Funding and Grantsmanship

Robert S. Sandler, MD, MPH, James D. Lewis, MD, MSCE,† Patricia R. Robuck, PhD, MPH,‡ and Bruce E. Sands, MD, MS§*

Abstract: Medical research funding in the United States has 4 predominant sources: the federal government; the pharmaceutical industry; institutions; and private foundations. In each case, the grant application process is the first step in obtaining funding. Successful grant applications are logical, organized, and easy to read. The research question should be both specific and significant. Comprehensive and detailed study methods addressing the study population, timeline, and data collection and management increase the likelihood of obtaining funding. Funding for inflammatory bowel disease preclinical and clinical research is available from the National Institutes of Health and Crohn's & Colitis Foundation of America.

Key Words: Crohn's & Colitis Foundation of America, National Institutes of Health, research funding, research grant

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Most clinical research, and in particular clinical trials, requires external funding. Funding for clinical research is normally obtained from 4 main sources: institutions; private foundations; the federal government; and industry. Institutions are often good sources of funding for pilot feasibility studies that provide essential groundwork for obtaining larger grants. Many foundations are willing to fund small clinical trials. These foundations usually offer both career development awards and larger research grants for independent investigators. The largest source of research funding in the United States is the National Institutes of Health (NIH). The NIH funds basic science research, epidemiological studies, clinical intervention trials, and prevention trials. Pharmaceutical companies are most likely to fund an investigator-initiated clinical trial that has some direct connection to their product line; however, industry sponsors may also be willing to fund pilot feasibility studies, proof-of-concept studies, or methodological studies that will facilitate a future clinical trial. Depending on the proposed research, industry support may range from supplying study drug to complete funding of a large-scale multicenter trial. Pharmaceutical companies also fund industry-sponsored studies that provide financial support for investigators and their staff and may provide opportunities for publication.

This article will provide practical information on the preparation and submission of grant applications and an overview of funding opportunities at the NIH and the Crohn's & Colitis Foundation of America (CCFA).

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From the *University of North Carolina, Chapel Hill, North Carolina; †University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania; ‡National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland; and §Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts.

Reprints: Marjorie Merrick, Vice President of Research and Scientific Programs, Crohn's & Colitis Foundation of America, 386 Park Avenue South, 17th Floor, New York, New York 10016 (e-mail: mmerrick@ccfa.org)

WRITING A RESEARCH GRANT

The most common reason that individuals within an institution are not funded is that they never submit a grant application.

Writing a successful research grant requires common sense, careful planning, and luck. A good idea and careful presentation are essential. The application should be logical, organized, and easy to read. Grant application reviewers have certain expectations about format and language. Following these conventions carefully will increase your chance of success.

General Recommendations

- **Plan ahead.** The most important recommendation (and the one that is commonly ignored) is to plan ahead. Most grant deadlines are announced months in advance. Starting early will help avoid the disasters that often occur when submissions are prepared at the last minute. A mentor and/or colleague should review early drafts and sufficient time should be allocated for final comprehensive review before submission.
- **Submit applications.** Grant writers become successful through practice. Assuming that the grant review process often has a random component to it, the likelihood of funding increases with the number of submissions. Keep in mind that poorly written applications will never be successful regardless of the number of submissions.

- **Take advantage of technology.** Confirm that the proposed study has not already been done. Conduct a thorough search of the literature and review the NIH Computer Retrieval of Information on Scientific Projects (CRISP) database to learn of ongoing studies.
- **Write clearly.** Each paragraph should begin with a strong topic sentence and every sentence should be relevant. Use simple declarative sentences and the active voice.
- **Make the application reader friendly.** A grant application that is easy to read improves the chance for success. A well-constructed presentation will include adequate font size, judicious use of white space, logical headings, and carefully constructed tables and diagrams.

The Question

Framing the research question is often the most difficult task when writing a grant application. The question should be important and answerable. The study must be feasible. A well-constructed research question should include:

- a clearly identified population (cases, target intervention)
- the type of exposure (e.g., risk factor, prognostic factor, intervention, diagnostic test)
- the control or comparison group
- the expected outcomes.

Specific Aims and Hypotheses

The research question is expressed in the specific aims. Experienced investigators usually use 1 or more introductory paragraphs to provide a context for the specific aims and to promote the central hypothesis of the study. This introduction can be extremely important because it is usually the first section read by the reviewer. The specific aims should unambiguously state the goals of the study. Many clinical research grant applications lack an explicit statement of the hypothesis. Clinical studies should have 1 or 2 primary objectives, with other aspects of the study described as secondary objectives. Many applications fail review for being too ambitious (i.e., too many objectives or questions). It is important to be realistic about what can be accomplished and to focus on the central question.

Background and Significance

The background section provides the justification for the research. A well-conceived background section should make the proposed study inevitable and irresistible. A common mistake is a background section that is too long. The background should be a critical, focused review rather than a comprehensive one. The background section should highlight limitations in our understanding and explain how the proposed research will contribute.

