The NIH K08 and K23 Awards

The National Institutes of Health (NIH) K08 and K23 Awards are designed for physicians who are still in training, i.e., they have usually not accepted a faculty position. Other K awards such as the K01, K18, K25 awards are designed for PhD researchers, for researchers studying specific problems or for those who are changing their research programs. The purpose of the K08/K23 awards is to provide both funding and mentorship to outstanding candidates during the 5-year period when they transition from fellow to independent principal investigator. The K08 award is intended for physicians who are engaged in basic research and intend to pursue basic research at the faculty level. The K23 award is designed for physician scientists engaged in clinical or patient-oriented research. Both awards provide up to 5 years of funding, allowing protected time for research, and also involve a formal didactic mentoring program involving more senior clinical researchers. Ideally a K08 or K23 award provides some of the funds for a trainee’s fellowship research as well as some of the initial funding for a new investigator’s laboratory. The recipients of K08 or K23 awards have a great advantage in the competition for faculty positions.

Planning a K08 or K23 application

When considering whether to apply for a K08/K23 award, consult with both senior faculty members at your institution and the Program Officials at the NIH (see contact information below) of the different institutes sponsoring the awards (NIDDK, NIA, NHLBI, NCI). There are appropriate and undesirable stages in your career to submit a K08/K23 application. As noted above, the K08 and K23 awards are designed for applicants who are in the middle in their fellowship training, and the reviewers of the applications will be expecting that the applicants will successfully compete for faculty positions during the funding period. If the applicant is too far advanced or just beginning their training, other awards are more appropriate. For example, if you have already begun a faculty position or you have a long track record of publications including senior author publications, it is probably more appropriate to apply for an R21 or an R01 award. Similarly, if a candidate is relatively early in the training period and will not likely be applying for faculty positions in 3-4 years, it may be more appropriate to apply for an NSRA F32 (Basic) or T32 (Clinical) award. The F32 and T32 awards are shorter-term awards designed for individuals who will still be in training at the end of the funding period.

Successful candidates for K08/K23 awards will have already demonstrated that they have the potential to become productive investigators and are committed to an independent career in biomedical research. Although there are many ways to demonstrate productivity, reviewers tend to focus on the publication of original results in the peer-reviewed literature. For K08 applicants, recent publications with the applicant as the first author carry the most weight. For a fellow who has not published any first author papers in their current lab, it may be advisable to delay the application for a year until original manuscripts have been published. Publication of manuscripts during MD or MD/PhD training will also positively reflect on the appraisal of a candidate. Many candidates mistakenly equate authorship on reviews with first authorship on original research manuscripts. Reviews and secondary author papers are certainly important markers of productivity, but reviewers are unlikely to credit these as highly as primary author papers.

For K23 applicants engaged in clinical research as fellows, productivity will not be measured strictly by published manuscripts, although publication would be a decided benefit to an applicant. In contrast to K08 applicants, the publication of a relevant review of the literature can be a great asset. The K23 applicant can demonstrate a leadership role by local recognition within the fellowship program, and should ensure that this recognition is part of their biosketch and their letters of recommendation. Independence can often be demonstrated by the development of a new arm or ancillary study within the mentor’s clinical trial. This new trial should be based on an observation made by the applicant and developed into an independent part of the Clinical Trial by the principal investigator (PI) and the mentor. The applicant should make sure that the letters...
from the mentor and colleagues demonstrate that the applicant has taken a leadership role in the development and execution of the clinical research.

Having determined that the time is right for submitting a K08 or K23 application, a candidate should investigate to which Institute and program the application should be sent. Great care should be taken in choosing a program, as the application will be rated based on the appropriateness to the program as well as the qualifications of the applicant. Depending on the applicant’s area of research (Clinical versus Basic, malignant versus benign, red cell or coagulation), programs within the different institutes may be better fits. Candidates should review the following websites to determine the institute and program that best matches their research:

- NIDDK: http://www.niddk.nih.gov/fund/training/training.htm
- NHLBI: http://www.nhlbi.nih.gov/funding/training/redbook/trgnprog.htm
- NCI: http://cancertraining.nci.nih.gov/

