

National Kidney Foundation, Inc.
RESEARCH, TRAINING, &
EDUCATION AGENDA
2004-2009

The National Kidney Foundation (NKF) has been providing funding for research and research training for over 35 years. The NKF research support program which began with Postdoctoral Research Fellowships has since been expanded to include Young Investigator Grants and Clinical Scientist Awards. As a result, the National Office of the National Kidney Foundation has a budget of up to \$2,385,000 during the current fiscal year for grants and awards.

With this level of commitment by the NKF to the support of biomedical research, it is prudent to periodically review its portfolio of research awards, in the context of the Foundation's evolving priorities and in light of evolution in alternate sources of research support from both public and private agencies. Five years have elapsed since the NKF last undertook such an examination and the time has come to 1) re-evaluate the relevance of the NKF research program, 2) develop a plan to maximize the effective utilization of the resources the public entrusts to research support through the NKF and 3) enhance the role of the Foundation in promoting scientific investigation that will enhance patient care and clinical outcomes.

In early 2004, I requested Joseph V. Bonventre, MD, to chair an ad hoc planning committee, and invited the following physicians to serve on committee: Sharon Andreoli, Thomas D. DuBose, Raymond Harris, Andrew Levey, Ravindra Mehta, Bruce Molitoris and Robert Toto. The committee met in Boston on March 5, 2004, and developed the attached report.

Brian J. G. Pereira, MD,
President

At its meeting on March 5, 2004, the ad hoc committee reviewed the recommendations from the last iteration of the National Kidney Foundation (NKF) Research, Training and Education Agenda and the implementation of these recommendations. A summary follows:

MAJOR RECOMMENDATIONS FROM THE RESEARCH, TRAINING AND EDUCATION 1999-2004 AND THE IMPLEMENTATION

General Considerations

There should be a major effort to attract more physician-scientists to renal investigation in order to take maximal advantage of the greater opportunities for research funding which currently exists.

Congress has fulfilled its commitment to double the level of appropriations annually provided to the National Institutes of Health (NIH) from the level it supported in 1998. However, this doubling has not reversed the decline in the participation of physician scientists in the research enterprise. Over the last 30 years, the number of physician scientists submitting NIH research grant applications has decreased significantly. In the 1970's 40% of NIH research applications were submitted by physicians (MDs). Now less than 20% of research applications submitted to NIH are from MDs. Similarly, the number of physician/scientists applying for NKF support has not increased as had been expected in 1999. Since MDs are critical for the interface between basic and clinical research, well-trained physician investigators are essential to assure that the explosion of findings from basic research are translated to clinical settings. Therefore, the recent National Research Council Report, "Addressing the Nation's Changing Needs for Biomedical and Behavioral Sciences," recommended that NIH and other research agencies intensify their efforts to train and retain physicians in the research workforce.

External Issues

1. *It is recommended that grants that fall outside of the expertise of a standing (NIH) study section (e.g. clinical research) should be reviewed by a special emphasis committee, consisting of individuals with experience and expertise required to provide true peer review.*
2. *It is recommended that training support be provided to competitively selected, established centers to provide specialty training in the practice of clinical trials, epidemiology and health services research as they pertain to diseases of the kidney.*
3. *Congressional directives for problem-oriented research could be improved by the establishment of a broadly-based independent Advisory and Planning Committee that would provide information and recommendations to the NIH as to those areas of nephrology which would benefit from additional research.*
4. *It is recommended that efforts be made to expand the scope of the United States Renal Data System project to include data collection and analysis on patients with progressive chronic renal failure before they develop ESRD.*

The NIH has convened special emphasis panels to review applications to participate in clinical trials and to conduct research in response to requests for proposals. In the last five years, the NIH has developed several promising new mechanisms to foster clinical research training, e.g. the K12, K23 and K30 programs. (See appendix). The NIDDK has instituted a clinical trials consortium, designed to provide opportunity for input from the kidney research community.

The USRDS has begun the process of analysis of data of patients with CKD who were Medicare-eligible prior to ESRD.

