Getting the Funding You Need to Support Your Research: Navigating the National Institutes of Health Peer Review Process

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Once an investigator has selected a general research topic, determined what others have already done, identified promising new research areas, planned a project, and estimated the budget required for it, she/he will need to obtain funding to perform the study. There are more opportunities than ever for clinical researchers to develop new diagnostic and therapeutic approaches to many diseases. Many public and private organizations support biomedical research and clinical trials, but most biomedical research conducted at research centers and academic institutions in the United States is funded by the National Institutes of Health (NIH).

Translational and clinical research can be broader in scope than laboratory research and more difficult to plan, describe, and carry out. Most clinician scientists also receive little training in grant writing. Recent studies at NIH show that the overall success rate of applications proposing clinical research and clinical trials is somewhat lower than the success rate for applications for basic or laboratory-based research. This was not due to the review panel assignment, the composition of the review committee, the cost of the proposed research, or whether clinical applications were reviewed in the same review group as basic research applications. It is likely that the applications are just not as well prepared.

Rejected grant applications can challenge the ego, cause critical delays, or result in loss of research opportunities, particularly if the research project is linked to ongoing clinical trials. A thorough understanding of the NIH peer review process will help both new and established clinical investigators be more competitive in applying for research funds. The purpose of this chapter is to provide (1) an overview of the NIH and the NIH peer review process, (2) suggestions for writing more competitive grant applications, (3) brief descriptions of some NIH grant programs for clinical researchers at various stages of their careers, and (4) ways to find current information about the NIH grants process when you are ready to apply.

OVERVIEW OF NIH

Mission and Organization of NIH

NIH is a federal agency that is part of the U.S. Department of Health and Human Services (DHHS). The mission of NIH is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability. NIH accomplishes this mission by conducting and supporting research, research training and career development, research infrastructure and resources and conferences related to

- the causes, diagnosis, prevention, and cure of human diseases;
- the processes of human growth and development;
- the biological effects of environmental contaminants;
- the understanding of mental, addictive and physical disorders; and
- the collection, dissemination, and exchange of information in medicine and health.

The structure of the NIH is shown in Figure 36-1. Most NIH components have both intramural programs, with laboratories and clinics staffed by NIH employees, and extramural programs, through which research is supported in institutions worldwide. It is important to note that although each NIH institute has specific scientific areas of primary interest, there are many areas of shared interest. For example, asthma is a shared interest of the National Institute of Allergy and Infectious Diseases (NIAID) and the National Heart, Lung, and Blood Institute (NHLBI); and the National Cancer Institute (NCI) and NIAID are both interested in transplantation biology and the life cycle of oncogenic viruses. Applicants should discuss potential research projects with program staff in all relevant NIH components before preparing a grant application.

The total budget of the NIH was approximately $31.2 billion in fiscal year 2010 (Table 36-1), excluding the one-time funds from the 2009 American Recovery and Reinvestment Act. About 85% of the NIH budget is used to support extramural research through different types of grants and contracts.

Responsibilities of NIH Staff

Each of NIH’s extramural research programs is managed by a program official, an NIH scientist who oversees scientific aspects of the program. Grants and contracts management staff provide financial stewardship and oversight of an institute’s extramural research programs. Each NIH funding component also has a review office that manages the scientific peer review of contract proposals and highly mission-oriented grant applications. Table 36-2 summarizes the responsibilities of NIH review, program, and grants and contracts management staff.
NIH Extramural Funding Mechanisms

NIH uses three types of funding mechanisms to support extramural research and development: grants, cooperative agreements, and contracts. The relationship between NIH and the awardees in each of these funding mechanisms is summarized in Table 36-3.

Most NIH grants are "investigator initiated"—which means that the principal investigator is responsible for developing the ideas, concepts, methods, and approaches for the project. The grantee files a yearly progress report, but NIH staff are not involved in carrying out the work. Cooperative agreements are similar to grants in that the purpose is to assist and support research or related activities. However, they include a substantial scientific and/or technical role by NIH staff, such as coordination of awardee activities or approval of phases or processes in the project. Cooperative agreement applications usually are solicited via a specific Request for Applications (RFA), which describes the activities that will be supported as well as NIH staff involvement.

In contrast, NIH uses contracts to purchase a service or product, and the awarding NIH component establishes the plans, parameters, and detailed requirements for projects.
supported by contracts. Contract proposals are almost always solicited through specific Requests for Proposals. Contracts have special submission and review processes, review criteria, mechanisms for reimbursement of costs, involvement of the funding institute, and delivery of the end product. Because most NIH support of extramural research is via grants and cooperative agreements, this chapter does not address contracts. For more information about NIH support of research and development contracts and contract opportunities, see http://ocm.od.nih.gov/.

NIH Funding Announcements

Funding Opportunity Announcements in Grants.gov

Most types of NIH grant applications are submitted electronically on the Standard Form 424 Research and Related (R&R) application form through the federal Web portal Grants.gov. Only complex multi-component applications are still submitted on paper on the PHS 398 grant application form. The Grants.gov portal allows you to search all federal grant programs through the “Find” option and to apply for grants through the “Apply” option. Applicant institutions also must register their project directors/principal investigators (PD/PIs) in the NIH electronic research administration (eRA) Commons. Registration volume peaks close to submission dates, so start the registration process at least four weeks before your target submission date.

All applications—including those that are “investigator initiated”—must be submitted in response to an open NIH Funding Opportunity Announcement (FOA). The NIH has posted generic (or “parent”) FOAs in Grants.gov for the most common types of grants. Specific FOAs are published for each RFA and Program Announcement (PA) and for NIH institute/center-specific grant mechanisms. Although most FOAs allow submission of only one type of grant application, some allow submission of multiple related types of grant applications.

Each FOA has an opening date and a submission deadline. Many FOAs are active for several years and include multiple submission/receipt dates. Applicants should read the entire FOA carefully to determine the specific submission/receipt deadlines. Applications submitted after the submission deadline may be rejected or may be held over to the next submission date.

Requests for Applications and Program Announcements in the NIH Guide

The NIH may invite submission of grant applications to address areas of special interest to an awarding institute by issuing an RFA or PA in the NIH Guide for Grants and Contracts (http://grants.nih.gov/grants/guide/index.html) with a link to the correct FOA in Grants.gov. Table 36-4 summarizes the key features of RFAs and PAs. RFAs generally have specific funds set aside to support research, training, or infrastructure on a given topic. RFAs also list NIH staff contacts, and it is a good idea to discuss your potential project with them to ensure that you meet all responsiveness and eligibility criteria. Peer review of applications for an RFA usually is managed by the peer review office in the issuing NIH component. In contrast, a PA usually indicates NIH’s interest in supporting research in a broad area without specific set-aside funds. Applications responding to PAs usually are reviewed with other “investigator-initiated” applications on similar topics through the usual channels in study sections organized by the NIH Center for Scientific Review. Both RFAs and PAs may have special eligibility requirements, application preparation procedures, receipt dates, and/or conditions of

**TABLE 36-2 Roles and Responsibilities of NIH Extramural Staff**

<table>
<thead>
<tr>
<th>NIH staff</th>
<th>Role and responsibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific review officer (SRO)</td>
<td>In Center for Scientific Review and in each NIH institute/center scientific review office</td>
</tr>
<tr>
<td></td>
<td>Organizes, manages, conducts, and reports scientific peer review of grant applications and/or contract proposals</td>
</tr>
<tr>
<td></td>
<td>Liaison between applicants and reviewers</td>
</tr>
<tr>
<td>Program officer/ director</td>
<td>In NIH institutes and centers</td>
</tr>
<tr>
<td></td>
<td>Manages a portfolio of awarded grants/contracts</td>
</tr>
<tr>
<td></td>
<td>Monitors scientific progress made on grants/contracts</td>
</tr>
<tr>
<td>Grants/contracts management officer</td>
<td>In NIH institutes and centers</td>
</tr>
<tr>
<td></td>
<td>Fiscal stewardship of portfolio of awarded grants/contracts</td>
</tr>
<tr>
<td></td>
<td>Negotiates fiscal aspects of awards</td>
</tr>
<tr>
<td></td>
<td>Monitors financial progress made on grants/contracts</td>
</tr>
</tbody>
</table>

**TABLE 36-3 NIH Extramural Award Mechanisms**

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>NIH role</th>
<th>NIH provides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grant</td>
<td>Patron</td>
<td>Assistance, encouragement</td>
</tr>
<tr>
<td>Cooperative agreement</td>
<td>Partner</td>
<td>Assistance, with substantial program staff involvement</td>
</tr>
<tr>
<td>Contract</td>
<td>Purchaser</td>
<td>Direction</td>
</tr>
</tbody>
</table>
award, so it is important to read the announcement carefully before preparing an application.