After identifying programs that seem to fit their research, applicants should contact the Program Official (also known as a Health Science Administrator) associated with that Program. The Program Official is responsible for most aspects of a grant application and can provide valuable insight into whether the research and the Program are compatible. The Program Official’s contact information can be found on the websites listed above. In most cases, the Program Official and the applicant’s judgments will be similar, and the Program Official may suggest that the application be submitted to their program. The Program Official can submit a form called an “Awaiting Receipt of Application” (ARA) on the applicant’s behalf, which will most likely get the application assigned to the study section reviewing applications in that Institute and program. In other cases, the Program Official may suggest contacting other programs to be sure that the applicant has identified the most appropriate program.

Preparing a K08 or K23 Application

The application package (including instructions) PHS 398 can be obtained at http://grants1.nih.gov/grants/funding/phs398/phs398.html. The deadlines for submitting K08 or K23 applications are February 1, June 1 or October 1. If one of these dates falls on a weekend or holiday, the deadline is extended to the next business day. Candidates must be aware that preparing the application will require several months and a considerable amount of time. It cannot be stressed enough that for any investigator the first grant application is the most complicated. In addition to the description of the proposed research, there are a daunting variety of forms, including those concerning Vertebrate Animals, Hazardous Materials and Human Subjects. It can take weeks or months to get the required signatures on these forms. To navigate this process smoothly, the applicant should consult frequently with the mentor, who will help him or her complete the application process. In addition, all applicants are strongly advised to enlist the counsel of senior investigators in their department for their advice about the process.

One of the unique features of any K08/K23 award is the requirement for a career development plan. The applicant will need to develop a specific plan that will demonstrate to the reviewers that the applicant is on a career path to become an independent investigator. The career development plan should make it clear that the candidate and the mentor have devised a plan that anticipates that the candidate will be in a strong position to compete for faculty positions in the latter stages of the funding period. This section of the grant is sometimes overlooked and not given the attention it deserves. It is carefully examined during the review process. A mentor with a track record of developing investigators who perform and publish independent research is a great asset to a candidate. The career development plan should be specific about the mentoring plans. Often the mentoring will involve a commitment of the mentor and the applicant for regular meetings about research, grant writing and job interviews. These sessions may involve other faculty members. Some candidates, particularly those pursuing a career in clinical research, may want to include in their career development plan course work in biostatistics and/or ethics. The career development plan should provide the content of the courses and describe how the candidate and the mentor agree that these courses would be an asset to the candidate’s development.

The applicant should keep in mind that a critical component of the K08/K23 award is concrete evidence that the applicant will successfully make the transition from trainee to independent investigator. Proposals that are extensions of the research conducted as a fellow or that overlap significantly with grants awarded to the mentor often do not appear to be leading to independence. A proposal to study a new problem that may be related to the work done as a fellow, but that is clearly distinct from ongoing work in the mentor’s laboratory, are reviewed much more positively. The mentoring sessions should be designed to assist the candidate in developing and initiating an area of research that is entirely distinct from that of the mentor’s research program. The career development plan and the letter from the mentor should agree on both the timing of the career development plan (e.g., whether the candidate will begin a job search in the third or fourth year) and what the direction of the proposed research will be. It is the responsibility of the candidate to make sure that the descriptions of the career development plan in the application and the mentor’s letter match.

Because the career development plan is a critical component of the K application, it is important to develop the career development plan in parallel with the research plan.
If the applicant needs to schedule regular meetings with a mentor, make sure that these can fit into a compatible schedule so that the mentor can be sure to mention it in his or her letter. If the applicant needs to enroll in classes, he or she should be registered and be sure that the class meetings are compatible with his or her schedule. A well-developed career development plan that is functioning at the time of the review of the application can set the application apart from the others.

**Writing a K08 or K23 Application**

When describing the proposed research, the candidate should be aware that all applications are evaluated on six criteria: Significance, Approach, Innovation, Investigator, Environment and the Career Development plan. The reviewers are instructed to consider all of these criteria in the review of the proposal.