Internal Recommendations

NKF Fellowship

1. *NKF should make a total of six third year Research Fellowships available to qualified applicants.*

Response to this new initiative has been good and as many as three third-year fellowships were funded in each of the succeeding years.

2. *The committee recommends that clinical investigators be encouraged to apply for NKF fellowship support for their trainees, that special consideration be accorded to qualified applicants and that the review committee include experts in clinical research.*

Beginning with the 2003 cycle, the review of grants was accomplished by two study sections - one for basic science and one for clinical research. This has allowed review of clinical grants by experts in the field of clinical research. Also, the Scientific Advisory Board which is the final decision making body with respect to allocation of grants has ensured that appropriate emphasis has been accorded to clinical research.

3. *The Committee recommends that the NKF Fellowship stipend be increased over the course of a three-year period, to a maximal \$35,000 per year.*

These fiscal changes have been instituted. Moreover, the fellowship stipend was raised an additional notch, to \$40,000 per year, beginning with awards that were effective on July 1, 2003.

NKF Young Investigator Grant

1. *The term of the award should be increased from two to three years.*

This has not been implemented, primarily because of budgetary limitations.

- 2. The level of the award should be doubled, from the current amount of \$25,000 annually to a maximum budget of \$50,000 per year.*

These fiscal changes have been instituted.

- 3. Up to \$25,000 of the grant should be available annually for salary support, provided that there is sufficient justification.*

The fraction that may be allocated to salary has been increased to \$15,000

NKF Clinical Scientist

- 1. The committee recommends that the maximum number of new Clinical Scientist Awards activated each year be increased gradually to five. Consideration should also be given to an increased level of funding in the future.*

Due to budgetary constraints the funding for the Clinical Scientist Award has remained at \$50,000 a year for three years. The issue of increasing the number of awards has not been relevant because the number of qualified applicants has been insufficient to make the existing three awards.

DEVELOPMENTS IN NKF EDUCATION PROGRAMS SINCE 1999

During the last five years NKF's clinical practice guideline program, the Kidney Disease Outcomes Quality Initiative (K/DOQI), has become one of the Foundation's most important services for patients and health care providers. While NKF has grown because of K/DOQI, the initiative itself has also grown, to pursue opportunities for improving outcomes for all

individuals with kidney disease, from earliest kidney damage through the various stages of progression to kidney failure, when replacement therapy becomes necessary.

To provide a unifying focus to K/DOQI, it was decided that its centerpiece would be a set of clinical practice guidelines on the evaluation, classification and stratification of chronic kidney disease (CKD). Those guidelines were published in February 2002. NKF's advocacy efforts relating to the federal support of biomedical research, as well as NKF's own program to fund research, should support and complement the K/DOQI initiative, particularly its focus on chronic kidney disease and the benefits of early identification and treatment of individuals with CKD.

CURRENT RESEARCH ENVIRONMENT

Federal Support of Kidney Research

As noted above, Congress has fulfilled its commitment to double the level of appropriations annually provided to the National Institutes of Health (NIH) from the level it supported in 1998. As a result of this achievement, however, we can expect only modest growth in funding for biomedical research from the federal legislative and administrative branches during the foreseeable future. Funding for kidney research has benefited from the doubling of the NIH budget that was completed in FY2003. Nevertheless, the federal support of investigation relating to kidney disease is still relatively modest, there is not a focus on kidney disease in any NIH study section, and NIH rarely funds clinical trials concerning kidney disease.

Elias Zerhuoni, Director of NIH, has designed a new "Road Map" initiative to define a limited set of priorities that will accelerate progress across the spectrum of the institute missions. The kidney research community should position itself to take advantage of these initiatives. The NIH "Road Map" has three themes: "New Pathways to Discovery," "Research Teams of the Future" and "Reengineering the Clinical Research Enterprise." Roadmap initiatives in the first category address technologies and approaches necessary to meet contemporary research challenges, including molecular imaging, the development of small-molecule libraries,

bioinformatics and computational biology, nanomedicine and structural biology. As for “Research Teams of the Future,” NIH wants to stimulate new ways of combining skills and disciplines in the physical and biological sciences, including nontraditional teams of biomedical scientists, engineers, mathematicians, physical scientists, computer scientists and others. This plan is based upon the perception that there is a converging set of unifying principles that link apparently disparate diseases through common biological pathways and therapeutic approaches.

