A GUIDE FOR
Developing, Writing, & Implementing
Scientific Research Grant Proposals

EDITED BY CLETE A. KUSHIDA, MD, PHD

A JOINT PUBLICATION OF THE AMERICAN ACADEMY OF SLEEP MEDICINE AND THE SLEEP RESEARCH SOCIETY
INTRODUCTION

You spent a considerable amount of time and effort developing a strong application. You have an important question with clear clinical relevance. After conversations with one or more program officers within the National Institutes of Health (NIH) institutes or centers (IC) appropriate for your specific area of sleep research you have developed related, yet independent Specific Aims with testable hypotheses. You have obtained critical preliminary data representative of each Specific Aim that demonstrate feasibility and a biological basis for your overall hypotheses, and you have written and polished a complete and balanced application. Finally, and hopefully not at the last minute, you have successfully navigated grants.gov and uploaded your application. Now what? For many, particularly junior faculty, the peer-review process is the consummate black-box. What happens from the moment the application is successfully submitted until you are able to access eRA-Commons and view the score your application received? In this chapter an overview is provided of the NIH grant application peer-review process, from submission to score, based upon experiences as a funded investigator, a former study section member and frequent ad hoc reviewer, discussions with study section chairs and NIH Scientific Review Officers.

THE SUBMISSION

CENTER FOR SCIENTIFIC REVIEW

The Center for Scientific Review (CSR) is the entity responsible for the peer review process for most research and research training applications submitted to NIH. The mission of the CSR is to “see that NIH grant applications receive fair, independent, expert, and timely reviews – free from inappropriate influences – so NIH can fund the most promising research.” Among its multiple tasks, and relevant to this chapter, the CSR serves as the central receipt point for applications, assigns NIH applications to appropriate institutes or centers for funding consideration and also assigns the applications to specific scientific review groups, called Integrated Review Groups (IRG) for review. In a normal year, the CSR will receive about 80,000 applications and will recruit more than 17,000 experts to review the applications for which it is responsible. The CSR has developed online resources that provide greater detail about the submission and peer-review process than is included in this overview chapter. Links to many of these resources are provided in the Useful Information section at the end of this chapter.

Upon receipt of your application, one (or more) referral officers of CSR will review your application to determine which NIH IC is best suited to fund the application should it be found to have sufficient merit. In some cases, particularly if the principal investigator (PI) specifically requests it (see later), the application will be assigned to as many as three different ICs. At this stage of processing, the CSR referral officer(s) will also determine the most appropriate IRG and study section for review of the application. The CSR referral officers follow guidelines when making assignments that are based upon established review boundaries for each study section. Currently, there are 25 IRGs within CSR, and each IRG is composed of multiple study sections. For example, many applications that focus on basic sleep research are assigned to the Integrated, Functional, and Cognitive Neuroscience (IFCN) IRG. IFCN at present consists of 11 study sections, including the Biological Rhythms and Sleep (BRS) and the Neuroendocrinology,
Neuroimmunology and Behavior (NNB) study sections, to which applications that focus on sleep are often assigned. Another study section to which more clinically-relevant applications are sometimes assigned is the Neural Basis of Psychopathology, Addictions and Sleep Disorders (NPAS) within the Brain Disorders and Clinical Neuroscience (BDCN) IRG. I will not review all IRGs that may be appropriate for sleep research application assignments. A complete listing of CSR IRGs and study section descriptions is found at (http://cms.csr.nih.gov/peerreviewmeetings/csrirgdescriptionnew/). Junior faculty and new investigators are encouraged to talk with funded senior PIs, program officers at NIH and others to determine IRGs and study sections that possess expertise relevant to the application being submitted.

