trained, and the work proposed should be appropriate for the experience of the principal investigator. Furthermore, the investigative team should bring complementary skill sets and have a prior record of achievement in the field. The **research environment**
should increase the probability of success of the project. There should be adequate patients, expertise in place, and institutional support to ensure completion of the project.

That being said, the reality of grants is that the proposal should withstand the scrutiny of a careful reviewer, but should also be clear to a hurried reviewer. It helps reviewers if grants are concise, clearly written, and use transparent language. Jargon should be discouraged and the grant should be entirely self-contained without requiring the reviewer to examine other references. One key point is to make the application look good. Fonts should be easy to read, margins should be adequate, headings and subheadings should help guide the reviewer through the project, and figures and tables should be used freely. Last, grammar and spelling should be carefully checked because sloppiness in this area reflects poorly on the investigator.

COMMON PITFALLS AND HOW TO AVOID THEM

A variety of pitfalls can sink a grant. A poorly stated hypothesis that is either unclear or overly ambitious is problematic. Other issues include inadequate preliminary data to support the specific aims, unsuitable methodology, inadequate information on data collection, management and analysis, and finally problems with feasibility. It is essential to be realistic about the expertise of the primary investigator and collaborators as well as to establish adequate institutional resources and access to adequate patients. Another pitfall is not following directions. The grant needs to follow the directions of the application!

RESUBMISSION

A reality of all grant applications by all levels of seniority is that rejection of initial grant applications is common. This happens to even the best of investigators. Reviews should not be taken personally in spite of human nature to do so. In fact, reviews provide useful information to improve a grant. Resubmission of a grant should graciously address all of the critiques in a systematic point-by-point fashion. Grant resubmission enhances the probability of successfully obtaining funding. In addition, the grant can be submitted to other funding agencies if need be.

SUMMARY

There is a variety of keys to grant success. A systematic approach as outlined here and elsewhere should emphasize the importance of considering a variety of variables in the grant-writing process. It is essential to allow adequate time for successful completion of the grant proposal and to stay persistent in both the initial grant development process and the resubmission phase. Hopefully, awareness of these variables should simplify the grant writing process for investigators.

DISCLOSURE

The author has no disclosures to make in regard to this article.

REFERENCE


Current affiliation: Department of Gastroenterology and Hepatology, The Cleveland Clinic, Cleveland, Ohio, USA.

Copyright © 2006 by the American Society for Gastrointestinal Endoscopy 0016-5107/$32.00
doi:10.1016/j.gie.2006.10.037