With regard to reengineering the Clinical Research Enterprise, Dr. Zerhouni notes that clinical trials can no longer be conducted in a single academic center. The NIH will promote creation of better integrated networks of academic centers that work jointly on clinical trials and include community-based physicians who care for large groups of well-characterized patients. Implementation of this vision will require new ways to organize how clinical research information is recorded, new standards for clinical research protocols, modern information technology, and new models of cooperation between NIH and patient advocacy alliances.

Trends in NKF Research Support

The number of proposals that NKF receives for fellowships and Young Investigator Grants fluctuates from year to year, but, overall, has remained relatively stable in the five years that have elapsed since the last *Agenda* was approved.

Fellowship Applications

2000-2001	86
2001-2002	94
2002-2003	76
2003-2004	107
2004-2005	98

Young Investigator Grant Applications

2000-2001	22
2001-2002	39
2002-2003	36
2003-2004	31
2004-2005	31

On the other hand, the number of candidates for Clinical Scientist Awards has dropped markedly, from 16 in 1998 to five in the most recent funding cycle. In addition, as noted above, there has been no increase in the number of physician scientists seeking NKF support. While these trends might be a cause for concern, the committee concluded that the growth in the number of investigators completing research training during the period of doubling at NIH, combined with the likelihood of constrained resources at NIH in the future, should insure a steady stream of qualified applications for NKF support over the next five years.

Research Support from the American Society of Nephrology (ASN)

In September, 2003, ASN President Norman Siegel announced that the Society planned to double its commitment to research grant funding, by adding \$1.5 million to its research budget over the next four years. While ASN does not support research fellowships, the resources that ASN is committing will expand funding opportunities for junior faculty. For example, eight Carl W. Gottschalk Research Scholar Awards will be supported each year, at an annual level per award of \$100,000.

RECOMMENDATIONS

Based upon its review of the current research environment and developments in kidney research since the issuance of the National Kidney Foundation Research, Training and Education Agenda, 1999-2004, the ad hoc research planning committee made the Following recommendations at its March 5, 2004 meeting.

1. INTERFACE WITH THE NATIONAL INSTITUTES OF HEALTH

1.1. ASN and NKF should join forces to develop a strategic agenda to secure as much benefit for kidney research as possible out of the NIH “Road Map” initiative. We should get behind the Road Map and give it specifics for kidney disease, e.g. biomarkers and fine needle aspiration. Otherwise, kidney investigation will be left behind as the scientific community moves into areas like proteomics, nanomedicine, regenerative medicine and stem cell regeneration. We have to be pro-active in pushing our research priorities at the National Institute of Diabetes and Kidney Diseases (NIDDK), including arranging joint meetings with the Director of that Institute. This could include advocacy for the NIH workshops that might lead to program announcements. ASN and NKF might “broker” a multi-institutional K12 award, involving centers where kidney research is conducted. Additional priorities, grounded in the themes already described, are explained in subsequent sections of this report.

2. RESEARCH ON CHRONIC KIDNEY DISEASE AND ITS COMPLICATIONS

2.1. The *1999-2004 Agenda* recommended that efforts be undertaken to expand the scope of the United States Renal Data System (USRDS) project to include data collection and analysis on patients with progressive kidney failure before they develop ESRD. While there has been some progress in that direction, additional resources should be provided to the United States Renal Data System (USRDS) so that its investigators will be able to analyze the data that are available regarding the demographics of chronic kidney disease (CKD) in this country.

2.2. To advance CKD research the International Classification of Diseases (ICD) should be revised to capture diagnoses that reflect early kidney disease.

2.3. It is recommended that efforts be made to enhance the involvement of the Center for Disease Control in prevention and assessment of chronic renal disease.

2.4 The Committee considered other opportunities to advance research on CKD and its complications that would require action by the federal government. They include the following:

2.4.1 The National Institutes of Health should design and support population-based cohort studies on the progress and prevention of CKD, like the Framingham study of cardiovascular disease. The resources of pharmaceutical companies and health plans should be mobilized in this search for new understanding.