THE COVER LETTER

One required component of the grants.gov application submission is the cover letter. Junior faculty and new investigators may not be aware that specific requests with respect to IC, IRG, and study section assignment may be made in the cover letter. As a PI it is important that you explicitly, concisely, and politely state your requests with respect to assignment of the application. CSR gives serious consideration to such requests, although referral officers are not obligated to honor them. There are several reasons why it is important to indicate your wishes to CSR. First, you have spent time speaking with program officers of relevant ICs prior to submitting the application so you know which ICs have an interest in adding your proposal to their portfolio. Discussions with IC program officers will provide you with a very good indication as to how your proposed study fits (or not) with the overall mission of a given IC. Referral officer(s) at CSR will not be aware of these discussions, and may not ascertain from a quick review of your application the critical features of the proposal that would make it more (or less) suitable for assignment to one or another of the 27 NIH ICs. It is important to be able judge the degree of interest by a particular IC in your application (by speaking before submission with program officers) and to convey that information to CSR, so your application does not suffer from lack of interest by an IC when final funding decisions are being made.

As previously stated, junior faculty and new investigators should speak with senior PIs with respect to requesting IC assignment. There are several NIH institutes that fund sleep research. These include, but are not limited to; the National Heart, Lung and Blood Institute (NHLBI), the National Institute of Mental Health (NIMH), the National Institute of Neurological Disorders and Stroke (NINDS), the National Institute on Aging (NIA), and the National Institute of Nursing Research (NINR). Other institutes that may fund sleep research include the National Institute of General Medical Sciences (NIGMS), the National Center for Complementary and Alternative Medicine (NCCAM), and the National Institute of Child Health and Human Development (NICHD). It is, however NHLBI, NINDS, NIMH, and NIA that over the years have funded the majority of sleep-related research. After consultation with others, it is likely you will decide that your proposed study would fit within the mission of more than one NIH IC. A second facet of requests included in the cover letter should be for a dual, or triple, IC assignment. One IC will be designated as the primary IC for the assignment and the others will be simply listed. Budgets and emphasis on/investment in sleep research differ across ICs such that after review your application may be transferred to one or the other of the alternate ICs for funding.

In addition to requesting IC assignments in the cover letter, it is also important to make suggestions with respect to the specific IRG and study section that you think will be the most appropriate to review your application. Although there are review boundaries that guide CSR referral officers in making decisions with respect to IRG and study section assignments, these boundaries frequently (in fact, invariably) overlap to
some extent, and more than one study section may have the expertise to review your application. Study section rosters are posted (http://www.drg.nih.gov/Roster_proto/sectionI.asp), and it is in your best interest as a grant applicant to know who are the permanent members of the study section. Such information is critical so you can determine if, in your opinion, appropriate expertise exists to review your application. Given the breadth and the multitude of techniques and approaches used to address questions that cover a broad spectrum of sleep research, it is not likely that expertise will exist among permanent members of the study section to review all applications submitted. If this is indeed determined to be the case, individuals who are not permanent members of the study section will be invited to serve as ad hoc reviewers (see later). These ad hoc reviewers will also be identified on the study section rosters.

There is one final type of request that may be made in the cover letter, but one for which careful consideration should be given. As an applicant, you may be of the opinion that some specific individual may have an inherent philosophic difference that would preclude an impartial review of your proposal. You may politely state such in your cover letter, but be advised that many factors are considered when the Scientific Review Officer (SRO, see later) decides who among the members of the study section, or potential ad hoc reviewers, will be assigned your application. It cannot be emphasized enough that requests to exclude from the potential reviewers of your application individuals with whom you have philosophical differences should be made with utmost respect and courtesy. Keep in mind that the SRO is under no obligation to honor such a request, but for a variety of reasons is likely to do so.

Upon successful submission of your application through grants.gov you will be notified by email and by notices posted in your eRA-Commons account that the application has been received. You will be notified when your application has been assigned to an IC and study section. The process of assignment by CSR referral officers may take several weeks given the number of applications received. CSR suggests that if a notice is not posted in your eRA-Commons account within three (3) weeks that you contact the referral office (301-435-0715). Questions about your application during the submission and assignment process should be directed to CSR. Similarly, if after you receive the IC and study section assignments you have questions, or think your application has been assigned to a study section lacking requisite expertise, you should speak with the CSR referral office. After IC and study section assignment, questions should be directed to the SRO, who will be named (with contact information) on your eRA-Commons account.