**Significance**

Most applications are focused on significant problems, but the outstanding applications make it clear to a reviewer why the work is highly significant. Applications can explore fundamental mechanisms underlying a specific disease or process (e.g., leukemia, coagulopathy, stem cell biology, signal transduction of erythropoiesis, apoptosis) or focus on a more applied research plan (e.g., screening a set of drugs for specific inhibition of a cellular disease process or a higher level of gene expression). Clinical research by its very nature is highly significant, but the applicant must make it clear to the reviewers how proposed research will increase the understanding and or treatment of the disease, as opposed to simply further defining the disease. It is the responsibility of the candidate to make it clear to the reviewer how the results will have a direct impact on human health.

**Approach**

The approach or experimental design is the largest section of the application and usually is where the best applications separate themselves from the others. Successful applicants carefully develop hypotheses for each part of the proposed research. The applicant should make sure that the hypotheses in the application and are well defined and experimentally testable. “Structure is related to function” is a fine hypothesis, but this hypothesis is vague and can be applied to almost any problem. In contrast, “mutations in a specific domain of a protein will affect one function, while mutations in a different domain will affect other functions of the protein by altering the conformation” is more precise and can be tested directly. Each hypothesis should lead to a description of an experimental design. Great care should be taken to make sure that each experiment contains the appropriate controls. It is critical that the applicant understands that the experimental design should test the hypothesis rather than further describe the problem.

The research plan should completely test the applicant’s hypothesis and address any competing hypotheses. The reviewers are instructed to consider whether the controls proposed will allow an unambiguous interpretation of the results. Many applicants make the mistake of proposing too many hypotheses and experiments. While these applications often have merit, they usually do not compete well with applications that focus on and thoroughly evaluate a clearly defined central hypothesis. The applicant should be aware that the reviewers will consider the amount of work proposed. For a beginning investigator it is almost always better to propose an in-depth study of a single problem that can be completed by the applicant and one or two other lab members rather than a comprehensive project that would require a large group of fellows, students and technicians to accomplish. If the application is focused on critical experiments, the workload should be within the capabilities of an investigator starting a new laboratory.

Research plans typically are divided into 2-4 specific aims, each of which describe a specific hypothesis and an experimental design to test that hypothesis. In successful applications the specific aims are independent, allowing information to be gathered from each aim. This information may be useful for conducting related or parallel studies outlined in other aims, but negative results from one aim should not preclude progress on the other aims. For example, applications where aim one is to clone a gene, aim two is to knock the gene out so that its function can be studied in aim three have dependent aims. These applications are generally not reviewed as positively because a negative outcome in aim one will prevent the work in aims two and three from proceeding. It would be better to design an application where the knockout experiments comprise one aim, a complementary approach using siRNA in primary human cells as a second aim, and a biochemical study of the mutant and normal protein in cell lines is the third aim. The three aims can each benefit from reagents that are developed (cells, antibodies) but do not depend on each other for progress.

**Innovation**

Most applications have a certain degree of innovation or novelty. A common mistake made by new investigators is the equating of a new technology with novelty. An innovative investigator will adapt a new technique developed for one purpose to solve a different problem. However, using the latest technology simply to define a previous observation more precisely would not be considered novel.

**Investigator**

The credentials of the investigator are a critical part of any K08/K23 application. As noted above, a great deal of the evaluation will involve the publication record of K08 applicants, and the evaluation of the Clinical involvement of K23 applicants. All K08/K23 applications require letters of recommendation. Choose the authors of these letters carefully. Seasoned reviewers have read hundreds of “ge-
neric” recommendation letters, 99% of which say nice things about the candidate’s published work or accomplishments and their personality. In 90% of such letters the applicant is ranked in the top 10% of all fellows. While complimentary, this type of letter does little to distinguish one applicant from another. On the other hand, a thoughtfully written letter that focuses on how the applicant solved a complicated problem encountered in the course of their work, the type of leadership skills exhibited in the lab or clinic, and a specific comparison to previous fellows who have gone on to successful careers carries much more weight. The applicant must impress upon the authors of their letters of recommendation that the reviewers will be looking for statements about the potential of the applicant to direct an independent research program.