2.4.2 The National Heart Lung and Blood Institute should collaborate with NIDDK to solicit research proposals as recommended at the Workshop on Cardiovascular Disease in Chronic Kidney Disease that was held on March 10-11, 2003.

2.4.3 The kidney research community should leverage the Consortium of Southern Health Studies REGARD project, involving risk factors for stroke and the ARIC study of atherosclerosis risk in the community.

2.4.4 The National Kidney Foundation, the American Society of Nephrology and the NIDDK should foster increased participation of kidney investigators in observational studies and, as a separate and distinct goal, encourage studies designed to improve care for patients with chronic kidney disease in different practice settings. One area of investigation, for example, could focus on factors that facilitate or frustrate the implementation of practice guidelines, e.g. what barriers limit the use of ACE inhibitors?

2.5 We need to confirm that the delivery of care and patient outcomes will be improved if practice guidelines are followed. We also need to evaluate whether resistance to the use of practice guidelines will be mitigated if the efficacy of the guidelines is confirmed.

2.6 Finally, the committee recommended that the kidney research community collaborate with the transplant societies to stimulate research on CKD in the transplant recipient.

3. RESEARCH ON ACUTE KIDNEY DISEASE (AKD)

3.1. Acute kidney failure is a growing problem in the United States because of the aging of the population and the increased use of chemotherapy. Therefore, additional resources should be devoted to the study of this illness. Furthermore, the focus of investigation should be extended beyond attention to the critical care component of health care delivery since acute kidney failure can progress to chronic kidney disease. Consequently, a new terminology is warranted to assist us in planning new initiatives. The committee recommended that “acute kidney disease” be substituted for “acute kidney failure.” We should use the Acute Dialysis Quality Initiative (ADQI) process to develop strategies for the prevention of AKD in vulnerable populations. Nephrologists should take the lead in addressing the lack of formalized training programs in AKD. There is currently no platform for the development of practice guidelines and more randomized controlled trials are needed in this area.

4. RECOMMENDATIONS FOR NATIONAL KIDNEY FOUNDATION RESEARCH AND EDUCATION PROGRAMS

4.1. General

4.1.1. The focus of the NKF research program has been career development and career development should remain NKF’s priority going forward. Considering budget restraints, new research activities should not be implemented at the expense of NKF’s career development mission. Specifically, NKF should not fund centers of excellence as has been proposed in the past. We should continue to emphasize

investigator-initiated research. Nevertheless, it would be appropriate for the Foundation to give special consideration to candidates for NKF research support who plan to address strategic areas or issues that have a priority in the context of NKF's overall mission. This would include research recommendations from K/DOQI practice guidelines and the NKF Kidney Early Evaluation Program (KEEP). In addition, NKF should redirect resources to the study of Acute Kidney Disease. The NKF Scientific Advisory Board (SAB) should develop (and periodically update) a list of such priority areas. That list should be posted on the NKF web site and included in any solicitations for research proposals that NKF issues.

4.1.2. NKF should develop a pro-active mechanism to track the careers of its awardees over time. We have focused in the past upon the likelihood of former fellows to accept faculty appointments after their training but they may ultimately opt for private practice. An on-going mechanism will provide a better assessment of NKF research support mechanisms. It will also afford the opportunity to evaluate mentors and to cultivate the devotion and loyalty of a committed constituency. Along that line it was suggested that there be an annual reception for current and former holders of NKF research awards, during which they can meet the leadership of the NKF, the members of the NKF SAB and the NKF study sections and each other.

4.1.3. In view of the fact that the number of physician scientists who seek support from NKF has not grown, and in response to the enormous opportunities to improve the care of patients with kidney disease through research undertaken by physician scientists, the Instructions to Applicants for all NKF award mechanisms should make it clear that MDs are strongly encouraged to apply for support for both clinical and basic studies. On the other hand, the committee concluded that it would be unwise to reduce the requirement that investigators funded by the NKF devote 75% of their time to research as a means of attracting more physician scientists to submit applications.