SUPPLEMENTAL MATERIALS

Although one of CSR’s initiatives is to streamline and shorten the review process, several months pass from the date of submission until the study section convenes and your application is formally reviewed. During this interval from submission to review, investigators may well continue to work on aspects of the project and may continue to generate data that are relevant to the submitted application. It is possible to submit supplemental information in support of your application after submission and prior to study section review. In addition to additional preliminary date, several types of information may be provided as a supplement to your application. For example, you may have learned that a submitted manuscript relevant to the application has been accepted for publication and wish to inform the reviewers. More generally however, supplemental information takes the form of additional preliminary data.

It is important that you discuss your plans with the SRO before you submit supplemental information. Your SRO will indicate the limitations for your proposed supplement. There are several considerations to keep in mind when deciding whether or not to submit supplemental information. First, the supplement will be submitted directly to the SRO, and must be done so with enough time for the information to be
forwarded to the reviewers assigned to your application. The SRO will indicate by what date s/he will need to receive the information, but it is likely to be a minimum of two weeks prior to the study section meeting date. Second, submission of supplemental information may annoy the reviewers. Keep in mind the reviewers will have applications to review other than yours, and depending on the number of applications to which they have been assigned their workload may already be heavy. Receiving additional information to review at the last minute may be perceived as more work, and result in the reviewers not giving it as much attention as you may think it deserves. With the impact on the reviewers in mind, every effort should be made to keep the supplement to one (1) page in length. If additional preliminary data are included in the supplement, there should be a brief explanation of the contribution these data make to one or more of the hypotheses and Specific Aims of the submitted application. A graphical representation of the data will have more impact, be easier for the reviewers to assimilate and is less likely to be considered an annoyance by the reviewers than if simply another page of text is provided. Also, although your SRO will likely have informed you during your discussions, the supplement is not to be used as a method to circumvent the page limitations of the overall application.

The Review

Reviewers are asked to assess your application with respect to each of five review criteria to determine scientific and technical merit. Each of the review criteria, as well as the overall impact and priority, is assigned a separate score (see later). The following descriptions of the review criteria are taken from information provided to study section members (or to ad hoc reviewers) when they are asked to review an application.

**Overall Impact/Priority.** NIH peer reviewers are asked to provide an overall impact/priority score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following five core review criteria, and the additional review criteria (as applicable for the project proposed).

**Significance.** Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project 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 preventative interventions that drive this field?

**Investigator(s).** Are the program directors/principal investigators (PD/PIs), collaborators, and other researchers well suited to the project? If Early Stage Investigators 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?

**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?

**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 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?

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.

In addition to the five core review criteria, reviewers are asked to consider additional items in the determination of scientific and technical merit, but not to give separate scores for these items. These additional items generally pertain to regulatory compliance issues, such as the use of vertebrate animals or human subjects in your research, among others. As with the core review criteria summarized earlier, the following descriptions are from information provided by CSR to reviewers prior to review of applications.

Protections for Human Subjects. For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46, reviewers are asked to evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: (1) risk to subjects, (2) adequacy of protection against risks, (3) potential benefits to the subjects and others, (4) importance of the knowledge to be gained, and (5) data and safety monitoring for clinical trials. If all of the criteria are adequately addressed, and there are no concerns, write “Acceptable Risks and/or Adequate Protections.” A brief explanation is advisable. If one or more criteria are inadequately addressed, write, “Unacceptable Risks and/or Inadequate Protections” and document the actual or potential issues that create the human subjects concern. Also, if a clinical trial is proposed, evaluate the Data and Safety Monitoring Plan. (If the plan is absent, notify the SRO immediately to determine if the application should be withdrawn.) Indicate if the plan is “Acceptable” or “Unacceptable,” and, if unacceptable, explain why it is unacceptable. For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt, evaluate: (1) the justification for the exemption, (2) human subjects involvement and characteristics, and (3) sources of materials. If the claimed exemption is not justified, indicate “Unacceptable,” and, if unacceptable, explain why it is unacceptable. NOTE: To the degree that acceptability or unacceptability affects the investigator’s approach to the proposed research, such comments should appear under “Approach” in the five major review criteria above, and should be factored into the score as appropriate. For additional information to assist you in making these determinations, please refer to [http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Protection_and_Inclusion_a5.pdf](http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Protection_and_Inclusion_a5.pdf) and [http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Worksheet_a5.pdf](http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Worksheet_a5.pdf).