**Electronic Submission of Applications through Grants.gov**

The electronic grant submission process through Grants.gov involves several steps that must be completed in sequence.

1. Search for and identify an open FOA on Grants.gov.
2. Download and complete the specific grant application package for that FOA. Some parts of the application (i.e., investigator and budget information) require entering information into specific templates and other parts (Biosketches, Research Plan, Bibliography) require PDF attachments with narratives prepared by the applicant.
3. An authorized official at the applicant organization submits the completed application package through Grants.gov. (Be sure to save a local copy!)
4. NIH eRA software retrieves the application from Grants.gov and checks the application against NIH’s business rules.
5. NIH notifies both the PI and signing official (SO) for the applicant institution by email to check the NIH eRA Commons for results of the NIH validations check.

   If the application *passed* NIH validations checks, there will be a grant image in the eRA Commons. If the image is not accurate, the PI and SO may reject the application in the eRA Commons, make the necessary changes, and submit the changed/corrected application again via Grants.gov. However, submission of the changed/corrected application must be completed by the deadline stated in the FOA—the deadline stated in the FOA—there is no “grace period” for correction of applicant errors!

   If the application *failed* NIH validation checks, the eRA Commons will show errors and warnings. The PI and SO must fix the errors and submit the entire corrected application again through Grants.gov by the deadline in the FOA.

6. eRA Commons saves the grant image, and NIH begins processing the application.

Each NIH grant application package in Grants.gov will include both SF424 (R&R) components and NIH-specific PHS 398 components as well as an application guide with complete instructions for submitting an application. The NIH logo indicates fields in the SF424 (R&R) components that are not mandatory on the federal-wide form but are required by NIH.

The NIH electronic receipt website (http://era.nih.gov/ElectronicReceipt) has a number of resources for applicants, including:

- SF424 (R&R) application guides, sample application packages, and related resources
- eRA Commons registration training
- Videotaped presentation, “A Walk through the SF424 (R&R)”
- End-to-end demo facility for applicants to “practice” the entire process from finding an opportunity in Grants.gov to viewing a submitted application in the eRA Commons.

**Multiple PIs**

For most types of grant applications, NIH allows applicants and their institutions to identify more than one PD/PI. The Multiple PI option is to encourage interdisciplinary and team approaches to biomedical research. Each FOA will indicate if the multiple PD/PI option is available for that type of application. The Multiple PD/PI option is not appropriate for individual career awards, individual fellowships, Dissertation Grants, Director’s Pioneer Awards, and Shared Instrumentation Grants. Investigators and the applicant organization are responsible for deciding whether to apply for the multiple PD/PI option.

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**TABLE 36-4 Key Features of NIH Program Announcements and Requests for Applications**

<table>
<thead>
<tr>
<th>Program announcement (PA)</th>
<th>Request for applications (RFA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addresses a relatively broad field/category of research</td>
<td>Addresses a well-defined area of research</td>
</tr>
<tr>
<td>Usually no set-aside budget</td>
<td>Set-aside budget</td>
</tr>
<tr>
<td>Usually submit on regular receipt dates</td>
<td>Submit on special, one-time-only receipt dates</td>
</tr>
<tr>
<td>Regular review criteria for type of applications requested</td>
<td>Often special eligibility and/or review criteria</td>
</tr>
<tr>
<td>Frequently more than one NIH component involved</td>
<td>Often special application format and/or submission instructions</td>
</tr>
<tr>
<td>Applications may be reviewed by CSR or the issuing NIH component</td>
<td>Usually only one NIH component involved</td>
</tr>
<tr>
<td></td>
<td>Applications usually reviewed by the issuing NIH component</td>
</tr>
</tbody>
</table>

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for a single or a multiple PI grant based on the scientific goals of the project. See the Multiple PI website (http://grants.nih.gov/grants/multi_pi/) for more information.

Applications with multiple PIs must include a Leadership Plan that describes the rationale for choosing a multiple PD/PI option, and the governance and organizational structure of the leadership team and the research project, including the roles and responsibilities of each PD/PI and plans for communication, decision making, and resolving conflicts.

THE NIH PEER REVIEW PROCESS FOR GRANTS

NIH draws on the national pool of scientists actively engaged in research to assist in evaluating the tens of thousands of grant applications received annually. These scientific “peers” advise NIH which applications are most likely to have a high impact in each field.

The NIH Dual-Review System

The cornerstone of the NIH grants process is the “dual-review system,” with two sequential levels of review that separate scientific assessment of the projects from policy decisions about scientific areas to be supported and the resources to be allocated (Figure 36-2).

The first level of review is by panels of experts organized by scientific discipline or research area to evaluate the scientific and/or technical merit of the applications. These scientific review groups (SRGs) also are commonly called “study sections.” Each SRG is managed by a scientific review officer (SRO), an NIH scientist with expertise in the SRG’s area of science. The second level of review is by an NIH institute’s or center’s national advisory board or council, which is composed of both scientific and public representatives noted for their expertise or interest in matters related to the mission of the institute. Council recommendations are based on scientific merit as judged by the SRGs plus relevance to an institute’s mission and programs.

NIH Review “Cycles”

The NIH receives 70,000 to 80,000 applications per year for about 200 different types of grants (http://grants.nih.gov/grants/funding/ac_search_results.htm). To handle this load, each type of grant application has a designated receipt date(s) indicated in the FOA, with three receipt dates per year for most types of applications (http://grants.nih.gov/grants/funding/submission-schedule.htm). RFAs and some PAs have special receipt dates.

Table 36-5 shows the three overlapping review cycles for grant applications that result from the standard NIH receipt dates. The review cycle for a grant application begins when an investigator submits an application to NIH and concludes when the applicant organization and the principal investigator are notified of the recommendation of the council (Figure 36-3).

Assignment of Applications to a Review Group and Funding Institute

All grant applications are processed centrally by the NIH Center for Scientific Review (CSR) Division of Receipt and

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**FIGURE 36-2** The NIH dual review system.
Referral, which determines if the application is appropriate for NIH and where it should be reviewed. Based on the type of application and the mission areas of the various NIH components, an application is assigned to a potential awarding NIH component and to either a CSR study section or an IC review committee for scientific merit review.

The rosters and scientific areas of the CSR study sections and links to other review committees are available at [http://cms.csr.nih.gov/](http://cms.csr.nih.gov/). Applicants are notified via the NIH eRA Commons (https://commons.era.nih.gov/commons) of the review group and the SRO within a few weeks after receipt of the application. The PD/PI of an application may provide suggestions about appropriate review groups and/or scientific expertise areas needed to evaluate the application in the cover letter attachment that accompanies the application. The SRO may invite additional temporary members to serve as reviewers if specialized expertise is required to review an application. If the research objectives and approaches of an application cannot be reviewed appropriately by an existing SRG, a Special Emphasis Panel may be constituted for the review.