4.1.4. Because of the increasing importance of interdisciplinary research, in the evaluation of applications and making recommendations about the award of support, NKF study sections should consider whether proposals will provide clinicians the opportunity to spend time in a basic science lab or give basic scientists an exposure to clinical investigation.

4.2. Postdoctoral Fellowships

As noted in the NIH “Road Map,” the individual investigator, working in isolation, is a thing of the past. Future research progress will depend upon collaboration of various disciplines and will be driven by investigators with multidisciplinary training. The National Kidney Foundation should encourage multidisciplinary training through its research fellowship program and dedicate a portion of its training budget for proposals that provide diverse training opportunities. However, fellowships should not be given funding priority simply because the candidate has multiple mentors.

4.2.2. NKF currently limits the number of fellowships that can be awarded to a single department or program at a medical school. With the increasing prevalence of multiple faculty appointments, however, that policy, adopted 25 years ago, is no longer practicable. In its place the committee recommended that NKF fund no more than two fellowships per institution per funding cycle, with no more than four fellowships active at any institution during any fiscal year. (Fellowships awarded pursuant to the Affiliate Matching Fellowship program could be funded in addition to these maximums.) Each fellowship funded in each funding cycle must have a separate sponsor. The process of applying for training support is in itself part of the career development experience. Therefore, it is recommended that the mentor be required to comment on the role of the candidate in preparing the proposal. Similarly, our trainees must be afforded a real opportunity for career advancement and the NKF research fellowship program should not be considered primarily as a source of supplemental manpower. Therefore, it is recommended

that the division director as well as the mentor be required to submit a statement of career expectations for the fellow.

- 4.2.3 Finally, it was recommended that NKF policy explicitly stipulate that NKF will fund a maximum of three consecutive years of fellowship training and that, if other agencies support a period of time during the fellowship training of a particular candidate, NKF funds will not be available to support more than four years of research fellowship training for that candidate.

4.3. Young Investigator Grants

- 4.3.1. In keeping with the overall strategy of facilitating career development through the use of NKF research funds, applications for Young Investigator Grants must include the candidate's own plans for his/her career development as well as a statement of how support through this funding mechanism will help the grantee to take steps towards an independent research career, rather than merely supplement funding from other agencies. (For example, the NKF Young Investigator Grant could prepare a grantee for a K24 award from NIH or provide seed money for a K24 application.) The applicant should highlight opportunities to acquire new skills and learn new techniques that the Young Investigator Grant will make possible, such as training in epidemiology and statistics, molecular biology, translation research and research methodology. Conversely, an NKF Young Investigator Grant may not entail enough funding, in and of itself, to enable a junior faculty member to develop into an independent investigator. Therefore, there must be explicit documentation of the availability of additional intramural or extramural support. In the case of a basic science application, this might consist of funding for supplies or technician time; for clinical research proposals, availability of a study coordinator or research assistant would be appropriate.

- 4.3.2. It was recommended that NKF policy be liberalized so that the Foundation could fund one Young Investigator Grant per institution, per funding cycle. Additionally,

in the future it should be permissible for a grantee under this program to have a mentor.

4.4. Clinical Scientist Award

4.4.1. Despite the downward trend in applications, the NKF Clinical Scientist Award should remain a part of the NKF research portfolio, provided that it is limited to supporting clinical investigators and that it is structured as a more supportive funding opportunity that is available earlier in the course of an academic career. In the future, the Clinical Scientist Award should be used only to support translational research or research leading to novel therapeutic interventions. If this recommendation is adopted, basic scientists would no longer be eligible for Clinical Scientist Awards. By way of analogy with the American Heart Association's research program, the NKF Clinical Scientist Award might be considered a "Clinical Established Investigator." In order to stimulate additional proposals for this funding mechanism, NKF should ask academic centers and division directors to nominate investigators for this Award and then urge nominees to apply. NKF could also solicit applications from holders of K23 awards.

4.5. Affiliate Research Activities

4.5.1. Many local affiliates of the National Kidney Foundation provide funding for research to investigators working in their service areas. These affiliates should be urged to develop programs and priorities similar to those that guide the national organization's program of research support.

4.6. Proposed Clinical Educator Award

4.6.1 This National Kidney Foundation should consider the establishment of a Clinical Educator Award that could ultimately facilitate the dissemination of skills in new technologies, including informatics, simulation, and computer science, advance the development of tools based on those new technologies and, capitalize on the opportunities these technologies present for nephrologists and for the patients that they serve. There are three promotion tracks in academic medicine today: basic science investigator, clinical researcher and clinical educator. On the other hand, the field of clinical education is not defined and there is a no established training track for clinical educators. This provides an opportunity as well as a challenge. The University of Pittsburgh offers a Master of Science Degree in Clinical Education and the National Science Foundation has a program in education and bioengineering. These could be used as models. As a first step a task force should be appointed to explore ways to formalize the field of clinical Education.

4.7. Collaborative Activities

4.7.1. NKF should explore opportunities for collaboration with sister organizations to develop and fund research and education programs. The proposed Clinical Educator Award, for example, could be planned in conjunction with the ASN. Because of the prevalence of diabetic kidney disease in this country, the American Diabetes Association might be a logical partner for the joint support of research.

4.7.2. NKF should work with the ASN to develop programs that could change the culture of kidney research. For example, ASN and NKF could co-sponsor courses on the conduct of patient-oriented research and courses on research mentoring.

4.8. Other Funding Arrangements

4.8.1. The National Kidney Foundation has entered into a three-year service agreement, which established a K/DOQI Center for Clinical Practice Guideline Development and Implementation at Tufts-New England Medical Center. The center's mission is to provide service to the NKF in K/DOQI guideline development and

implementation, conduct research on K/DOQI guideline implementation in various healthcare settings, and to train fellows in the applications of evidence-based medicine in kidney diseases. Deliverables include but are not limited to: evidence reports, draft guideline statements, physician education materials, data analysis and peer-reviewed publications concerning the effects of guideline implementation on diagnosis, treatment and outcomes. In the future, the SAB should ask NKF to develop a process for solicitation and evaluation of applications for support for guideline development as well as for other service agreements, e.g. data collection and analysis for the KEEP program.

APPENDIX

K12 MENTORED CLINICAL RESEARCH SCHOLAR PROGRAM AWARD

Institutions can apply for K12 Awards that support career development programs for physicians, including activities that provide candidates a comprehensive understanding of clinical research approaches that are not necessarily disease-specific. The didactic and research phases of this program must include acquiring expertise across a broad spectrum of research methodologies, technologies, concepts, use and management of large datasets, bioinformatics and other research tools. Allowable costs include \$90,000 per year per candidate for salary support and up to \$30,000 per candidate for expenses, including tuition. Funds are also available to defray salary for the Program Director and the Lead Mentor and well as a part time secretary. Finally, there is an 8 percent add-on for “Facilities and Administrative Costs.” Funding for the K12 Program became available in 2002.

K23 MENTORED PATIENT-ORIENTED RESEARCH CAREER DEVELOPMENT AWARD

An individual investigator can apply for the K23 Award, which was first offered in 1999. The K23 supports three to five years of supervised study and research for clinically trained professionals who have the potential to develop into productive, clinical investigators focusing on patient-oriented research. This award forms an important part of the NIH initiative to attract talented individuals to the challenges of clinical research. The objective of the award is to encourage research-oriented clinicians to develop skills and gain experience in advanced methods and experimental approaches needed to conduct patient-oriented research. Most NIH components will provide up to \$75,000 to offset the full-time salary requirements of the candidate. In addition, NIH will generally provide up to \$25,000 per year for expenses.

K30 CLINICAL RESEARCH CURRICULUM AWARD

The NIH has provided 59 K30 Awards to institutions to support the development and expansion of dedicated programs in clinical research. These programs must include formal course work on:

- Design of clinical research projects
- Hypothesis development
- Biostatistics
- Epidemiology
- Legal, ethical and regulatory issues related to clinical research

This award has a duration of five years, with funding at the level of \$200,000 per year, per institution.