Inclusion of Women, Minorities and Children. When the proposed project involves clinical research, reviewers are asked to evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children. 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. NIH 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. Each project involving human subjects must be assigned a code using the categories “1” to “5” below. Category 5 for minority representation in the project means that only foreign subjects
are in the study population (no U.S. subjects). If the study uses both then use codes 1 thru 4. Examine whether the minority and gender characteristics of the sample are scientifically acceptable, consistent with the aims of the project, and comply with NIH policy. For each category, determine if the proposed subject recruitment targets are “A” (acceptable) or “U” (unacceptable). If you rate the sample as “U”, consider this feature a weakness in the research design and reflect it in the overall score. Explain the reasons for the recommended codes; this is particularly critical for any item coded “U”. NOTE: To the degree that acceptability or unacceptability affects the investigator’s approach to the proposed research, such comments should appear under “Approach” in the five major review criteria above, and should be factored into the score as appropriate.

For additional information to assist you in making these determinations, please refer to: http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Protection_and_Inclusion_a5.pdf and http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Worksheet_a5.pdf

Vertebrate Animal. Reviewers are asked to evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: (1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; (2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; (3) adequacy of veterinary care; (4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and (5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia. For additional information to assist you in determining if the Vertebrate Animals section is “Acceptable” or “Unacceptable,” please refer to: http://grants.nih.gov/grants/olaw/VASchecklist.pdf.

Biohazards. Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Scoring of the Application

In March, 2009, the CSR implemented a new scoring system based on a nine-point scale (Table 1). The old scoring scale was based upon a 1 to 5 scale in 0.1 point increments, which allowed a total of 41 “score bins” across the full scoring range. Making 41 discriminations was deemed difficult for reviewers, and more importantly, scores were becoming compressed at the positive end of the scale. The shift to a nine-point scale in which only whole integers are provided as scores reduces the number of discriminations dramatically. The representative list of descriptors (Table 1) indicates that the intent of the scoring system is to broadly categorize applications into thirds. Whereas discriminating between an application scored 1.4 and one scored 1.5 using the old scale may have been difficult, it is felt that using the new scale the discrimination between an application scored as a 3 vs. one scored as a 4 should be easier.

After the discussion of your application is completed (see later), each member of the study section will vote an integer score using the 1 – 9 scale. The average of all scores is determined and multiplied by a factor of 10 to obtain the final score ranging between 10 and 90. Your application will be ranked by score, which is the primary, although not only factor used by NIH program when making funding decisions. As this new scoring system has only been recently adopted, it is not possible at this point to assess whether the desired goals of this system are being achieved.

Perhaps the most important change to the scoring system from your perspective as a PI is the feedback obtained by having each of the five criteria assigned a numeric score. Whereas the old scoring system
provided one overall score, the new scoring system provides a score for each of the criteria in addition to the overall score. This means that you will know the numeric designation used by the reviewer in ranking Significance, Investigator(s), Innovation, Approach, and Environment. This type of feedback should make it easier as a PI to determine the areas of the application that were viewed as being weaker or deficient as compared to the old system, in which such information from the reviewers was often disguised within the text of the critique.

THE STUDY SECTION MEETING

STUDY SECTION COMPOSITION AND ATTENDEES

The study section is composed of individuals who play three distinct roles. The Scientific Review Officer (SRO) is the designated federal official responsible for conducting the peer review meeting. The SRO will determine who among the study section members are most appropriate to review your application. Some SROs will make decisions as to who reviews your application after consultation with the Chair of the study section. The Chair of the study section conducts the review meeting with the SRO and serves to direct the discussion of each application. Each application is assigned to three reviewers. At least two of the reviewers will provide written critiques of your application, although generally each of the reviewers provides a written critique. These three individuals lead the discussion of your application during the study section meeting, and it is these individuals who are to serve as advocates for the application. Reviewers of your application may be permanent members serving multi-year terms on the study section, or they may be ad hoc members serving for a specific study section meeting. If the SRO determines that no permanent members of the study section have appropriate expertise, s/he will solicit reviews from experts in the field who are not members of the study section but do possess such expertise. These ad hoc reviewers will contribute written critiques, but they may participate in the study section meeting by conference call. If an ad hoc reviewer has been assigned more than one application to review, they may be invited to attend the study section meeting.