Assignment of an application to an NIH funding component is based on the institute’s congressionally mandated program responsibilities. If the subject matter of an application relates to two or more institutes, a dual, or multiple, assignment may be made. The CSR has no responsibility for either decisions about funding or the management of funded grant programs.

**How are Reviewers Selected?**

The primary requirement for serving on an SRG is demonstrated achievement as an independent investigator. Service also requires mature judgment, balanced perspective, objectivity, ability to work effectively in a group, and a commitment to complete review assignments, maintain confidentiality of applications and discussions and avoid conflicts of interest. NIH also considers geographic distribution and representation of ethnic minority and female scientists in the selection of SRG members.

Members usually are appointed to an SRG for four years, with staggered terms, so about one-fourth of the members of each SRG change each year. Several NIH

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### TABLE 36-5 NIH Grant Application Receipt, Review, and Award Cycles

<table>
<thead>
<tr>
<th>Application receipt dates</th>
<th>Scientific review group meetings</th>
<th>National advisory council meetings</th>
<th>Earliest possible award date</th>
</tr>
</thead>
<tbody>
<tr>
<td>January 25–May 1</td>
<td>June–July</td>
<td>September–October</td>
<td>December 1</td>
</tr>
<tr>
<td>May 25–September 1</td>
<td>October–November</td>
<td>January–February</td>
<td>April 1</td>
</tr>
<tr>
<td>September 25–January 2</td>
<td>February–March</td>
<td>May–June</td>
<td>July 1</td>
</tr>
</tbody>
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**FIGURE 36-3** Flow of a typical grant application from the applicant through the NIH peer review and funding process.
institutes also include patient representatives or advocates on SRGs reviewing clinical research applications, especially those involving clinical trials. Patient advocates have expertise in the impact of the disease on patients and caregivers, strategies and approaches likely to succeed in patient recruitment and follow-up, and quality of life issues. Patient advocates are full voting members of the review panels.

How Does the Review Proceed?

Standing SRGs ("study sections") normally meet three times a year for one to three days each time, depending on the number and types of grant applications to be reviewed. Typically, a CSR study section is responsible for the review of 60–100 research project grant applications at each meeting. The SRO assigns each application to three or more members of the SRG, who provide detailed written reviews listing specific strengths and weaknesses of the applications related to each of the review criteria. Each member may be assigned to prepare detailed critiques for 5–10 applications and as a discussant (reader) on additional applications. Reviewers receive the applications and instructions for preparing their reviews four to six weeks before the SRG meeting.

The SRO is the designated federal official in charge of the meeting and handles all communications with applicants and reviewers during the review process. The SRO and the chairperson, one of the members of the SRG, conduct the meeting. The chairperson calls on the assigned reviewers and discussants to present their critiques and then moderates a discussion among all SRG members. Other members of the SRG question assigned reviewers about the application or their critiques. SRG members score each application on the basis of their own assessment of its strengths and weaknesses, scientific merit, and potential impact on the field.

To use the time at the review meeting most effectively, many SRGs use a streamlined review process in which only the top half of all applications to be reviewed are discussed at the SRG meeting; the rest of the applications are not discussed. Applications may be discussed in the order of the preliminary overall impact scores provided by the assigned reviewers.

Review Criteria for Research Project Grant Applications

The review criteria were updated in 2008 as part of the NIH Enhancing Peer Review initiative (http://enhancing-peer-review.nih.gov/) and are summarized in Table 36.6.

Core Review Criteria

Reviewers consider each of the following five core review criteria in their determination of the scientific merit of the project, and assigned reviewers give a separate score for each.

1. Significance: Does this study address an important problem or a critical barrier to progress in the field? If the aims of the application are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventive interventions that drive this field?

2. Investigators: Are the PD/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators (ESI) or New Investigators, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance, and organizational structure appropriate for the project?

3. Innovation: Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

4. Approach: Are the overall strategy, methodology, and analyses well reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? If the project

<table>
<thead>
<tr>
<th>TABLE 36-6 NIH Review Criteria for Research Project Grant Applications</th>
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</thead>
<tbody>
<tr>
<td>Review criteria:</td>
</tr>
<tr>
<td>Significance</td>
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<tr>
<td>Investigator</td>
</tr>
<tr>
<td>Innovation</td>
</tr>
<tr>
<td>Approach</td>
</tr>
<tr>
<td>Environment</td>
</tr>
<tr>
<td>Types of applications:</td>
</tr>
<tr>
<td>Unsolicited R01s, R03s, R21s, P01s</td>
</tr>
<tr>
<td>R01s, R03s, R21s, P01s for PAs</td>
</tr>
<tr>
<td>Most R01s, R03s, R21s, P01s for RFAs</td>
</tr>
</tbody>
</table>

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involves clinical research, are the plans for (1) protection of human subjects from research risks, and (2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

5. Environment: Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment, and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Some RFAs and PAs may list additional review criteria and/or additional elements under each of the standard core review criteria that relate to the specific requirement(s) of the program announced in the FOA.

Additional Review Criteria

The following items also are considered in the determination of scientific merit and the impact/priority score for research project grant applications, but do not receive individual scores.

1. Protection of human subjects from research risk: Most clinical research projects will involve human subjects, either living persons with whom you will interact directly or identifiable specimens from them. The reviewers evaluate the proposed use of human subjects, the risks to the subjects, the plans to protect them from risks, whether the risks are reasonable in relation to the anticipated benefits to the subjects, and the importance of the knowledge that may result from the research. For projects that claim an exemption, the reviewers evaluate the justification for the exemption. Serious deficiencies in the plans to protect human subjects may be considered weaknesses under the “approach” review criterion. In addition, there is a bar to award until all reviewer concerns about protection of human subjects have been resolved.

2. Inclusion of women, minorities, and children in research: Reviewers evaluate the proposed plans for the inclusion of minorities and members of both genders, as well as the inclusion of children. Serious deficiencies in the plans to include women, minorities and/or children will be considered weaknesses under the “approach” review criterion and may result in a bar to award.

3. Vertebrate animals: Reviewers evaluate the proposed use of live vertebrate animals, including the strains, ages, sex and number of animals; justification for using animals; adequacy of veterinary care; procedures for limiting distress, pain and injury; and methods for euthanasia. Serious deficiencies in the plans to protect vertebrate animals will be considered weaknesses under the “approach” review criterion and may result in a bar to award.

4. Resubmission applications: Reviewers evaluate the application as now presented, considering the responses to the previous review and changes to the project since the previous submission.

5. Renewal applications: The reviewers consider progress made in the last funding period.

6. Revision applications (formerly called competing supplement applications): The reviewers consider the appropriateness of the proposed expansion of the scope of the project.

7. Biohazards: Reviewers assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and, if so, whether adequate protection is proposed. An award cannot be made until all concerns about hazardous conditions have been resolved. Serious deficiencies in the plans to protect against biohazards may be considered weaknesses under the “approach” review criterion.

Additional Review Considerations

As applicable for the proposed project, reviewers address each of the following items, but do not give scores for them and do not consider them in the overall impact/priority score.

1. Applications from foreign organizations: If the application is from an institution outside of the United States, or involves a substantial foreign component, the reviewers comment on whether the research could be done in the U.S., or if the foreign location offers specific advantages, such as resources, equipment or study populations that are not available in the U.S.

2. Select agent research: Federal policy requires applicants proposing research with certain biological agents and toxins, termed “select agents,” that have the potential to pose a severe threat to public, animal or plant health, to disclose the proposed use in NIH grant applications and for reviewers to evaluate the plans to handle and contain such agents (see http://www.selectagents.gov/ and http://grants.nih.gov/grants/policy/select_agent/ for policies related to grants involving select agents). Although this item is not scored, serious deficiencies in the experience of the research team or the plans for handling such agents may be addressed under the “investigators,” “approach,” or “environment” review criteria.

3. Resources Sharing Plans: NIH expects awardees to share research data and to make the results of the projects that it funds available to the public. Reviewers comment on whether the following Resource Sharing Plans are reasonable.
Data Sharing Plan. Applications requesting more than $500,000 direct costs in any year must include a data sharing plan (http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm). Some RFAs and PAs may request a data sharing plan for all applications regardless of costs.

Sharing Model Organisms. All NIH grant applications are expected to include a plan for sharing and distributing unique model organism research resources generated using NIH funding or to state why sharing is restricted or not possible (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html). Model organisms include both mammalian models, such as mice and rats, and non-mammalian models, such as yeast, amoebae, worms, flies, zebra fish, etc. Investigators may request funds to defray costs associated with sharing. For some special initiatives and grant programs specifically directed toward the development of model organisms, reviewers’ evaluation of the plan for sharing model organisms may factor into the overall score.

Genome Wide Association Studies (GWAS). All applications that include GWAS are expected to include a plan for submission of GWAS data to the NIH designated data repository or an appropriate explanation for why submission to the repository will not be possible (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-013.html).

Research Project Grant Applications from New/Early Stage Investigators

New and Early Stage Investigators (ESIs)—a new investigator who is within 10 years of completing his/her terminal research degree or 10 years of completing medical residency—are encouraged to apply for traditional NIH research project grant (R01) applications to accelerate their transition to an independent scientific career. Wherever possible, the NIH will cluster applications from New and ESIs for discussion during initial peer review. When reviewing applications from New/ESIs, reviewers consider the experience of and the resources available to the investigator, and apply the five review criteria in a manner appropriate to the expectations for, and problems likely to be faced by, a new investigator. Specifically:

- Investigator: More emphasis is placed on the applicant’s training and research potential than on his or her track record and number of publications.
- Approach: More emphasis is placed on demonstrating that the techniques and approaches proposed are feasible than on the presentation of preliminary results.
- Environment: Reviewers look for evidence of institutional commitment in terms of space and time to perform the research.

NIH also has special receipt dates that allow resubmission of R01 applications from New/ESIs for the very next review meeting, saving approximately four and a half months in the overall resubmission process. However, since NIH allows only one resubmission of an application, New/ESIs need to consider carefully whether this option is appropriate for their situation. Consultation with NIH program staff and senior colleagues about the specific weaknesses cited in the summary statement, and whether they are amenable to a “quick fix,” is very important.


Possible SRG Actions

Scientific review groups have several options for each application that is discussed.

- Score: If the SRG members have sufficient information to make a final recommendation about the application, they will score the application.
- Deferral: In the rare instance that an SRG cannot make a recommendation without additional information, it may defer the application to the next review cycle. The SRO will contact the applicant to obtain the necessary information, or, if the information can be obtained only by discussion with the applicant or by direct observation, a telephone conference with the applicant or a project site visit may be scheduled. Deferred applications are usually reviewed again by the same SRG during the next review cycle. Deferral usually is not an option for applications received in response to a one-time RFA.
- Not recommended for further consideration: In reviews that are not streamlined, applications may be “not recommended for further consideration” if they lack significant and substantial merit or if they involve procedures that are gravely hazardous or pose very serious risks to human subjects or vertebrate animals. The advisory councils do not consider these applications and they cannot be awarded.

Overall Impact/Priority Score and Percentiles

Reviewers provide an overall impact/priority score to reflect the likelihood that the project will exert a sustained, powerful influence on the research field(s) involved. Each of
the review criteria is considered in assigning the overall impact/priority score, with reviewers weighting them as appropriate for each application. An application does not need to be strong in all categories to be judged likely to have a major scientific impact—for example, a project that is not innovative may be essential to advance a field. However, it is unlikely that projects with low significance or serious problems in the approach will have a high impact. Reviewers provide a one-paragraph overall impact evaluation summarizing the factors that led to the impact score.

Each reviewer who is not in conflict with an application assigns an impact/priority score ranging from 1 (exceptional) to 9 (poor). A score of 1 indicates an application with essentially no weaknesses that will have an exceptionally high impact, whereas a score of 9 indicates an application with serious and substantive weaknesses, very few strengths and little likelihood of making an impact. Reviewers consider not only the number of strengths and weaknesses, but also their relative importance; for example, a major strength may outweigh many minor weaknesses. (See http://grants.nih.gov/grants/peer/guidelines_general/scoring_system_and_procedure.pdf.)

After the meeting, the individual reviewers’ numeric ratings for each scored application are averaged and multiplied by 10 to provide the final two-digit impact/priority score. The best possible score is 10 and the worst is 90. In addition to the impact/priority score, percentile ranks also are calculated for most research project grant (R01) applications. The percentile represents the relative position or rank of a priority score on a 100 percentile scale; the first percentile is the best and the 100th percentile is the worst. Percentiles are calculated using a reference base of R01 applications reviewed by a study section at three consecutive meetings. Percentile ranking is currently the primary factor used by most NIH institutes in deciding which applications to fund, although each may set a different percentile “payline” for applications.

**The Summary Statement Tells you what the Reviewers Thought about your Application**

Immediately after the SRG meeting, the SRO prepares a summary statement for each application which documents the deliberations of the SRG and is the official record of the review. Summary statements generally include the assigned reviewers’ essentially unedited written comments and the scores they gave for each of the five core review criteria. For applications that were discussed, the SRO also prepares a resume and summary of discussion to convey the highlights of the discussion (i.e., major strengths and weaknesses of the application). Summary statements for scored applications also may include budget recommendations and administrative notes with reviewer concerns about research involving human subjects or animals or potential overlap with other ongoing projects.

Applicants should expect to be able to access the summary statement through the NIH eRA Commons within four to six weeks after the review meeting. Summary statements for applications from New/ESIs are generally available within two weeks after the review meeting, since there are special deadlines for resubmission of amended applications for new and ESIs.

**Review by National Advisory Councils and Boards**

The second level review for grant applications is by each institute/center’s advisory council or board which assesses the quality of the scientific merit review by the SRG, considers the relevance of the proposed research to the institute’s programs and priorities, and advises the institute/center on policy issues. Generally, councils review only scored applications. Most types of NIH grants cannot be awarded without consideration by a council/board.

Advisory council members use summary statements as the main source of information about applications. For most applications, councils concur with the recommendation of the SRG. If the council disagrees with an SRG recommendation, it may recommend re-review of the application. In addition, the council may advise the institute, based on the relevance of the project to the institute’s mission, that an application should receive more or less favorable consideration for funding than would be indicated by the impact/priority score and/or percentile rating.

**What Determines which Applications are Awarded?**

Awards are made based on the scientific and technical merit of the application, as reflected by its impact/priority score and/or percentile rating, the relevance of the application to the mission and programs of the institute, and the availability of funds. Each NIH institute/center generally sets a payline for each of the different types of applications. Paylines may differ considerably among the NIH institutes/centers, depending on their overall budgets, their portfolio of award mechanisms, and the advice of their advisory councils about portfolio balance. Paylines also may differ from program to program within an institute/center.

**Confidentiality and Conflict of Interest**

Confidentiality of review proceedings is essential to maintain the integrity of the peer review system. Under no circumstances may reviewers discuss the review proceedings outside of the SRG meeting or advise applicants or
others of SRG recommendations. The SRO in charge of the SRG handles all inquiries from applicants and from reviewers. In addition, reviewers may not solicit opinions or reviews from experts outside the SRG. Review materials and the proceedings of review meetings are privileged communications for use only by reviewers and NIH staff.

Conflict of interest in scientific peer review occurs when a reviewer has a personal or financial interest in an application or when an application involves a close relative or a close professional associate of the reviewer, such as a collaborator on any research project. The SRO for the review identifies conflicts of interest among the reviewers before the review and reviewers sign a certification before the review meeting stating that they will not participate in the discussion of any application with which they are in conflict. At the beginning of each SRG meeting, the SRO again explains the NIH confidentiality and conflict of interest policies and review staff keep a record of which members leave the room during the meeting because of conflicts of interest. At the end of the meeting, reviewers sign a second confidentiality and conflict of interest certification and also must leave all review materials with the SRO.

HINTS FOR PREPARING BETTER GRANT APPLICATIONS

After you have decided on your research area and designed a specific project, the most important element in increasing the chances that you will be successful in getting funding for your project is a well-prepared grant application. The reviewers assigned to your application will be scientists working in the general area of your research project. Consider them “informed strangers.” The application is your marketing tool—it must convey a large amount of information while generating excitement about the project. After reading the application, the reviewers must understand the rationale for and objectives of the project, see where it fits in the “big picture” and why it is important, and feel confident that you can actually design, carry out and interpret the proposed experiments to have an impact on the field. A well-prepared application leads the reviewers through the project logically and says much about you as the PD/PI, particularly that you “think like a scientist.” Therefore, the process for preparing an NIH application requires a significant amount of time, a high level of organization, and attention to detail.

Planning your Application

Allow Sufficient Time to Prepare the Application

A first-time applicant for a traditional “R01” research grant should allow at least three months to prepare and finalize the application. Establish deadlines for the preparation of each part of the application, particularly when collaborating investigators are involved. Be aware of administrative deadlines for sign-off within your institution, and be sure to leave enough time to correct validation errors through Grants.gov before the submission date, if necessary. Prepare a draft of the application early enough that objective experts (e.g., successful grantees or an institutional panel) can review it and provide extremely frank feedback and suggestions for revision—friends and close associates are rarely as critical as reviewers on an NIH study section.

Get Help

Find someone in your institution to help you understand the NIH grant application process and forms. Incomplete applications may not pass eRA validations checks or may be returned without review. Ask colleagues for copies of successful recent NIH grant applications to get a more concrete idea of what each section should include. NIH updated the organization and page limits for research grant applications (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-149.html) as part of the Enhancing Peer Review initiative (http://enhancing-peer-review.nih.gov/), so be sure to look at an application in the new format! Talk to program representatives from the NIH institutes with interests in your research area about whether your project falls within the scope of an existing RFA or PA or an area of special program emphasis.

Follow the Instructions Closely—Submit a Complete and Carefully Prepared Application

Before you begin writing your application, download the application package and read the SF424 (R&R) instructions carefully to become familiar with all the requirements and certifications necessary. If you are submitting your application in response to a specific PA or RFA, read the announcement in detail for special eligibility requirements, formatting instructions, and/or submission deadlines. NIH frequently updates policies, procedures, and application requirements, so check the NIH website and do not rely on “hearsay.”

Your application must be complete for review as submitted. If several people are contributing to writing the application, decide who will do the final editing. Reread your application. Have someone else read it. Proofread it again before submission. You, and only you, are responsible for making sure your application is written with good grammar, that the flow of experiments is clear, that the references and figure legends are accurate, and that information is organized and displayed legibly and in the correct
order. Once the submission deadline has passed, NIH accepts update materials, such as revised budgets or additional information, only in a limited number of specific circumstances and cannot “change pages” to correct mistakes in the application. See http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-115.html for examples of acceptable and unacceptable update materials.

Hints and Suggestions for Preparing Each Part of your Application

This section should be used in conjunction with the Grants.gov Application Guide for the SF424 (R&R) forms package. The items discussed here are important parts of the application on which reviewers focus; many first-time applicants have problems with them. (Note that they are not listed here in the order in which they are attached to the SF424 (R&R) application.)

SF424 (R&R) Project Summary/Abstract

The purpose of the Project Summary/Abstract is to convey succinctly the major aspects of the proposed project. It is used in the application referral process to determine what study section is most appropriate to review the application and to what NIH funding component(s) it is most relevant. Members of the review committee who are not primary reviewers may rely heavily on the Project Summary/Abstract to understand your project. If an award is made, the Project Summary/Abstract will be available to the public, so do not include any proprietary information.

- View the Project Summary/Abstract as your one-page advertisement.
- Be complete but concise. Include the rationale for the project and its potential impact on the field. Summarize the specific aims and hypotheses, the short- and long-term objectives, the unique features of the project, the types of methods (i.e., genetic, immunologic, genomic, proteomic, population surveys, etc.) you will use, and the expected results and how you will evaluate them.
- Do not exceed the space allotted or your application may fail validation in Grants.gov.
- Write the Project Summary/Abstract last so that it reflects the entire project.

PHS 398 Specific Research Plan Component

Table 36-7 summarizes the key features of the PHS 398 Specific Research Plan component of successful applications. This is the most important part of the application and will largely determine whether the application receives a high—and potentially fundable—impact/priority score. The Research Plan includes the Specific Aims and Research Strategy of the project. The Research Plan as a whole should answer the following questions.

- Why is this work important and what impact will it have on this and related fields?
- How is the work innovative?
- How will the research be accomplished and how will the results be analyzed?
- What have you and/or others done to establish the feasibility of what you are proposing?

A strong and clear Research Plan establishes your credibility as the principal investigator. One person should revise and edit the final draft. Make sure that all sections are internally consistent and support each other. The thought processes behind the project should be clear. Emphasize how the combination of a strong hypothesis, important preliminary data, and a new experimental system and/or approach will enable important progress to be made. Emphasize biological mechanisms in your hypotheses, experiments, and interpretation of results as much as possible. Use a numbering system and/or subheadings to lead reviewers through the Research Plan. Use diagrams for complex processes, relationships, or organizational schemes.

<table>
<thead>
<tr>
<th>TABLE 36-7 Key Features of Successful Research Grant Applications</th>
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</thead>
<tbody>
<tr>
<td><strong>Hypothesis</strong></td>
</tr>
<tr>
<td>A meaningful hypothesis and a means of testing it</td>
</tr>
<tr>
<td>A sound rationale for the hypothesis</td>
</tr>
<tr>
<td>A set of related aims focused on the hypothesis</td>
</tr>
<tr>
<td><strong>Preliminary data</strong></td>
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<tr>
<td>Shows proper training for the research proposed and the ability to interpret results</td>
</tr>
<tr>
<td>Include alternative interpretations of results and address limitations of methods</td>
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<tr>
<td><strong>Well-organized research plan</strong></td>
</tr>
<tr>
<td>Aims focused, not diffuse</td>
</tr>
<tr>
<td>Clear experimental plan, with rationale for methods chosen, criteria for proceeding from one aim to the next, alternatives if experiments do not work</td>
</tr>
<tr>
<td><strong>Research priorities clearly indicated</strong></td>
</tr>
<tr>
<td>Emphasize mechanism—avoid “descriptive data gathering”</td>
</tr>
<tr>
<td><strong>Clear plans for data analysis, with alternative interpretations addressed</strong></td>
</tr>
<tr>
<td><strong>Access to key reagents, patients, specimens, facilities, etc., well documented</strong></td>
</tr>
</tbody>
</table>
Section 2 of the PHS 398 Specific Research Plan: Specific Aims

The Specific Aims should concisely state the goals of the proposed research and summarize the expected outcome(s) including the impact that the results could have on the field. The Specific Aims section may not exceed one page. Succinctly list broad, long-term goals (e.g., the hypothesis to be tested) and provide a list of specific time-phased research objectives.

- State the hypotheses or problem(s) to be solved clearly and definitively. Make sure the hypotheses are understandable and testable within the proposed time frame.
- Be brief and specific. State each aim in one sentence. Use a brief paragraph under each aim if more detail is needed.
- Do not “bite off more than you can chew.” A small, focused project with a feasible timetable is generally better than a diffuse, multifaceted “fishing expedition.” Most successful applications have two to four specific aims.
- Make sure that all aims are related to the stated hypothesis or problem.
- Focus on aims where you have good supporting preliminary data and scientific expertise.

Section 3 of the PHS 398 Specific Research Plan: Research Strategy

The Research Strategy section describes how the research actually will be carried out and is crucial to how favorably an application is reviewed. This section is organized to address the Significance, Innovation and Approach criteria (listed previously in “Core review criteria,” above) and is limited to 12 pages for an R01 application. The page limits for other types of applications are listed at http://enhancing-peer-review.nih.gov/page_limits.html.

In the Significance section, you must make a compelling case for your proposed research project and excite the reviewers about your project. Explain why your objectives and specific research questions are important and what barriers to progress in the field the project addresses, given the current state of the art in the field. How will the results advance the field?

In the Innovation section, show how your project challenges or seeks to shift current paradigms in the field, or has novel concepts, approaches or methods.

In the Approach section, describe the overall strategy, methodology, and analyses that you will use to accomplish the specific aims. Emphasize the rationale for selecting the proposed methods and approaches, how the data will be collected and analyzed, and the criteria for moving from one aim to the next. Discuss alternative approaches that will be pursued if the proposed approach is not successful.

Include a projected sequence or timeline for the project. Address precautions to be used for work that may be hazardous to project personnel or human subjects. The approach for clinical projects should be developed with input from a statistician. Be sure to address statistical issues in study design and data analysis, with appropriate power calculations.

Include data from any preliminary studies you have done, as well as citations to published reports that establish the feasibility of the proposed work in the Research Strategy section.

- Number the sections to correspond to the numbered Specific Aims. Be sure to explain how the results from the experiments proposed address your stated hypotheses!
- Use active voice and be specific. For example, it is not sufficient to state, “A variety of viruses will be grown in cells in standard systems.” The reviewers will want to know which viruses, cells, and systems; your rationale for selecting them over others; how they will be used; and if you have ever done work like this previously.
- You will not have room for all of the experimental details within the 12 page limit. Cite publications for standard methods and explain new or unusual methods in more detail.
- Be realistic about how much work can be done with the time and resources proposed.
- Use diagrams or flow charts to convey the flow of experiments, samples and/or data.
- Include specific, definitive letters of collaboration for critical patients, populations, specimens, equipment, or reagents that will be provided by others.

PHS 398 Specific Research Plan: Human Subjects Sections

You must include these sections if you answer “yes” to the question “Are human subjects involved?” on the SF424 R&R Other Project Information form—failure to do so will result in validation errors in Grants.gov. Applications that do not adequately address research on human subjects may be returned without review, or the review or award may be delayed. Therefore, before preparing an application, you should review the instructions in the SF424 (R&R) Application Guide (http://grants2.nih.gov/grants/funding/424/index.htm) and the Office for Human Research Protections’ (OHRP) website (http://www.hhs.gov/ohrp/) for guidance on and decision charts for research involving human subjects. There is no page limit for these sections; be thorough but succinct. You may not use these sections to get around the page limits in the Research Strategy section, but you may include statistical analyses and power calculations justifying the numbers or types of patients or
Section 6: Protection of Human Subjects

Provide a complete description of the proposed involvement of human subjects as it relates to the work outlined in the Research Plan. If an exemption is claimed, explain why it is justified. If no exemption is claimed, address all four items listed in Part II, Supplemental Instructions for Preparing the Human Subjects Section of the Research Plan. The application must include a plan for monitoring data and safety of all clinical trials. Large-scale (Phase III) trials must have a full Data and Safety Monitoring Board.

NIH policy allows submission and review of grant applications before they are approved by your IRB. If your application is likely to be funded, NIH will ask for documentation of IRB approval. Work with human subjects cannot begin without documentation of IRB approval.

Sections 7 and 8: Inclusion of Women and Minorities and Targeted/Planned Enrollment Table

As described in Chapter 13, Public Law 103-43 requires that women and minorities must be included in all NIH-supported clinical research projects involving human subjects, unless a clear and compelling rationale establishes that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. All applications proposing clinical research must contain explicit plans for including both genders (except for projects on gender-specific conditions like prostate cancer, ovarian cancer, or pregnancy) and minorities in the subject population. You also must complete a “Targeted/Planned Enrollment” table (see the Supplemental Instructions for Preparing the Human Subjects Section of the Research Plan) for each clinical study. Cost is not an appropriate justification for limited representation, and it is not sufficient to state that no one will be excluded on the basis of gender or race.

Section 9: Inclusion of Children

NIH also requires that children (individuals under the age of 21) of all ages be involved in all human subjects research supported by the NIH unless there are scientific or ethical reasons for excluding them. To determine if inclusion of children applies to your application, follow the instructions in the Supplemental Instructions for Preparing the Human Subjects Section of the Research Plan. Justification is required if there is limited or no representation of children.

Budget and Justification

The purpose of the Budget section is to present and justify the costs you are requesting to accomplish the project aims and objectives. For multi-institutional applications, there must be a separate sub-award/consortium budget component for each sub-awardee/consortium organization that will perform a substantive portion of the project. The application package for most NIH FOAs will include two budget components: the SF424 (R&R) Budget Component and the PHS 398 Modular Budget Component. Each NIH application will use one of these budget forms.

The modular budget format is applicable for research grant applications requesting $250,000 or less per year for direct costs in all years; consortium/contractual facilities and administrative costs may be requested in addition to the $250,000 direct costs per year limit. For modular budgets, applicants estimate the total research budget required for each year in multiples of $25,000 (e.g., $125,000, $150,000, or $225,000) and do not itemize categories such as glassware, reagents, animals, equipment, and travel. The budget justification should specify the roles and person-months of effort proposed for each of the listed project personnel and explain any large costs, unusual items, or unapparent costs that contribute to the overall estimate for the first year of the project. The budget for future years of the project should be similarly estimated, and any increases or decreases in the number of requested budget modules should be explained. For grants with modular budgets, the award will not be increased by an inflation factor each year.

Many clinical research studies will require more than $250,000 in any year. Such applications must include a complete SF424 (R&R) Budget Component, with a detailed budget for each year of support requested. The SF424 (R&R) Budget Component includes three separate...
data screens. Read the instructions carefully and include all required fields. The form will generate a cumulative budget for the total project period. The budget should include costs for all personnel, consultants, equipment, supplies, travel, patient care, and other expenses (e.g., animal maintenance, equipment service contracts, and offsite space rentals). The Budget Justification attachment should explain the roles of the proposed personnel and the need for items requested.

- Be realistic. Both “padding” and deliberately under-budgeting reflect naiveté or lack of appreciation of the scope of the work proposed. They undercut your credibility as the principal investigator and are viewed as weaknesses by the reviewers.
- If possible, identify specific individuals for each position requested. “To be named” personnel often are deleted by reviewers.
- Justify all requested equipment. Acquisition of major equipment is scrutinized carefully, especially equipment that is not project specific, such as fax machines and computers.
- Break out supply costs into major categories (e.g., reagents, disposables, or animals).
- Explain any year-to-year fluctuations in the budget, particularly the level of effort of personnel. Changes should parallel the research plan and project aims.
- If there is a co-investigator at another institution who will require salary and/or supplies in order to work on the project, be sure to include her or him in your budget.

**Senior/Key Personnel Profiles Component and Biosketches**

The biosketches showcase the expertise and experience of you and the research team involved in your project. Reviewers use the information in the biosketches to address the “investigators” review criterion and evaluate whether the proposed research team has the qualifications and experience to carry out the proposed work and overcome any problems that may arise. Be sure that each biosketch includes a Personal Statement that is customized to the role of the investigator in this particular project.

**Facilities and Other Resources**

Reviewers use the information in this section to evaluate Environment. This section should show the reviewers that you have all of the equipment and space, including clinic and clinical laboratory space, necessary to perform the proposed project successfully. Do not assume the reviewers will know what is in your institution or what is actually available for your use. For applications from ESIs, this section also should describe the institutional investment in the success of the investigator, such as resources for training or travel, career enrichment programs, protected time for research, etc.

- Make sure this section addresses all of the requirements of the proposed research plan.
- Justify any reliance on resources external to your research laboratory. Include strong and definitive letters of collaboration from the providers of those resources.
- Show that all subcontractors/consortium members have the capability to perform the tasks assigned to them.
- Make certain your resources and budget requests are consistent. Do not request funds for equipment listed in the Resources section as already available to you.

**Appendix**

There are specific limits on the types of information that may be included in the Appendix (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-018.html) and some FOAs do not allow Appendix materials at all. The Appendix may not include elements that belong in the Research Plan, and cannot be used to circumvent the page limit for the Research Plan. All Appendix materials must be submitted in PDF format; applicants must contact the SRO for the review to make special arrangements to send materials that cannot be submitted electronically (such as medical devices or prototypes) or cannot be converted to PDF format.

**Revising Unsuccessful Applications**

Competition for NIH research and career development awards is tough, and it is common for applicants not to succeed on the first attempt. Table 36-8 lists some of the most common problems with unsuccessful NIH grant applications.

<table>
<thead>
<tr>
<th>Problem Not Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothesis is not scientifically sound</td>
</tr>
<tr>
<td>Poor scientific rationale for the project or proposed approach</td>
</tr>
<tr>
<td>Diffuse, superficial, or unfocused research plan</td>
</tr>
<tr>
<td>Poor choice of experimental methods, models or technologies</td>
</tr>
<tr>
<td>Insufficient statistical power for clinical studies</td>
</tr>
<tr>
<td>Lack of knowledge of published relevant work</td>
</tr>
<tr>
<td>Lack of new or original ideas</td>
</tr>
<tr>
<td>Unrealistically large amount of work</td>
</tr>
<tr>
<td>Uncertainty concerning future directions</td>
</tr>
<tr>
<td>Lack of experience in the essential methodology</td>
</tr>
</tbody>
</table>

**Table 36-8** Most Common Problems with Unsuccessful NIH Grant Applications
most common reasons for unsuccessful applications. Although a rejected grant application can be hard on the ego, the reality is that most investigators have to resubmit applications before securing funding for their research. Revising an application provides an opportunity to rethink weaknesses in your design, approach, and methods and to address the reviewers’ concerns.

How to Decide Whether to Revise your Application

Read and reread the summary statement. Look for the main problems identified by the reviewers. Discuss the summary statement with the NIH program officer responsible for your application. If the reviewers thought the main ideas and research question are worthwhile and important, then it is worth revising the application. Common fixable problems include unclear organization of the project, insufficient preliminary data, diffuse or unclear aims, too much work for the project period requested, inadequate experience of the proposed personnel, inadequate controls, and insufficient attention to potential problems or how the data will be interpreted.

If the reviewers identified fundamental problems in the significance, scientific rationale, hypothesis, or approach, then it may be best to begin with a new idea and develop a new project. For example, the critiques may state that the objective is not very important, the project will add little to advance the field, the hypothesis is not sound, the work has already been done by others, or the proposed design or methods are not appropriate for testing the hypothesis.

How to Revise and Resubmit your Application

NIH allows one resubmission of an unsuccessful application within 37 months of the original application (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-140.html). Resubmission applications must include significant changes in the Research Plan and a one-page Introduction that summarizes the changes made in the application since the original review. If you disagree with weaknesses noted in the previous review, you may use the Introduction to try to convince the reviewers of your point of view. However, regardless of how you feel, be courteous and do not insult the reviewers—some of them may still be on the review committee!

The key to revising and resubmitting your application successfully is to address the reviewers’ main concerns. Clarify the objectives and rationale for the project. Add preliminary data or an experienced collaborator. Delete weak and peripheral aims or experiments, and refocus diffuse projects tightly on the hypothesis. Change the approaches or methods that will be used if necessary. Rethink the design of a clinical trial to address concerns about statistical power. Ask a colleague who is experienced in your field and in grantsmanship, but who is not involved in your project, to read your application and the summary statement and provide advice.

Even if you respond to all of the reviewers’ comments, your resubmitted application may still not receive a fundable score. This may happen for several reasons. When you make changes to the project, you risk introducing new problems. In addition, science “moves on,” so a project with high significance when first submitted may not be as important by the time the resubmission is reviewed. The membership of review committees also changes, so new reviewers with different perspectives may review your resubmitted application. Still, do not be discouraged. You can still submit a new application, but it must be significantly different, with a new hypothesis, different aims, model systems and/or methods, and different potential outcomes.

What if it Appears that the Study Section was Inappropriate or Biased?

If it appears that there was not sufficient expertise on the review panel (e.g., a molecularly oriented study section reviewing a clinical trial), or you have reason to believe that there was a bias in the review, you should revise and resubmit the application and request a different study section for the review in the cover letter attachment. Real bias in the review is very rare. Reviewers are alert to potential bias among competitors on the review group and argue against it vigorously. SROs also are alert to potential bias among reviewers.

NIH GRANT PROGRAMS FOR CLINICAL RESEARCHERS AT VARIOUS STAGES IN THEIR CAREERS

Although the R01 research project grant is the most well known and popular of NIH’s grants, NIH has several types of awards specifically designed to support clinical researchers at various stages in their careers. In addition, other types of grants, such as career transition awards and small (R03) and exploratory (R21) grants, are useful ways for new clinical investigators to obtain the preliminary data and proof of concept that are needed to prepare a competitive R01 application. Finally, the Loan Repayment Program (LRP) can help clinicians repay educational debts in return for a commitment to research.

Individual Career Development (“K”) Awards

Detailed information about career development awards can be found at the NIH K Kiosk at http://grants.nih.gov/training/
There are a number of different types of career development awards, and not all NIH institutes and centers participate in all of them. In addition, each participating NIH component may have its own guidelines and requirements for a particular career development award to accommodate the career needs of researchers working in different fields. Therefore, you should contact the training and career development office in the NIH institute closest to your research interests before preparing an application. At the time of award, candidates for most NIH career development awards must be citizens or noncitizen nationals of the United States or permanent residents. The exception is the K99/R00 Pathway to Independence Award.

Note that the review criteria for career development awards are different from the review criteria for research project grants discussed previously. Review criteria for the various career development awards vary somewhat, but generally focus on the following.

- Qualifications of the candidate
- Career development plan
- Research project to be conducted as part of the career development plan
- Qualifications of the sponsor(s) for mentored awards
- Environment and institutional commitment to the candidate.

**Mentored Career Development Awards**

The candidate must identify a mentor with extensive research experience and must devote at least 75% effort to career development research activities during the period of the award.

**Mentored Clinical Scientist Development Award (K08)**

The Mentored Clinical Scientist Development Award (K08) provides support for clinical professionals to develop into independent investigators. In general, K08 awards support more laboratory-oriented, translational, or preclinical research projects; clinicians who wish to pursue patient-oriented research training should see the section on the K23 award. There is substantial variability among the sponsoring NIH institutes in eligibility requirements, allowable costs, and application procedures. Applicants should contact the individual institutes for specific guidelines.

Candidates should hold a clinical doctoral degree and should have initiated postgraduate clinical training. The requested project period may be for three, four, or five years, depending on the candidate’s prior research experience, additional experiences needed, and the policy of the awarding NIH institute. Awards are not renewable.

**Mentored Patient-oriented Research Career Development Award (K23)**

The purpose of the Mentored Patient-oriented Research Career Development Award (K23) is to support the career development of investigators who have made a commitment to patient-oriented research (POR) and have the potential to develop into productive clinical investigators. For the purposes of this award, POR is defined as research conducted with human subjects (or on material of human origin, such as tissues, specimens, and cognitive phenomena) for which an investigator directly interacts with human subjects on research on mechanisms of human disease, therapeutic interventions, clinical trials, or development of new technologies.

Candidates must have a clinical degree or its equivalent and must have completed clinical training, including specialty and, if applicable, subspecialty training, before award. Candidates may request three to five years of support, depending on their previous training and experience.

**Career Transition Awards**

**K99/R00 Pathway to Independence (PI) Award**

One of the most challenging transitions in any research career is from postdoctoral trainee to independent scientist. This award is designed to help the most promising, exceptionally talented, new investigators make the transition from trainee to independent investigator. Candidates must have no more than five years of post-doctoral research training experience. The K99/R00 award will provide up to five years of support in two phases. The initial mentored K99 phase will provide support for salary and research expenses for up to two years to complete research, publish results, and bridge to an independent research position. Candidates must commit at least 75% effort to the grant during the mentored phase.

The candidate must propose a research project that will be pursued as an independent investigator during the second R00 phase of the award. The R00 phase may be up to three years to support transition, as an independent scientist, to an extramural sponsoring institution where the candidate will be a tenure-track assistant professor or equivalent. This support will allow the awardee to continue to work toward establishing an independent research program and prepare an application for regular research grant (R01) support. Support for the independent phase, however, is not automatic and is contingent on being accepted by an extramural institution and NIH programmatic review of progress during the mentored phase of the award.

For more information about this program, see [http://grants2.nih.gov/grants/guide/pa-files/PA-10-063.html](http://grants2.nih.gov/grants/guide/pa-files/PA-10-063.html) and the NIH K Kiosk.
K22 Career Transition Awards
K22 career transition awards are intended to facilitate the transition of investigators, particularly clinical investigators, from the mentored to the independent stage of their careers. K22 awards provide “protected time” for newly independent investigators to develop their initial research programs in a research institution of the candidate’s choice. The unique feature of this award is that individuals may apply without a sponsoring institution while they are still in a “mentored” position. Because policies about the K22 awards differ markedly among NIH institutes, potential applicants should contact the training office in the NIH component most closely associated with their research interests before preparing an application.

Independent Scientist Awards
The Independent Scientist Award (K02) provides up to five years of salary support for newly independent scientists who can demonstrate the need for a period of intensive research focus as a means of enhancing their research careers and enabling them to expand their potential to make significant contributions to their field of research. A candidate must have a doctoral degree and independent, peer-reviewed research support at the time the award is made; some NIH institutes and centers require the candidate to have an NIH research grant at the time of application, whereas others will accept candidates with peer-reviewed, independent research support from other sources.

The candidate must devote at least 75% effort to conducting research and research career development during the award. In addition, the candidate must be able to demonstrate that the requested period of three to five years of salary support and protected time will foster his or her career as a highly productive scientist in the indicated field of research.

Midcareer Investigator Award in Patient-oriented Research
The purpose of the Midcareer Investigator Award in Patient-oriented Research (K24) is to provide protected time for clinician investigators to devote to POR and to act as research mentors primarily for clinical residents, fellows, and/or junior faculty. This award is primarily intended for clinician investigators at the associate professor (or equivalent) level who have an established record of independent, peer-reviewed federal or private research grant funding in POR. It is expected that investigators will obtain new or additional independent peer-reviewed funding, assume leadership roles in collaborative POR programs, and increase efforts and commitment to mentor beginning clinician investigators in POR, thereby increasing the pool of well-trained clinical researchers.

Exploratory/Development Grant (R21) Applications
The R21 award mechanism is intended to encourage exploratory and developmental research projects in innovative new research areas by supporting early and conceptual stages of these projects. R21 applications are suitable for novel ideas that break new ground and need feasibility testing or high-risk/high-reward studies. Not all NIH institutes and centers accept investigator-initiated R21 applications under the R21 Parent FOA. However, those that do not may have RFAs or PAs to solicit R21 applications to meet specific program needs. Consult the NIH R21 website at http://grants.nih.gov/grants/funding/r21.htm before preparing an application.

The review criteria are the same as for R01 research project grant applications described previously. However, the Research Plan for a R21 application is limited to six pages. Accordingly, reviewers will focus on the conceptual framework, the level of innovation, and the potential to significantly advance knowledge or understanding. Because this type of grant is designed to support innovative new ideas, preliminary data as evidence of feasibility are not required. Justification for the proposed work can be provided through literature citations, data from other sources, or, when available, investigator-generated data. R21 grants are generally limited to a total budget request of $275,000 for two or three years of support and generally are not renewable.

Small Research Grant (R03) Applications
Small research grants provide research support that is limited in time (usually one or two years) and amount (usually $50,000—$100,000 direct costs per year) and are nonrenewable. R03s are generally for support of preliminary studies or short-term projects. The results of an R03 grant often provide the preliminary findings for an R01 grant application. The review criteria for R03s are the same as those for R01s. Not all NIH institutes support R03 awards, and of those that do, different institutes have different objectives, guidelines, and requirements for their small grant programs. Not all NIH institutes and centers accept investigator-initiated R03 applications under the R03 Parent FOA. However, those that do not may have RFAs or PAs to solicit R03 applications to meet specific program needs. Consult the NIH R21 website at http://grants.nih.gov/grants/funding/r03.htm before preparing an application.
Loan Repayment Program

The NIH Loan Repayment Programs (LRP) were initiated in 2002 to attract health professionals to careers in clinical, pediatric, health disparity, or contraceptive and infertility research. There is also a Loan Repayment Program for Clinical Researchers from Disadvantaged Backgrounds. In exchange for a two- or three-year commitment to a research career, NIH will repay up to $35,000 per year of your educational debt from qualifying types of student loans. In addition, NIH will make corresponding federal tax payments to your Internal Revenue Service tax account to cover your increased federal taxes and also may reimburse other tax increases incurred as a result of your LRP benefits. For more information, see the LRP website at www.lrp.nih.gov.

To qualify, you must have a doctoral or equivalent degree and be a U.S. citizen, national, or permanent resident, and your research must be funded by a domestic nonprofit or U.S. government (federal, state, or local) entity. You must commit 50% of your time (at least 20 hours per week) for two years to the research and your educational debt must equal at least 20% of your “institutional base salary.” NIH issues payments directly to lenders on a quarterly basis. To remain eligible for the LRP program, student loans must remain segregated from non-educational loans and loans held by another person, such as a spouse or a child.

HOW TO STAY INFORMED ABOUT NIH PEER REVIEW

NIH periodically updates specific policies, forms, and procedures regarding the peer review process. Therefore, before you prepare a grant application, you should visit the NIH website (www.nih.gov) to obtain the latest information and discuss current application and review procedures with NIH program or review staff. The following are a few of the “starting points” for finding current information when you are ready to apply for research support.

“About Grants” Page (http://grants.nih.gov/grants/about_grants.htm)

This page covers many topics, from the basics of the grants application and review process to management of awards.

NIH Institute/Center Home Pages

Each of the NIH component institutes also has a home page. The general format for the Internet addresses is “www.Institute acronym.nih.gov” (e.g., www.nci.nih.gov, www.nhlbi.nih.gov, etc.) Each institute home page will have a way for you to find a contact for each general area of science that the institute supports, as well as the office responsible for managing the institute’s training and career development portfolio. The NIAID website has a particularly well-developed section on the grants process, with flow diagrams for investigators at different career stages and different types of grants (http://funding.niaid.nih.gov/researchfunding/grant/pages/default.aspx).

The CSR Home Page (www.csr.nih.gov)

Potential applicants are encouraged to visit the CSR home page for additional information about CSR and peer review. You can find the schedules for CSR study section meetings, study section rosters, information about review criteria and review procedures, and resources for applicants, including advice to investigators submitting clinical applications. Particularly instructive for new applicants is a video of a mock study section that illustrates the peer review process and how reviewers discuss applications.