Environment—Career Development Plan

The largest component of the Environment evaluation will be the career development plan. As noted above, the best career development plans are in place at the time of the application. They should include formal, regular mentoring sessions as well as opportunities for interactions with other investigators. The latter aspect is very important, especially if the research plan involves techniques and procedures that are new to the applicant. The availability of expertise locally or through formal collaborations to give the applicant the assistance needed can be critical to the success of the proposal.

The budgets for the K08 and K23 awards are not intended to fully fund the applicant’s research program. It is understood that primary support for the applicant’s research as a fellow should be provided by the mentor. Depending on the institute, K08 and K23 awards can provide up to $75,000 in salary support and $25,000 to $30,000 for supplies, travel and/or the hiring of a part-time assistant. The applicant should work closely with the Program Officer in developing the budget.

Most important of all, before submitting the proposal, the applicant should have several more senior colleagues read and critique the proposal. This is extremely valuable to the applicant as colleagues may discover correctable flaws that reviewers would use to rate the application behind other applications. Ideally the proposal should be critiqued 4-6 weeks before submission so that problem areas or administrative details can be corrected and critical control experiments performed. The failure to get input from colleagues about a proposal is one of the most common mistakes made by young investigators and, sadly, it is the easiest mistake to avoid.

The Review Process

After the applications are received, the candidate will receive notification that the application has been assigned to a Scientific Review Administrator (SRA) and a study section. The SRA is a different person from the Program Officer, and becomes the contact person for the applicant during the review process. If the applicant feels that their application has been assigned to a different study section than the one discussed with the Program Official, the candidate should contact the SRA, not the Program Officer to clarify the decision. After the proposal is submitted, some institutes allow an applicant to submit supplementary material that will assist the reviewers in evaluating their proposal. Supplementary materials would include the acceptance of papers that were being reviewed or submitted at the application deadline, IRB approval of a Clinical Trial or amendment or the results of a critical experiment. Applicants should check with the SRA before submitting supplementary materials.

The study sections for K08 and K23 applications are known as special emphasis panels. The members of the study section are chosen by the NIDDK, NIA, NHLBI or NCI based on their expertise in the programs of that institute. The SRA will forward the application (along with 6-10 other applications) to 2 or 3 individual study section members. These reviewers study the applications assigned to them in detail and prepare detailed critiques to be shared with the other members of the study section at the meeting. The purpose of a study section is to rank the applications relative to each other so that the outstanding applications are identified to the funding authorities. The problem confronted by a reviewer is that almost all of the applications contain meritorious experiments, and the difference between very good applications and outstanding applications is not very large. The reviewer’s task is to distinguish between the very good and the outstanding, and to help the study section reach a consensus about the ranking of each application.

After reading the proposal the reviewer must decide on a ranking for the proposal. Here the reviewers will consider the other applications assigned to them in for this particular study section and their evaluation of ongoing work in this field by others. Often reviewers will rank applications using a percentile scale. Outstanding applications are ranked in the top 10%, excellent but not outstanding applications in the top 20%, very good applications in the top 30%, and applications that could be very good or excellent if certain aspects were better in the top 50%. Applications with serious flaws, including the significance of the problem addressed, vague or descriptive hypotheses and research plans, or incomplete experiments will be ranked in the bottom 50%. Reviewers are encouraged to use the entire scale for ranking the assigned applications.

The reviewers prepare written reviews for the K08 and K23 applications assigned to them. The written reviews plus the executive summary statement (crafted by the SRA following discussion of the application at study section) are the information the applicant receives about the review of the application. The written reviews should be organized around the 5 criteria, and should point out the strengths and weaknesses. For applications not given a high percentile ranking the reviewers should attempt to constructively point out weaknesses, explain why a particular part of the application was judged to be weak and suggest a means to improve the weaknesses. For example, if an
application is too diffuse, a reviewer may constructively calculate the number of experiments proposed for the funding period to show the applicant how much work has been described. Suggestions by the reviewer about which are the most important experiments can be very useful in rewriting the application. If the reviewer feels that the hypothesis is not clear or does not attempt to resolve controversy in the area, this should be pointed out to the applicant. Unsuccessful applications may be modified and resubmitted, and the comments of the reviewers can be an invaluable resource to the applicant in the resubmission process.