Individuals in addition to permanent and ad hoc members of the study section will also attend the meeting. For example, there will be a Grants Management Specialist who will provide administrative support to the

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**Table 1** Nine-point scoring system adopted by the Center for Scientific Review in 2009

<table>
<thead>
<tr>
<th>Impact</th>
<th>Score</th>
<th>Descriptor</th>
<th>Strengths/Weaknesses</th>
</tr>
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<tbody>
<tr>
<td>High Impact</td>
<td>1</td>
<td>Exceptional</td>
<td>Exceptionally strong with essentially no weaknesses</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Outstanding</td>
<td>Extremely strong with negligible weaknesses</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Excellent</td>
<td>Very strong with only some minor weaknesses</td>
</tr>
<tr>
<td>Moderate Impact</td>
<td>4</td>
<td>Very Good</td>
<td>Strong but with numerous minor weaknesses</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Good</td>
<td>Strong but with at least one moderate weakness</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Satisfactory</td>
<td>Some strengths but also some moderate weaknesses</td>
</tr>
<tr>
<td>Low Impact</td>
<td>7</td>
<td>Fair</td>
<td>Some strengths but with at least one major weakness</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Marginal</td>
<td>A few strengths and a few major weaknesses</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Poor</td>
<td>Very few strengths and numerous major weaknesses</td>
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SRO. Of most importance to you however, is the presence of NIH extramural staff, i.e., program officers. Program Officers, or their designees, make every effort to attend the study section meetings at which applications to which they have been assigned will be reviewed. These individuals may not participate in the discussion of applications, and they do not vote a score. After the review is completed and you have received your score and critiques, you may speak with your Program Officer about the review. If your Program Officer, or designee, was present when your application was reviewed they will have notes about the discussion and will often be able and willing to provide insight into the review, particularly with respect to weaknesses in the application, that may not be totally apparent or clear from the written critique.

MEETING AGENDA

The study section meeting agenda will vary somewhat among SROs, but there are some components that are common to all meetings. The meeting will begin with formalities such as a statement by the SRO of Conflict of Interest (COI) policies and polling the study section members to determine if any COI were inadvertently missed during assignment of applications for review. COI may include, among other things, being from the same institution as the applicant, or being a collaborator/mentor with/of an applicant. The general rule of thumb is that if you have collaborated or published with an individual during the last 5 years, you have a COI that will preclude your participation in the review process for that application. In addition, if you have stated in your cover letter that you have philosophic differences with a member of the study section that may preclude an impartial review of your application, that individual is likely to be identified as having a COI. Any individual who is indentified as having a COI will be excused from the room during the discussion of that particular application and will not vote a score for that application.

The SRO will at some point turn the meeting over to the Chair of the Study section and the actual review of the applications will begin. When it is time for your application to be reviewed, the Chair will ask the three reviewers for their preliminary scores. Each reviewer will give an initial score and then the individual designated as the primary reviewer will begin the discussion. The discussion of your application should focus first on the overall hypothesis and an assessment as to the importance of the potential results to the field, and then on the details of the proposed approach.

ASYNCHRONOUS ELECTRONIC DISCUSSION (AED) REVIEW

The AED Review protocol was initiated in 2005. This type of review “meeting” is conducted electronically over a period of (generally) two days. The stated goal of AED Review is to “provide a new, viable method of scientific peer-review for grant applications submitted to NIH—without the need for concurrent assembly or teleconference.” The expected benefits include, “greater flexibility for scheduling peer-review meetings, expanding the potential reviewer base, enhancing the dynamics of discussion at the meeting, simplifying management of conflicts, and reducing costs.” Limited AED Review began with the January round of submissions in 2007, and expansion of the AED Review process is still being discussed.