Preliminary Studies

Once the reviewers agree that the study is a good idea, the next task is to convince them that the study design is rational and logical. One of the most common reasons a study is not funded is that the reviewers believe that the study is impossible to conduct. Often a small pilot study can show that a study is feasible. If it is not possible to conduct a small pilot study, other experience relevant to the proposed research should be described. The reviewers must be convinced that the research team is competent and has adequate resources.

Methods

The methods section describes all aspects of the study design and conduct in full detail. Attention to detail in the development of the methods section will help detect and eliminate errors before review. The methods section should begin with an overview describing the study in general terms and should include the following:

- **Study setting.** Describe how study subjects will be identified, recruited, and enrolled and designate the personnel responsible for these tasks.
- **Subjects.** Describe eligibility and exclusion criteria in great detail and characterize the available pool of patients. The criteria should not be so rigid as to make enrollment in the study impossible. Pilot studies can help determine if eligibility/exclusion criteria and available patient pools are adequate to support a larger study.
- **Data collection.** Describe what you plan to measure, how you will measure it, when you will measure it, and the tools you will use to collect and manage the data. Whenever possible, choose instruments, scales, and criteria that have been used successfully. If you are going to measure quality of life, use a well-accepted instrument. If you choose to develop an instrument, make sure it is reliable and valid. Avoid collecting extraneous data because it increases the cost and makes the study appear cluttered and unfocused.
- **Quality control.** Attention to quality marks you as a careful researcher. Describe the training and qualifications of all personnel involved in the trial. Include methods for validation of outcomes measures (e.g., laboratory certifications, recording of telephone interviews, etc.) and describe methods used to maintain blinding and avoid bias.
- **Data management.** A careful plan to monitor progress of the study should be in place before initiation. Data entry, validation, and security should be well thought out and thoroughly described. Make sure that computer files are backed up and store back-ups in a separate location.
- **Sample size.** The research study must have an adequate sample size to detect a meaningful difference between treatments. Differences in treatment should not only be statistically significant but clinically relevant. If a study cannot enroll sufficient numbers of patients, it is neither feasible nor ethical. The sample size depends on several factors:
  - the level of type 1 error (α error, usually 0.05)
  - the power of the study to detect a difference ($1 - \beta$, often pre-specified as 0.80)

- the extent of the difference the study is designed to detect.
- **Data analysis.** Poorly written data analysis sections are a common problem in clinical research grant applications. Find a statistician to help write and/or review the data analysis section before submission. A poorly written data analysis section may create concern that study data will not be analyzed or interpreted correctly.
- **Timeline.** Provide realistic estimations of how long each step will take.

Summary

This summary should include a brief restatement of the aims of the study and describe the study's strengths, weaknesses, and potential problems. Addressing the weaknesses shows understanding of the process and helps immunize the proposal from criticism by the reviewers. This section may also include commentary on the potential implications of the study results.

References

Cited references should be complete and current but not exhaustive. Older references (i.e., >5–10 yr) should be used only to show historical perspective. If the reviewing committee membership is known, it may be helpful to include their publications where relevant.

Appendix

A carefully composed appendix can be crucial to the success of a grant application. Page limitations may not allow for inclusion of all necessary information in the main body of the application. The appendix may include the study protocol, data collection forms, letters to patients, study brochures, and pertinent references. Information that describes prior experience as a researcher in the field can be helpful. The appendix is not designed to circumvent page limitations. Critical information should be in the body of the application and not the appendix.

Study Administration

- **Personnel.** The personnel conducting the trial should be experienced and competent. If the principal investigator is inexperienced, the addition of a senior investigator or collaborator may instill a level of confidence among the reviewers. Senior researchers or experts in the field may be included in the submission as consultants. It is particularly important that the personnel assigned to the study have the capability to get the work done.
- **Budget.** The budget must be sufficient to complete the work described in the application. A careful and complete budget justification will convince reviewers that the investigators understand the complexity of the project and the resources needed to complete it. The budget justification must coincide with the study methods described. If the requested budget is not sufficient to complete the study, indicate how the deficit will be handled.
- **Letters of support.** Letters of support from collaborators or investigators at other institutions should be included in the application. Under no circumstances should these be form letters! Collaborators unwilling to develop their own letters are unlikely to be enthusiastic participants in the study, and reviewers are not impressed when all the letters of support are exactly the same.

Resubmission

It is unusual for a grant to be funded on its first submission. Reviewers' comments should be carefully examined and addressed in the resubmission. Second and third applications are more likely to be funded. Don't give up!

NATIONAL INSTITUTES OF HEALTH

The NIH offers funding in many different forms. The number of grant applications to the NIH and the success rate have remained fairly stable over the 10 years between 1990 and 2001.

The **K-series awards** are designed to provide funds for a junior faculty member to conduct research under the guidance of a mentor and to obtain training in research methods. These 3- to 5-year grants provide salary support (typically $75,000/yr) and research funds (typically $25,000/yr). While it is possible to conduct a clinical trial as part of a K-series award, the trial would need to be conducted on a relatively small scale at a single center and may require additional support from other sources.

R03 grants are designed specifically to support small research projects that can be carried out in a short period of time with limited resources. Individual institutes within the NIH use this mechanism differently. These 2-year grants typically provide $50,000 to $100,000 per year in research support. At the NIDDK, the R03 mechanism is used to fund pilot feasibility studies for future clinical trials. The expectation is that these studies will lead to more substantial R01 grants (see below) to support large-scale clinical trials. The competition for R03 grants at the NIDDK is less intense than that for R01 level funding, but still requires careful planning and a well-prepared grant application.

R01 grants are generally viewed as the "gold ring" of research support. R01 grants provide support for 3 to 5 years. These grants are generally capped at $500,000 per year in direct costs, although with special permission, larger grants can be awarded. R01 grants are extremely competitive and often require multiple applications to obtain funding. The reviewers will expect evidence that the applicant is an independent investigator, has experience conducting research in the field, has appropriate resources available, and can prove the feasibility of the proposed research. Junior faculty are rarely

successful in receiving R01 grants without having obtained prior research funding from the NIH or other agencies.

In addition to unsolicited, investigator-initiated applications, NIH solicits applications on topics of interest through mechanisms such as *Program Announcements, Requests for Applications,* and *Requests for Proposals*.

The typical timeline for a new individual research project grant application is 11 months from submission to grant award. Grant applications submitted to the NIH receive 2 levels of review:

- The Scientific Review Group provides initial scientific and technical merit review and makes recommendations for appropriate support level and award duration.
- The Institute's National Advisory Council provides second-level peer review of grant applications that have been scored by the Scientific Review Group and advises the institute on the relevance of the research to the institute's priorities and public health needs.

CROHN'S & COLITIS FOUNDATION OF AMERICA (CCFA)

CCFA's mission is to find the cure for Crohn's disease and ulcerative colitis by supporting outstanding peer-reviewed research and to provide education and supportive services to patients, health care professionals, and the general public. Applicants must hold an MD, PhD, or equivalent degree and be employed by a public nonprofit, private nonprofit, or government institution engaged in health care and/or health-related research. Eligibility is not restricted by citizenship.

CCFA research funding has 4 goals:

- To identify and fund the best peer-reviewed, investigator-initiated research in IBD
- To provide seed money to allow investigators to generate enough preliminary data to compete for funding at the NIH
- To encourage outstanding young investigators to choose a career in IBD research
- To identify and support emerging areas of research to increase understanding of the causes and disease course of IBD

The types of funding available include the following:

- **Senior Research Awards.** These grants are awarded to established investigators for projects conducted at hospitals, universities, and research laboratories around the world. Senior Research Awards are a maximum of $143,000/yr for 3 years.
- **Training Awards.** CCFA offers Career Development and Research Fellowship Awards for young investigators who are engaged in postdoctoral training programs. Applicants must be employed by a public nonprofit, private nonprofit, or a government institution engaged in health-related research within the United States and its possessions. Eligibility is not restricted by citizenship. These awards are primarily salary support to insure protected research time for the trainee.
  - **Career Development Awards.** These awards are for investigators who are in the final phase of their post-doctoral training and are beginning to transition to independence. This award is a maximum of $90,000/yr for 3 years and includes salary support, fringe benefits, and funds for supplies, tuition, travel, etc. Two tracks are available:
    - *Clinical Research*: includes funds for tuition toward a Master of Public Health Degree (MPH) or equivalent. Investigators are required to complete this degree within the 3-year window of this award. If the researcher has already obtained an MPH, the funding can be used for expenses related directly to the project.
    - *Basic Research*: to be used for salary, fringe benefits, and expenses related directly to the project.
  - **Research Fellowship Awards.** These awards are for the new investigator who has at least 1 year of IBD-related research experience. Awards are a maximum of $58,250/yr for 3 years and include salary, fringe benefits, and travel support.

Further information, guidelines, and application forms for all of CCFA's grant programs may be found online at www.ccfa.org/science.

CONCLUSION

To obtain funding for clinical research you must have a good question, write clearly, and be organized and meticulous. Writing the application demands an organized and deliberate approach. Senior colleagues are usually happy to read drafts and provide advice. Don't be discouraged if early efforts are not successful. Writing successful applications is a learned skill, and the more you practice, the better you get.

ADDITIONAL RESOURCES

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NIH New Investigators Web Site: http://grants1.nih.gov/grants/new_investigators/index.htm

NIH Office of Extramural Research Web Site: http://grants1.nih.gov/grants/oer.htm