Review at the Study Section

All K08 and K23 submitted are discussed at the study section. At the meeting of the study section the reviewers will present their preliminary rankings for each application. Usually this is given as a percentile. The primary reviewer is charged with explaining the application to the other members of the study section. This explanation should include why the application is important, what methods will be used and what new information can be obtained. The applicant can help the primary reviewer by writing in clear language and avoiding jargon that the reviewer and many members of the study section may not be familiar with. If the applicant is clear about the significance of the work, it will be easy for the primary reviewer to communicate that to the study section. For example, data from a Disease Foundation website about how common a disease is or how much it costs to treat a disease takes only a few moments to collect, but hands the reviewer concrete data that can be used to establish the significance. Likewise if the hypotheses are identified (perhaps in bold type) and stated clearly, the reviewer will only have to repeat these words to the study section. The applicant can ensure that the proposal is clear and easy to read by having colleagues read and critique it prior to submission.

After presenting the application, the primary reviewer will give a critique pointing out the strengths and weaknesses that the reviewer has identified. The secondary reviewer and the reader complement the critique of the primary reviewer with those parts of their critiques that are different from that of the primary reviewer. After the discussion each reviewer recommends a numerical score based on the percentile scale. Study sections make a good faith effort to distribute the scores according to merit over a wide range so that all of the applications have different scores and fall into a rank order. This allows the funding authorities (who actually decide which applications to fund) to make the best choices.

When the reviewers have different opinions about the ranking of the application, the reviewers present their differences of opinion to the rest of the study section in more detail. Many times a reviewer will pick up a point that another reviewer has missed or misinterpreted. Often disagreements reflect a current controversy in the field, and it is important for the reviewers to distinguish between controversial points and scientific flaws. These disagreements will be part of the written critique by the SRA. The purpose of the extended discussion is to better inform the other members of the study section so that they can decide for themselves how to score the application.

After the Review Process

About two weeks after the study section meets, the applicant will be notified of the priority score his or her application received. This number may not mean very much, but it can be compared to those posted on http://grants1.nih.gov/training/outcomes.htm#funded.

At this point the contact person reverts to the Program Officer. About eight weeks after the review, the applicant will receive a Summary Statement with a letter from the Program Officer. The Summary Statement will include the reviewers’ written comments and the SRA’s summary of the discussion of the application. The applicant should contact the Program Officer immediately if there are questions about any administrative aspects of the application (Human Subjects, Vertebrate Animals etc.) so that these can be resolved before the funding decisions are made.

After the review by the study section is complete, the rank and scores of the applications are forwarded to the Institute’s Advisory Councils for the final funding decisions. The Program Officer will notify all applicants about the Council’s decision. For those applications that are selected for funding, an official Notice of Grant Award will be emailed to the institutional business official. The time from when the application is submitted to when the successful applicant receives the first of the funds usually is between 9 and 12 months.

Although the funding authorities would undoubtedly like to fund many more applications, the pool of money allotted to the K08/K23 awards is a fixed amount. Therefore, many excellent applications cannot be funded. For most applications that do not receive funding, resubmission is an option the applicant should strongly consider. The applicant should begin the resubmission process by contacting the Program Officer. The written critiques of the proposal should provide the applicant with valuable information about how to improve the proposal. If the reviewers question a particular set of experiments, the applicant can address these concerns with either some preliminary experiments or a more careful explanation. If the productivity of the applicant was an issue, the publication of papers will positively address this concern. Many applicants may be unsure about exactly what the reviewers were questioning. In this situation the applicant should contact the Program Officer and consult with colleagues about the ambiguity before deciding on which corrective measures to take. It is important to note that even applications that were ranked in the bottom 50% can be revised and resubmitted. There are many examples of applications that were originally ranked in the bottom half being revised, resubmitted and funded at the next study section. A positive attitude on the part of the applicant is a major factor in turning constructive criticism into an improved application.