From your perspective as PI, and although an overly-simplified statement, you may think of AED as a fancy threaded message board on which your application is being discussed. There have been several iterations of the software developed for use in the AED review, and I will not discuss technical aspects of the software. The general workflow for this type of review is as follows: your application is submitted and assigned as previously summarized. As with traditional face-to-face study section meetings, reviewers involved in AED Review post by a specified date and time their critiques on a secure website accessed via eRa Commons, termed Internet Assisted Review. Other reviewers involved in the AED Review meeting then
have access to read the critiques for a period of several days. On a particular date and time the AED Review website becomes available to reviewers, and threaded discussions begin about each application. Comments posted by the reviewers assigned to a specific application are viewable to all study section members involved in the AED Review. Any study section member of the AED Review meeting is able to post comments, ask questions, etc., about any of the applications under review. The thread of comments for each application is maintained such that one can go back and review the entire “discussion” for a particular application.

In addition to the thread of comments, the initial scores of the three reviewers assigned to a particular application are posted. Provision is made for dynamic changes to be made to the scores during the course of the threaded discussion. For example, a reviewer may post a threaded comment indicating that “on the basis of the comment of Reviewer 1, I now have less concerns about the ability of the PI to successfully target brain stem nuclei for microinjection of compounds and am changing my score for approach from a 4 to a 3.” The new score (3) would be posted in a grid that is visible to all reviewers. The intent of posting “interim” scores is to provide feedback to other reviewers involved in the meeting as to changes in levels of enthusiasm for the application as the threaded discussion progresses. On a specific date and time, the AED Review meeting will end and the threaded discussions cease. There is then a period of several hours when the final scores for each application are entered into the scoring grid. Each member of the study section votes a score electronically for each application. During the days that follow, critiques of the applications may be edited to reflect the threaded discussion.

Although there are benefits to CSR for conducting this type of review meeting, it is not clear there will be benefits to you as a PI. As with face-to-face study section meetings, if the initial assessment/scores of the three reviewers are in very close agreement, there is likely to be little threaded discussion and the scores may not change much from their initial values. However, if there are differences in scores that generate a significant amount of threaded discussion, the inability of AED Review to provide visual and auditory feedback among the reviewers (i.e., assessment of “body language”) may well lead to less effective advocacy for a particular application. In addition, whereas much can be verbally communicated in one minute (for example), for most it takes much longer to type a similar amount of information. To what extent threaded discussions lead to less discussion, rather than more, about a particular application has to my knowledge not been determined. Similarly, to my knowledge there has not been a direct comparison of scores voted to specific applications that have been reviewed by AED Review and by traditional face-to-face study section meetings to assess differences due to the type of review meeting used. In 2007, CSR surveyed reviewers who had used AED Review during the June and December 2006 review cycles. Of the 232 reviewers who responded, roughly one-third felt the discussions were not as rigorous or there were compromises in the review process (http://cms.csr.nih.gov/NR/rdonlyres/5DBA768C-5C75-469B-922D-E96142CB6160/14849/AEDReviewerSurveySummaryDec2006.pdf.) A second survey was planned for the October 2008 review cycle, but I am not aware as to whether the survey was actually conducted or where the results have been posted, if they exist. Having participated in AED Review, the personal perspective of this author is that this form of review meeting may well (in general) be less effective in advocating for applications and much more effective at moving scores toward the “poor” end of the scoring scale. However, it must be pointed out that the change to the new nine-point scoring scale and the increase in the use of AED Review are occurring at the same time. There will be a period of re-calibration for reviewers for changes to the scoring system and to the use of AED Review. It will take some time to fully assess whether the savings to NIH of AED Review come at too high a cost to the PI due to potentially less vigorous discussion and debate relative to the extensive discussion that can take place during face-to-face study section meetings.
THE CRITIQUE ("PINK" SHEET)

Within a week or so (generally) of the study section meeting, the critique of your application will be available on eRA Commons. The critique historically was referred to as the “pink” sheet because of the color of the paper on which NIH printed the grant application review (although it has been decades since paper of any color was used by NIH for the critique and for many years the review has been transmitted electronically). As part of the initiative to streamline the review process, in 2009 CSR adopted a critique template that has simplified and standardized the written critique. Written critiques no longer will consist of free-flowing text that often rivaled the grant application itself in terms of length and complexity. Instead, the written review for each scored criteria and for the overall impact/priority of the application is limited to one-quarter page of bulleted statements. Early feedback from reviewers suggests this new template has been generally well-received because it has dramatically reduced the time taken to produce a written critique and it provides incentive to focus the critique only on the big issues of the application. However, the new critique template does not appear to have been well received to date by investigators. The previous review system often resulted in a critique of 5 pages or more, and although the major weaknesses of the application were supposed to be the focus of the critique, there was often a lot of text devoted to issues that in many cases were not central. As an investigator, it was often difficult to extract from these long and complex critiques the most salient information intended by the reviewer. Nevertheless, a lot of feedback was usually provided to the investigator with the old critique format. The new critique template may make it difficult to determine the scope of issues felt by reviewers to be important. As an investigator, you may feel you are getting less information as feedback from the reviewers when reading your critique on this new template. As with other newly-adopted changes to the peer-review process, it will take some time for both reviewers and investigators to adjust to the new critique template.

THE RESUBMISSION

Unfortunately, the vast majority of applications submitted to NIH will fail to achieve a fundable score on the first submission. For many years NIH policy allowed for two revisions to an unfunded application. Recently however, NIH has adopted a policy that applications may be revised only once. That is, an application may be submitted only twice. This reduction in the number of submissions increases the pressure on you as an investigator to make sure every aspect of “grantsmanship” is perfect, insofar as possible. The decision making process as to when an application is “strong enough” to submit now becomes even more critical as there will be minimal margin for error. There are many aspects of the grant application that have been discussed in other chapters of this volume. Suffice it to say that it will now be more important than ever that applications are physically “perfect.” Those applications that are “sloppy” (typos, misspelled words, poorly formatted, poor quality graphics for figures, difficult for reviewers to read, etc.) will be at even a greater disadvantage than before. Nevertheless, even applications that are scientifically strong, that pose important questions that can be answered to provide new information that will advance the field, will more often than not require revision.

One of the most important components of the revised application to be re-submitted is the Introduction to Revised Application section. The Introduction to Revised Application section is to be used to provide a detailed response to concerns raised by the reviewers. Beyond the response to concerns raised, it is also important that the Introduction clearly and succinctly articulates the changes that have been made to the application. It is a good idea to begin the Introduction by thanking the reviewers for their insightful comments and to point out the positive aspects of the application identified by the reviewers. Since much of
the *Introduction* is devoted to addressing the “negative” aspects of the review, it is also important to briefly remind the reviewers of the strengths of the application.

Every effort should be made to make it easy for the reviewers to know exactly what the major changes were and how these changes address the identified weaknesses. After thanking the reviewers for their insightful review, and summarizing the strengths of the application identified by the reviewers, it may be a good idea to provide as an itemized or bulleted list a synopsis of the major changes made to the application. One could state, for example:

“As suggested by the reviewers: (1) Experiment 1 of Specific Aim 1 has been omitted, (2) the number of compounds proposed for testing has been reduced, and (3) an experiment in which \( X \) will be antagonized has now been included in Specific Aim 2. In addition, (4) we present new preliminary data demonstrating that antagonizing \( X \) abolishes \( Y \)...”

Such a synopsis will make it much easier for the reviewers to understand the extent to which you have addressed their suggestions.

Although termed *Introduction*, this section is often viewed by investigators as “The Rebuttal.” Keep in mind however, that the *Introduction* is all about the reviewers, and not about you. An overly aggressive or argumentative tone on your part will not ingratiate you to the reviewers. Similarly, this is not a debate. Even though you may feel compelled to do so, this is not the time to prove to the reviewer that you actually know more about your proposed project than s/he does. The adage that the “reviewer is always right” is for the most part true when it comes to this section of the application. Some aspects of the review will be inaccurate, and these must be respectfully pointed out. Pointing out information contained in the application that was missed by the reviewer must be done with courtesy and respect. Phrases such as “I did not clearly articulate that …” are likely to be received in a more positive manner than “as indicated on page 10 of the application, which the reviewer apparently did not read, …”.

The fundamental purpose of the peer-review process is to guide NIH in funding decisions that will result in the best use of tax-payers dollars to the benefit of our physical and mental health. The fundamental purpose of the grant application critique, much like that of a manuscript submitted for publication, is to point out weaknesses, which if resolved would make the project stronger, more meaningful, and perhaps increase the probability of success. It is a fact of life, however, that reviewers do not possess expertise in all areas of sleep research and on occasion are not able to/do not give a meaningful review. There will invariably be suggestions as to which experiments should be deleted, or ideas for new/different experiments to be conducted. Some suggestions by the reviewers are just not tenable, whether because of biology, scope of available resources or many other factors. In these instances, you must politely state your reasons and the rationale for not implementing the suggestions of the reviewers. However, in most instances you will agree with the expert advice provided by the reviewers and omit or add experiments, or change the experimental approach/design as suggested. Remember, at this point in the NIH funding process it is definitely not about you, it is all about the reviewers.

There is one aspect of the review to which you should always agree. If there are phrases in the critique such as “overly ambitious,” or “this project is unlikely to be completed within the time frame of funding”, your application has taken a substantial hit. Often junior faculty or new investigators do not carefully evaluate the total work load of the proposed project. When blood or tissue samples are to be used as sources of RNA, DNA or protein which will be assayed by various methods, take the time to calculate the number of all the samples that will be collected across the entire study, determine exactly how many assays/plates/reactions, etc., will need to be run and estimate the time it will take to do that. Carefully assess the time it will take...
to manipulate animals or get human subjects through the entire protocol. The easiest way to assure a poor score upon review is to propose to conduct more work than can be achieved in a reasonable amount of time. Therefore, if comments are made in the critique as to the “overly ambitious” nature of the project, you will always agree with the reviewer and reduce the workload by eliminating experiments of manipulations.

The Introduction is to be used to address in a point-by-point manner the major issues raised by the reviewers. You must also demonstrate where changes have been made and what changes have been made to the body of the text of the application. There are several ways in which changes to the text may be indicated. One may choose to use boldface type or italics font, but the general principle is that the manner in which changes to the text are indicated should not make it physically difficult to read the application. If extensive changes are made, it may be better to use a vertical notation in the margin, such as available in the Microsoft Word track changes feature. Using a notation in the margin will indicate to the reviewers where changes have been without cluttering text with extensive boldface type or italics font. This approach will also allow you to use boldface type and italics fonts for your headings and subheadings, without confusing them with changes to the text. One final note, it is not necessary to indicate every single change you have made to the text. Corrections of inadvertent typos or grammatical errors do not need to be indicated, nor does minor editing to the text. “Reserve” identification of changes that you have made to those of substance that are in response to the critique.

Resources

The CSR website contains much useful information about the submission and peer-review process. The major aspects of the submission and peer-review process have been summarized in this chapter, and much of this information was obtained from the CSR website. However, there is much more information available, and interested readers, particularly new investigators, are encouraged to make use of these resources during the development and submission of the grant application. The following list of links is arranged more-or-less in a sequence corresponding to the workflow of the submission and peer-review process.

Center for Scientific Review (CSR) home:
http://cms.csr.nih.gov/

Welcome to CSR:
http://cms.csr.nih.gov/AboutCSR/Welcome+to+CSR/

Submission and assignment process:

What happens to your application:

Insider’s guide to peer review for applicants:
http://cms.csr.nih.gov/nr/rdonlyres/60b2d32e-ae00-4358-8c51-2e11cc46eac8/15100/insiderguideapplicantsfinal.pdf

Mock study section video:

The “peer review process”:

Asynchronous Electronic Discussion Review:

Quick links: answers for applicants: