ADMINISTRATIVE GUIDELINES FOR PEDIATRIC CENTERS OF EXCELLENCE IN NEPHROLOGY

National Institute for Diabetes and Digestive and Kidney Diseases

6/1/2011

Contents

I. DESCRIPTION

Background

The NIDDK-supported Pediatric Centers of Excellence in Nephrology (PCEN) are part of an integrated program of kidney disease research. These Centers were originally established as Specialized Research Centers in 1991. Center grants such as these have proven to be a valuable way to promote multidisciplinary interactions and to provide the shared resources needed to address complex biomedical problems in pediatric kidney disease. Centers also can provide the basis for generating technologies that can be applied by other investigators and clinicians in many medical centers throughout the nation.

General Description

The studies proposed by the PCEN should foster and extend the development of new approaches into the causes, early diagnoses, and improved treatments for kidney disease in children. Institutions selected for this program are domestic and have extensive scientific expertise in the areas of cellular and molecular biology, genetics, protein chemistry, structural biology, immunology, pathology, physiology, nutrition, epidemiology, animal models, and clinical trials. The objectives of the PCEN are to bring together basic and clinical investigators from relevant disciplines in a manner which will enhance and extend the effectiveness of their research. The Center consists of several components: a single Administrative Core, Biomedical Research Cores, interrelated Research Projects and a Pilot and Feasibility Program. A Center must be an identifiable unit within a single university, medical center or a consortium of cooperative institutions, including an affiliated university.

II. ADMINISTRATIVE CORE COMPONENT

Description

The overall goal of a Center is to bring together, in a cooperative, multidisciplinary and integrative manner, basic science and clinical investigators to enrich the effectiveness of research on pediatric kidney disease. To accomplish the overall goal of these Centers, an ongoing program of excellence in biomedical research related to the study of pediatric kidney disease should exist at the applicant's institution. However, the research program need not be exclusively in kidney, and can include elements related to development, creation of animal models for use in fundamental studies, and the development of innovative, pioneering human investigation protocols. Close cooperation, communication, and collaboration among all participating center personnel of many professional disciplines are characteristics of a successful PCEN.

Requirements

A PCEN will involve the interaction of broad and diverse elements within a single institution, or a consortium of cooperating institutions; thus the lines of authority and sanction by the appropriate institutional officials must be clearly specified. The administration of the PCEN will include the responsibility of coordinating the various functions of the Center.
Each applicant institution will specify a Center Director to be responsible for the organization and operation of the PCEN. It would be highly desirable that the Center Director, as well as the applicant institution, has a commitment to the investigation of basic science, translational or clinical topics relevant to the kidney. The Center Director should be an experienced and respected individual who can provide scientific and administrative leadership for the total program. This individual must be able to coordinate, integrate, and provide guidance in establishing new programs in pediatric kidney disease research. This commitment will require significant effort from the Center Director. Each Center Director is expected to commit 2.4 person months (calendar year) overall effort to the Center. An Associate Center Director should be named who will be involved in the administrative and scientific efforts of the PCEN and will serve as acting director in the absence of the Center Director.

It is expected that the administrative organization of the PCEN will include a supportive structure, such as an internal executive committee to ensure accomplishment of (1) Coordinating and integrating the Center components and activities; (2) Review the use of funds for pilot and feasibility studies; (3) Provide advice to the Director about the productivity and effectiveness of the activities of the Center; and (4) Interact with the NIDDK and other appropriate individuals or groups including the scientific and lay communities, in order to help develop relevant goals.

The final administrative structure of the Center will be left largely to the discretion of the applicant institution (subject to review by NIH peer review mechanisms). However, NIH's experience has demonstrated that the effective development of the Center programs requires close interaction between the Center Director, the principal investigators, appropriate institutional administrative personnel, the staff of the awarding agency, and the members of the community in which the Center is located. Therefore, each Center applicant should establish an administrative structure that will permit the development of such interaction. Within this structure, each applicant institution must also establish a mechanism to oversee the use of funds for the proposed Pilot and Feasibility Program. This mechanism must include review by appropriate consultants from the scientific community outside the Center institution or consortium institutions. Consultants who will serve on advisory committees should not be specifically identified in the application, but the process by which they will be selected should be described. These same consultants may be utilized, if desired, for review of other activities of the Center. The mechanism for reviewing the use of the pilot and feasibility funds will be considered by the initial review groups in the evaluation of the Center applications. Further details regarding this mechanism will be found below in the discussion of the Pilot and Feasibility Program. The projects selected to receive these funds will be described by the Centers in their annual reports and will be reviewed by the NIDDK Staff for eligibility in its annual evaluation of the Center program. Funds for the Pilot and Feasibility Program should be listed in the Other category in the budget of the Administrative Core. The Center grant may also include limited funds for program enrichment (i.e., seminars, etc.) that should be included in this core (see below).

Although facilities available should be described for each element of the application, a more general description of overall facilities and a statement regarding institutional commitment to the Center should also be included here.

Educational Enrichment Programs

The PCEN grant can budget for and provide limited support for an enrichment program, whose description and budget may be included within the administrative core. It may provide support for visiting scientists, seminars, and research forums. Students, fellows, and junior faculty should be encouraged to take full advantage of all Center-sponsored seminars, courses, workshops, and symposia. If appropriate, Centers may waive fees for attendance at such events for interested students, fellows, and junior faculty members. Enrichment program-sponsored mini-sabbaticals, or other instructional opportunities, also may be appropriate for postdoctoral fellows. Stipends for fellows are never an allowable Center expense, but travel, per diem, and registration expenses may be paid from enrichment program funds. Limited travel support is allowable for PCEN investigators to travel to present scientific findings, learn new laboratory techniques, develop new collaborations, or engage in scientific information exchange. In all cases, the enrichment program should further the overall aims and objectives of the PCEN as well as of the scientific cores.

III. BIOMEDICAL RESEARCH COMPONENT

Biomedical Research Cores

Definition: A biomedical research core is a shared facility that provides a needed service to Center investigators, enabling them to conduct their funded individual research projects more efficiently and/or more effectively. Cores should be designed to furnish a group of investigators with materials, techniques, determinations, instrumentations, and/or quality control to enhance research and contribute to cost effectiveness. It is acceptable to develop a cost recovery system to help defray costs to the Center. This system would charge a fee to Center participants for services provided by the Core, but at a reduced rate. If such a cost recovery system is developed, a detailed charge justification must be presented and the program income section on the checklist of the PHS 398 must be completed. Participating Center members must also be informed to include such costs with their full budget justifications in their applications for individual grant support. Cores may be proposed to support any research activity of the Center, but usually fall into one of the following categories:

- Collection, storage and distribution of data and samples;
- Provision of specialized tools and technologies or access to specialized expertise;
- Development, standardization, and distribution of reagents and/or protocols;
- Provision of technical assistance, training, and enrichment programs;
- Recruitment of patients and coordination of patient studies;
- Beta-testing and dissemination of specialty assays, methods, and services on an institutional level;

- Increasing interdisciplinary interactions at the institution through cross-project/ laboratory exchange; and
- Sharing of specialized tools, technologies and expertise between collaborating investigators.

Clinical and translational research cores could provide biostatistical expertise for study design and data management and analysis; bioinformatics support; infrastructure for recruiting and managing clinical research subjects and/or tracking and analyzing clinical samples; technologies useful for phenotyping and characterizing subjects or exploring clinical pathophysiology; and expertise for behavioral assessment or intervention.

Regional/National/International Cores: Centers are encouraged to propose Cores that provide unique resources to a community outside the Institution. These could be on a regional level, a national level, or an international level.

Justification for proposing a core: The establishment of and continued support for biomedical research cores within a PCEN must be justified on the basis of use by Center investigators. The minimum requirement is significant usage by two or more principal investigators each with a Center project. While investigators holding awards from the Center's Pilot and Feasibility Program are appropriate users of the Core facilities, their use does not contribute to justification for establishment or continued support of a Core. Additionally, the minimum of two independently funded users does not in itself provide sufficient justification and will receive close scrutiny in review. The organization and proposed mode of operation of each core should be described, with a plan for prioritizing investigator use of the core and criteria for determining core users or potential users.

Each core must have in place a procedure to evaluate efficiency and to maintain appropriate quality control. Limited developmental research is an additional appropriate function of a core facility, so long as the research is related directly to enhancing the function or utility of the core and is not an undertaking that should be funded through other mechanisms. Cores should develop policies and procedures for change as technology progresses. Cores must also have well-defined policies to ensure that intellectual property is identified and appropriately protected, but these issues should not impede the sharing of resources. Teaching the investigators and/or their staff members' new techniques and methodologies is also an important function of the cores. The cores are not intended to supplant investigator capabilities; rather, they are intended to enhance the opportunities of investigators to learn and become proficient in the technologies available through the core.

Personnel: A director must be named for each core. A core director must contribute at least 0.6 person months. A core director with requisite expertise may devote a greater effort to the core and with justification could devote up to 12 person months. Where appropriate, an established expert in the core activities could also be included as a consultant to the core. Technicians, etc., are allowable in accordance with the volume and type of work in the core.

Facilities, space, and special arrangements: Particularly in initial applications, the description of the physical arrangements and instrumentation for each core should be given special attention. In renewal applications, any changes should be carefully documented. Cores

are encouraged, whenever possible, to enter into cooperative arrangements with established cores in other Centers or resources offering a similar type of service. However, it should be clear that the PCEN can function independently.

Recharge System: A recharge system may be developed to allow investigators to utilize any core. Recharge fees are allowable budgetary items in the investigators' individual research project grants. A system of payment management/accounting must be established such that it is clear to the individual users, the institutional business office, and the NIDDK what the recharge system covers and how funds recovered are being used. This will enable Center investigators to appropriately adjust the budgets on their own grants and ensure accountability.

Management of the core: The organization and proposed mode of operation of each core should be presented. A plan for prioritizing investigator use of the core should be included, as well as a definition of qualified users. If use by investigators outside the parent institution is proposed, the mechanism by which such investigators will apply and be evaluated and selected should be detailed. The definition of qualified users should not be too narrow. Any proposed, ongoing, or completed developmental efforts should be described. If the core is used to train investigators in special techniques, the mechanism for this training should be included.

Renewal applications: Information relative to cores in renewal applications should generally cover all of the same points as initial applications. In addition, past performance, usage, and accomplishments should be described. The effect of the service provided by a core on investigator productivity and cost effectiveness should also be addressed.

Individual Research Projects

Criteria for designating an investigator as a PCEN participant should be defined. Subsets of participants based on degree of participation or other measures are acceptable. Each PCEN is encouraged to develop guidelines for PCEN participation by investigators. Individual research projects should be interrelated and may be basic, translational, or clinical in nature.

Pilot and Feasibility Program

Definition: A Pilot and Feasibility (P&F) study provides modest research support for a limited time (one to two years) to enable eligible investigators to explore the feasibility of a concept related to the mission of the Center and generate sufficient data to pursue it through other funding mechanisms. The pilot and feasibility studies are intended to (1) provide initial support for new investigators; (2) allow exploration of possible innovative new leads or new directions for established investigators, and (3) stimulate investigators from other areas to lend their expertise to research in this area. Pilot and feasibility study support is not intended for large projects by established investigators that would otherwise be submitted as separate research grant applications. Pilot and feasibility funds are also not intended to support or supplement ongoing funded research of an established investigator**.**

Requirements: Each Center must contain a P&F program with a minimum of two projects. A maximum of four projects can be requested. The funds for the pilot and feasibility program are included in the budget of the Center within the $750,000 direct cost cap.

Eligibility and related guidelines: Investigators eligible for pilot and feasibility funding generally fall into three categories: (1) new investigators without current or past NIH research support (R01, P01) as a principal investigator (current or past support from other sources should have been modest); (2) established investigators with no previous work in kidney disease who wish to apply their expertise to a problem in this area; and (3) established investigators who propose testing innovative ideas that represent clear departure from ongoing research interests. It is expected that the majority of the investigators will fall into the first category. All eligible investigators, however, must have faculty appointments and be independent investigators. Postdoctoral fellows or their equivalent are **not** eligible. Each pilot and feasibility study proposal should state clearly the justification for eligibility of the investigator under one of the above three criteria.

A proposed pilot and feasibility study should present a testable hypothesis and clearly delineate the question being asked, detail the procedures to be followed, and discuss how the data will be analyzed. It must be on a topic related to the objectives of the Core Center. Projects should be focused, since funding for these studies is modest and is limited to two years. Any one investigator is eligible only once for this support, unless the additional proposed pilot and feasibility study constitutes a real departure from his/her ongoing research.

For new Center applications only, applicants should provide an abstract for each proposed pilot and feasibility project, followed by the biographical sketch of the investigator of the proposed pilot and feasibility project.

Pilot and feasibility projects proposing clinical studies are encouraged. Clinical and Translational Science Awards (CTSA), provide services and resources to enhance clinical research (http://www.ctsaweb.org/). Research Centers supported by the NIDDK are encouraged to collaborate with CTSAs at their institution to avoid duplication of effort and enhance utilization of services and resources.

The application should clearly describe and justify the pool from which potential pilot and feasibility applications will be solicited. This can be limited to investigators at the parent institution or expanded to include investigators at institutions with well-defined affiliation with the Center. The mechanisms by which information on the availability of P&F awards will be disseminated and by which applicants will apply and be selected for these awards must be described and will be an important element in the review of the P&F component of the Center.

Initial review and management of the pilot and feasibility program: By the very nature of this program, a significant responsibility for its management will be left to the Center administration during the project periods. Each Center should include project descriptions for the pilot and feasibility projects they propose to fund. For new Center grant applications, the pilot and feasibility proposals are reviewed for scientific merit and eligibility by the initial review group as an example of the selectivity of their review process. These initial pilot and feasibility studies must have been reviewed by the Center in the manner proposed for review of future studies so that only those considered to be the highest quality are included in the grant application. The recommended budget for the Pilot and Feasibility Program for the first year

will be based on the review of the proposed projects. The budget for future years is recommended by the initial review group, based on the quality of the proposed pilot and feasibility studies and the proposed method for management and review (as evidenced by this set of projects). Also considered will be the review group's evaluation of the future justification for continued pilot and feasibility support.

Since pilot and feasibility studies can be awarded for any period of time up to two years, studies end at various times. In addition, the studies may also be terminated by the Center administration before their approved time limit for various reasons: for example, (1) the investigator may receive outside funding for the project; (2) the project was found not to be feasible; (3) the investigator may leave the Center institution; etc. When this occurs, the Center may make new awards for pilot and feasibility studies with the remaining funds.

While a Center's administrative framework for management of the Pilot and Feasibility Program is basically left up to each Center (subject to NIH peer review), certain minimal requirements must be met. The program must have a director who is an established investigator in PKD research. There must also be a committee representing all the aspects of the Center that will assist the director in the management of the program. The major responsibilities of the director and the committee should be as follows:

(1) Maintain oversight and review of ongoing pilot and feasibility studies.

(2) Make recommendations regarding termination or other actions to the Center Executive Committee (or equivalent).

(3) Prepare and ensure appropriate distribution of announcements of the availability of pilot and feasibility funding.

(4) Arrange and preside over the scientific merit review of proposals. At least one reviewer from outside the parent institution must be used for each proposal. All reviewers should assign priority scores in accordance with the NIH system. Copies of all of the proposals with written documentation of their reviews, priority scores, and final action must be retained by the Center. These records must be made available to reviewers if requested at the time of a renewal application.

(5) Maintain, insofar as is possible, a record of subsequent career events of each pilot and feasibility study recipient. This record must also be made available to reviewers at the time of the renewal application.

(6) Make recommendations to the Center Executive Committee (or equivalent) for final decisions. A record of actions by this committee must be documented and be available if requested by the initial review group.

All applicants should describe how these requirements will be met and have been met in the case of renewal applications. Also included should be an assessment of the relevancy of the proposed

individual P&F studies and of the program as a whole to research on pediatric kidney disease and to the specific goals and objectives of the Center program.

Review of the pilot and feasibility program in renewal applications: After the initial review of P&F proposals as described above, all responsibility for review and funding during the remainder of the project period will reside within the Center itself. This approach provides each Center with the needed flexibility for effective and efficient management of the program. In competing renewal applications, the review of this program will be based on the past track record, the management of the program, and an assessment of overall potential needs and opportunities.

In general, a competing renewal application will include the following:

1) an historical overview;
2) a description of Center management of the program;
3) a description of the method for solicitation for pilot and feasibility projects and the number of respondents received for each solicitation;
4) a listing of all previous, ongoing and approved proposed pilot and feasibility studies with reports on those which were supported by the Center during the last project period; and
5) a statement relating to benefits of the program to the Center as well as the contribution of the uniqueness of the Center environment to the program.

These points are detailed in the following paragraphs.

The historical overview will cover the pilot and feasibility program since the inception of the Center. This should include, in summary format, all pilot and feasibility projects ever awarded. For each project listed, the following should be included:

1) publications as a result of the studies;
2) peer-reviewed funding as a result of the studies; and
3) whether the recipient is still active in the area of pediatric kidney disease.

The P&F program director may wish to highlight certain studies or certain aspects of the past studies. Collaborations that resulted in lasting relationships, acquisition of new skills by the study recipient, or other significant outcomes should be identified. The relationship of the scope of the various studies to that of the Center should be emphasized. Details such as back-up documentation (described earlier in relation to the arrangement of the P&F program) should not be included, but should be available for examination by the reviewers if requested.

The description of center management of the program will present in detail the current system used to manage the P&F program, including its integration with and relationship to the rest of the administrative structure. The use of outside consultants for review should be included in the discussion. Important features of the solicitation process should be provided including the distribution and the number of respondents.

The description of the accomplishments of the P&F program should include a list of all NIDDK-supported pilot and feasibility studies awarded. For each P&F project awarded during the last project period, include a brief report (1-2 pages) containing the following:

1) the name of the investigator, degree(s), professional career status at the time awarded, and current professional career status (if known);
2) an overview of the project including its significance and salient results;
3) a list of resulting publications; and
4) peer-reviewed subsequent funding in the same or related area.

The proposals should be available, if requested by the reviewers.

Funding levels for the pilot and feasibility program on renewal applications: The format for renewal of P&F programs will depend on whether the applicant is requesting: (1) a number of pilot projects less than or equal to that for the previous project period, or (2) an increase in the number of pilot projects.

If the applicant wishes to maintain the same number of pilot projects in a renewal application, the recommendation of the initial review group will be based on the overall performance of the center's pilot and feasibility program as documented in the application. This recommendation will be based on

1) the extent to which awarded funds were fully utilized during the previous project period;
2) whether awards were made to investigators who fully met the eligibility criteria for P&F support as outlined above;
3) Center-relatedness; and
4) the success of previously supported P&F studies (e.g., publications, subsequent independent R01 or other peer-reviewed support, and/or attraction of a new investigator into Center-related research).

Conversely, should the applicant institution feel that an increased level of funding for the P&F program is justified, new P&F studies, over and above the number currently awarded, must be submitted with the competing renewal applications. These proposals would be reviewed by the initial review group in a fashion similar to the review of P&F studies during the initial review. The initial review group would assess the new proposals, along with the overall performance of the program during the previous grant period to arrive at a recommendation for a possible increased P&F funding level.

IV. PRE-APPLICATION PROCESS

It is the policy of the NIDDK that new and competing continuation Center applications are accepted only in response to a Request for Applications (RFA) announced in the NIH Guide for Grants and Contracts. It is strongly encouraged that potential applicants for the Centers submit a letter of intent. The letter should be sent at least one month prior to submission to allow NIDDK staff to identify potential opportunities and problems early in the development of the application. The letter of intent needs to include only the following:

1) names of the principal investigators and principal collaborators;
2) identification of the organization(s) involved; and
3) the announcement to which the potential application is responsive.

The purpose of the letter of intent is to establish communication between the potential applicant group and NIDDK staff. It is not part of the peer review material. Upon receipt of the letter, the appropriate NIDDK program director contacts the prospective principal investigator to assist in a number of areas that include scientific content and objectives, organization, and clarifications. However, applicants should not construe advice given by the NIDDK staff as assurance of favorable review. The staff will not evaluate or discuss the merit of the scientific aspects of the proposal.

V. PREPARATION OF APPLICATION

Description

Applications must be submitted using the most recent PHS Form 398.

Submit the signed original application, including the Checklist, plus three signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Suite 1040, MSC 7710
Bethesda, MD 20892-7710 (U.S. Postal Service Express or Regular mail)
Bethesda, MD 20817 (Express/Courier Non-USPS Service)

At the time of submission, two additional copies of the application and all copies of the appendix material must be sent to:

Chief, Review Branch
Division of Extramural Activities, NIDDK
6707 Democracy Boulevard, Rm. 752, MSC 5452
Bethesda, MD 20892-5452
(for express/courier service: Bethesda, MD 20817)

The arrangement of materials should follow both the instructions in the PHS Form 398 application kit and the more specific guidance detailed below. Applications not in accordance with Center guidelines will be returned to the applicant.

Applicants should keep in mind that the written application is the basis for the merit review. Particular attention should be given to the format of the application. Awards for Center grants will be made only for five-year project periods. Some basic information useful for preparing the application follows. Applicants may also consult with NIDDK staff concerning the technical aspects of preparing the application.

Content Order for Applications

SECTION 1: CENTER OVERVIEW

Face Page, Descriptive Abstract, Key Personnel and Table of Contents should be prepared as per standard instructions.

Budgets
Detailed Budget for Initial Budget Period (PHS 398-Form Page 4)
Budget for Entire Proposed Project Period (PHS 398- Form Page 5)
Consolidated budget for first year of requested support (See Illustration I; budgets for each individual Core should immediately precede the narrative for each Core; budgets for each individual project should immediately precede the narrative for each project)
Distribution of Professional Effort on this Center application (See Illustration II)

Biographical Sketches for all Center investigators in alphabetical order (key personnel, research base investigators, consultants and collaborators)

Biographical sketches for principal investigators on proposed P&F projects should be included within the P&F program section.

Summary of total current and pending support of all Center participants, including professional effort levels. List support related to Basic Kidney Research first, followed by Clinical Kidney Research and then non-Center-related research support. (See Illustration III)

Resources Format Page:
Facilities and Major Equipment: general overall description of research facilities (space, equipment, collaborations, etc.) and the major, shared pieces of equipment to be used by Center members should be provided.
Specific core facilities, equipment, and special resources should also be listed in each core component.

• Specific Aims (limited to 1 page): Provide the broad, long-range objectives and goals of the proposed Pediatric Center of Excellence in Nephrology.

• Research Strategy (limited to 12 pages): This narrative section summarizes the overall plan for the proposed or established multi-component Center. The multi-component application should be viewed as a confederation of interrelated research resources that are complementary to one another. This is an important section for it provides the group of investigators an opportunity to give conceptual wholeness to the overall Center – by giving a statement of the general problem area and by laying out a broad strategy for attacking the problems. As the strategy develops, each individual research component/core should be cited briefly as to its place in the overall scheme. Summarize the special features in the environment and/or resources that make this application strong or unique. If the application is a renewal, the Center Program Overview section should also highlight past performance and the major accomplishments from the prior funding period as described in the PHS 398 Instructions. For Renewals: Changes from the original Center design should be highlighted.

SECTION 2: ADMINISTRATIVE COMPONENT

• Description (PHS 398- Form Page 2)
Key personnel (PHS 398- Form Page 2 cont'd)
Budget with comprehensive budgetary justifications (PHS 398- Form Page 4); funds requested for the P&F and enrichment programs should be included in the "other expenses" category of the budget for the Administrative Core.
Biographical Sketches: Director and Associate Director(s) (PHS 398 Form page)
Specific Aims (limited to 1 page): Describe the broad, long-range objectives and goals of the Administrative structure within the context of the proposed Center.
Research Strategy (limited to 6 pages): Presentation of the administrative structure; Relationship and lines of authority and sanction by appropriate institutional officials; Description of the process that would be used to recommend a successor to the Director, if needed; Committee structure (Internal advisory boards and the pilot and feasibility program oversight committee; include External advisory boards for renewal applications but not for new applications); Description of plans for website development, maintenance and curation; General overall description of facilities and institutional commitment; Other Considerations (include listing of other relevant Centers and cores at the institution and affiliated hospitals, and plans to integrate, harmonize and reduce redundancies in activities)

SECTION 3: BIOMEDICAL RESEARCH COMPONENT

• Overview of ongoing research and impact of Center on this research.

• New applications: Emphasize the anticipated impact of the establishment of a Pediatric Center of Excellence in Nephrology on the research at, and outside your institution. Include an indication of how the establishment of a Pediatric Center of Excellence in Nephrology will provide added dimensions and new opportunities for kidney research, along with increased cooperation, communication, and collaboration among investigators. Discuss how a Pediatric Center of Excellence in Nephrology will add to any resources that may already be provided to kidney investigators by other NIDDK centers at the institution(s).
For Renewals: Progress including description of significant findings and new participants.

Document collaborative efforts by using a format such as in the Guidelines Illustration IV to aid in the review process.

• Biomedical Research Cores (present each core separately; Research Strategy limited to 12 pages per core)

1. Description (PHS 398- Form Page 2)
2. Key Personnel (PHS 398- Form Page 2-cont'd)
3. Budget with justifications (PHS 398- Form Page 4)
4. Biographical sketches: Core Director and key personnel (PHS 398- Form Page)
5. Specific Aims (limited to 1 page): List in priority order, the broad, long-range objectives

and goals of the proposed core. In addition, state the core's relationship to the Center goals and how it relates to the other cores at the applicant institution and in the application.

6. Research Strategy, including: Objectives of the core; Core function, including quality control; Benefits from core; Proposed developmental research or training; Future directions and plans to ensure continuing evolution & relevance of the core; For renewals: Core progress and productivity (include 2-3 examples of literature citations, grant awards, and 2-3 key advances supported by core activity); to assist reviewers, for each core also refer to the page numbers of the individual core-specific research publications in Guidelines Illustration VII; if applicable, describe any recharge system that may be in place to allow investigators to utilize a core, including information on any proposed F&A charges to outside users of the core.
7. New applications: Funded investigators who will use the core and proposed extent of use (see Guidelines Illustration V). For Renewals: Core Use during the last grant period (see Guidelines Illustration V)

- Individual Research Projects (present each separately; Research Strategy limited to 12 pages per project

1. Description (PHS 398- Form Page 2)
2. Key Personnel (PHS 398- Form Page 2-cont'd)
3. Budget with justifications (PHS 398- Form Page 4)
4. Biographical sketches: Project Director and key personnel (PHS 398- Form Page)
5. Specific Aims (limited to 1 page): List in priority order, the broad, long-range objectives and goals of the proposed project. In addition, state the project's relationship to the Center goals and how it relates to the other projects and the cores at the applicant institution and in the application.
6. Research Strategy

• Pilot and Feasibility Program

Description (PHS 398- Form Page 2)

1. Key Personnel (PHS 398- Form Page 2-cont'd)
2. Budget with justifications (included in Administrative Component budget; justify any changes for future years).
3. Biographical sketches: Program Director and Committee (PHS 398- Form Page)
4. Specific Aims (limited to 1 page):
5. Research Strategy (limited to 12 pages): Management of the pilot and feasibility program; Program progress and productivity (include key publications supported by the P&F program, grant awards resulting directly from P&F awards, and 2-3 key advances supported by the P&F program); Future directions and plans; For initial applications include: eligibility requirements, selection process, abstracts of proposed P&F awards, and justification for core usage by P&F awards; For competing renewal applications include: Total number of all P&F submissions received each year during the prior project period, selection process and funding success rates, single paragraph synopses of Pilot & Feasibility studies awarded during the last project period.
6. For Renewals: Pilot and Feasibility Project Outcomes (see Guidelines Illustration VI)

- Enrichment Program (limited to 6 pages, exclusive of form pages)

Description (PHS 398- Form Page 2)

1. Key Personnel (PHS 398- Form Page 2-contd)
2. Budget with justifications (to be included in Administrative Component budget)
3. Biographical sketches: Program director and key personnel (PHS 398- Form Page)
4. Specific Aims (limited to 1 page)
5. Research Strategy (limited to 6 pages): New applications: Describe plans for the enrichment program; Renewal applications: Describe the enrichment program and indicate the program's value to Center members. Indicate how the program has grown or been adapted to better serve Center members' needs during the past funding period; Future directions and plans to ensure continuing evolution and relevance of the enrichment program; Other considerations (include plans to enhance interactions with relevant NIDDK supported T32 training programs; letters of acknowledgment and support from T32 PIs should be provided separately)

SECTION 4: CENTER-RELATED INFORMATION (suggested Illustrations only)

Suggested Illustration for Renewal Applications: Publications Citing Support from this Center during the past project period. List only those publications that clearly used Center resources; do not list all publications from Center members (see Guidelines Illustration VII; include PMCID numbers).

- Checklist (PHS 398- Form Page)
- Appendix (Follow PHS 398 instructions)

VI. BUDGET CONSIDERATIONS

Unless otherwise indicated in the Notice of Grant Award, allowable costs and policies governing the research grant program of the NIH will prevail. The anticipated award will be for five years. The annual direct costs requested may not exceed $750,000. Each pilot/feasibility study is limited to $50,000 per year and a two-year duration of support. An exception to the $750,000 cap will apply to Center applications that include subcontracts. Subcontract facilities and administrative costs are not included in the direct cost cap of $750,000 (Notice OD-04-040; http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-04-040.html). Equipment may be included in the first year of the grant that will not be included in the direct cost cap.

Budget Categories

Professional Personnel: This category may include support for salaries of key personnel within the Center who contribute to allowable activities of the Center. The salaries derived from the Center grant will depend on the effort provided and institutional salary as well as existing NIH policies; however, current NIDDK practice limits annual increments to 3 percent. The Center Director is expected to devote at least 2.4 person months of his/her efforts to the Center. The Center application should include salaries for individual principal investigators only to the extent that they provide an essential Center function. No overlap of time or effort between the Center and separately-funded projects is permitted.

Salaries of professional personnel engaged in research activities supported by pilot and feasibility funds of the Center are an allowable cost item, as are salaries of professional personnel in core facilities.

Technical and Support Personnel: This may include salaries for identified positions to be filled in the Center. No overlap of time or effort between the Center and separately funded projects is permitted.

Equipment: Requests for large equipment costs must include documentation of similar equipment already available at the institution and provide a clear justification in terms of core need and service to Center investigators. General purpose equipment needs should be included only after surveying the availability of such items within the institution.

Supplies: Consumable supplies related to the operation of the Center are allowed and include office materials, as well as scientific supplies, but should not be supplement to separately funded projects.

Research Patient Care Costs: Research patient care costs (both in-patient and out-patient expenses) will be considered in the context of other existing institutional clinical resources. Attempts should be made by the applicant institution to utilize existing clinical facilities, such as CTSAs and individually supported beds. Costs relating to the clinical research efforts of Center investigators may be funded through the Center, provided there is no overlap of funding. Costs already budgeted in individual projects should be appropriately reduced if such costs are to be transferred to the Center budget. The Center is not intended to be a facility for health care delivery; thus, only those patient costs directly related to research activities may be charged to the Center.

Travel: Domestic and foreign travel of project personnel directly related to the activities of the Center are allowable. Travel of Center participants for attendance at annual Center directors meetings is allowable.

Consultants: Consultants and any associated costs (consultant fees, per diem, travel) may be included when their services are required within the Center.

VII. APPLICATION REVIEW INFORMATION

Review Criteria

Overall Impact. Reviewers will provide an overall impact/priority score to reflect their assessment of the likelihood for the Center to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria, and additional review criteria (as applicable for the Center proposed).

Scored Review Criteria - Overall. Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a Center that by its nature is not innovative may be essential to advance a field.

Significance. Does the Center address an important problem or a critical barrier to progress in the field? If the aims of the Center 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? What is the relevance of the separate research projects to the Center objectives and what is the likelihood for meaningful collaboration among Center investigators? What is the potential of the cores for contribution to ongoing research, including their appropriateness, impact, relevance, uniqueness, modes of operation, and suitability of facilities? Do renewal applications document the use, impact, quality control, and cost effectiveness of each core, and demonstrate progress of any developmental research in the cores? Are a minimum of two users (exclusive of Pilot and Feasibility projects) documented for each core?

Investigator(s). Are the PD/PIs, collaborators, and other researchers well suited to the Center? 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? Are the Center investigators responsible for the individual research projects willing to interrelate with each other and contribute to the overall objectives of the Center? What are the scientific and administrative leadership abilities of the proposed Center Director and Associate Director and their commitment and ability to devote adequate time to the effective management of the program? Is appropriate administrative organization proposed for the following:(a) Coordination of ongoing research between the separately projects, including mechanisms for internal monitoring;(b) Establishment and maintenance of internal communication and cooperation among the Center investigators;(c) Mechanism for selecting and replacing professional or technical personnel within the Center;(d) Mechanism for reviewing the use of and administering funds for the P&F program;(e) Management capabilities that include fiscal administration, procurement, property and personnel management, planning, budgeting, and other appropriate capabilities?

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 Center? 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 Center 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? Is there institutional commitment to the program, including lines of accountability regarding management of the Center grant and the institution's contribution to the management capabilities of the Center? Is there clear potential for interaction with scientists from other departments and institutions? Is there efficient and effective use and/or planned use of the limited enrichment funds, including the contribution of these activities in enhancing the objectives of the Center?

Additional Review Criteria. As applicable for the Center proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall priority/impact score, but will not give separate scores for these items.

The following additional review criteria apply to all new and renewal Pediatric Center of Excellence in Nephrology applications.

- Does the researchers to be supported by the Center show evidence of a strong and consistent record of productivity and peer-reviewed funding in Center-related research areas?
- Is the requested budget directly correlated to the breadth, quality and relevance to pediatric kidney disease and related areas of research being served by the Center?
- Do the proposed cores fill a need present in the pediatric kidney research community, and will they provide services that would otherwise be unavailable, or be more cost-effective to conduct centrally? Is the necessary technical and analytical expertise available?
- Does the application demonstrate ability to monitor use and utility of the cores, and provide approaches to ensure continuing development and evolution of services as needs of the community change?
- Do the existing Centers show clear evidence of successful implementation of a recharge structure to support expanded and/or evolving Center activities?
- Do the new proposals document a clear intent to implement a recharge structure to support expanded and/or evolving Center activities?

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, the committee will 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.

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the Human Subjects Protection and Inclusion Guidelines.

Inclusion of Women, Minorities, and Children. When the proposed Center involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children. For additional information on review of the Inclusion section, please refer to the Human Subjects Protection and Inclusion Guidelines.

Vertebrate Animals. The committee will 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 on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section.

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.

Resubmissions: For Resubmissions, the committee will evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Renewals: For Renewals, the committee will consider the progress made in the last funding period.

Biomedical Cores:

- Are the number and impact of papers that acknowledge the Center sufficient to justify each core?
- Is there a significant fraction of papers that acknowledge the Center but do not have core personnel as co-authors?

- Are the number and listing of Center investigators who have used the core and resultant key advances consistent with the level of core investment?
- Do the number and listing of investigators who have used the core multiple times indicate satisfaction and continuing need for core services?
- Are there sufficient numbers of users who are not core personnel or their collaborators?
- Are the number and listing of users who are not Center personnel or members consistent with the best utilization of the core by the community?
- Are the numbers of tests completed for each core indicative of a growing need and sufficient to justify continued support?
- Is the capacity of each core with current resources sufficient to serve the needs of the Center community?
- Does the Center provide evidence of ability to evolve cores to meet changing needs of the research community?
- Does the Center provide evidence of Program Income and sufficient institutional support?
- Does the Center website show evidence of continuing maintenance and a high level of quality and usability?

Pilot & Feasibility Program:

- Are the numbers and types of P&F awards well justified?
- Were papers generated under these awards and key advances linked to these awards well documented and consistent with the level of support provided?
- Did the individual pilot projects lead to independent grant funding?

Additional Review Considerations – Overall As applicable for the Center proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact/priority score.

Foreign Applications — Not applicable.

Select Agent Research Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: 1) Data Sharing Plan; 2) Sharing Model Organisms; and 3) Genome Wide Association Studies (GWAS).

Budget and Period of Support Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

Review and Selection Process

Applications will be evaluated for scientific and technical merit by an appropriate Scientific Review Group convened by the NIDDK , in accordance with NIH peer review policy and

procedures, using the stated review criteria. Review assignments will be shown in the eRA Commons.

As part of the scientific peer review, all applications:
• May undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review), will be discussed and assigned an overall impact/priority score.
• Will receive a written critique.

VIII. AWARD CRITERIA

Funding decisions will be based on the quality of the proposed Center as determined by peer review, overall balance in the Pediatric Center of Excellence in Nephrology program, and the availability of funds.

IX. EVALUATION AND REPORTING REQUIREMENTS

When multiple years are involved, awardees will be required to submit the Non-Competing Continuation Grant Progress Report (PHS 2590) annually and financial statements as required in the NIH Grants Policy Statement.
A final progress report, invention statement, and Financial Status Report are required when an award is relinquished when a recipient changes institutions or when an award is terminated.
The Federal Funding Accountability and Transparency Act of 2006 (Transparency Act), includes a requirement for awardees of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later. All awardees of applicable NIH grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) available at www.fsrs.gov on all subawards over $25,000. See the Statement for additional information on this reporting requirement.

X. SPECIAL CONSIDERATIONS

While each Center will be expected to develop its own program in accordance with local talents, interests, and resources, each must be responsive to national needs to develop new approaches to the prevention, treatment and cure of pediatric kidney disease and must be willing to work with the NIDDK and other organizations in furthering the overall goals of the Pediatric Center of Excellence in Nephrology Program. In this regard, the Center Director and selected other Center participants may be invited to meet periodically with NIDDK staff and its consultants to review progress, identify emerging needs and opportunities, and plan approaches for future investigations.

Within the context of these guidelines, potential applicants for Center grants are encouraged to exercise the flexibility necessary to utilize the strengths of their particular institutions in preparing a plan which will eventually cover the spectrum of required activities. While types of activities that should be included are indicated in the guidelines, specific approaches for their accomplishment are left to the individual applicant.

Because of resource limitations and in light of the size of the Center grants, it is unlikely that NIDDK will be in a position to provide hardship allowances in the event that an application for renewal of Center support is not funded.

ILLUSTRATION I: CONSOLIDATED BUDGET FOR FIRST YEAR OF REQUESTED SUPPORT

Budget Category	Admin	Core A	Core B	Core C	P&F Projects	Total
Personnel						
Consultant Costs						
Equipment						
Supplies						
Domestic Travel						
Foreign Travel						
Patient Care Costs						
Alterations and Renovations						
Other Expenses						
Contractual Costs						
Total						

ILLUSTRATION II: DISTRIBUTION OF PROFESSIONAL EFFORT (calendar months) ON THIS APPLICATION

Participating Investigators*	Admin	Core A	Core B	Core C	Project A	Project B	P and F	Application Total	Other Support
Dr. A.	*1.2							2.4	6.0
Dr. B.		1.2					*1.2	2.4	4.8
Dr. C.	0.6		1.2					0.6	
Dr. D.			1.8	*1.2				3.0	6.6
Etc.									

***Star the calendar months (See Admin) when that individual is the core director or the principal investigator on a pilot and feasibility study. Minimum effort for Core Director is 0.6 calendar months. Minimum total effort for Center Director is 2.4 calendar months.**

ILLUSTRATION III: SUMMARY OF TOTAL CURRENT AND PENDING SUPPORTOF ALL CENTER PARTICIPANTS

Principal Investigator Co-Investigator*	**Supporting Organization and Grant Number**	**Title**	**Project Period**	**Current Annual Amount**	**Effort (Calendar months)**
BASIC KIDNEY RESEARCH BASE Current Support					
Example: Doe, John	**P01 DK00000**	**Murine Models of Kidney Disease**	**4/1/07-3/31/12**	**$500,000**	**4.8**
Smith, Lisa (Doe, John)	**K08 DK00000**	**Nedd4 in ENaC Trafficking**	**6/1/09-5/31/13**	**$75,000**	**6.0**
Jones, Steve	**R01 DK00000**	**Mechanisms of Glomerular Scarring**	**7/1/10-6/30/15**	**$200,000**	**1.8**
Pending Support					
Principal Investigator Co-Investigator	**Supporting Organization and Grant Number**	**Title**	**Project Period Requested**	**First Year Support Requested**	**Effort Requested**

CLINICAL / TRANSLATIONAL KIDNEY RESEARCH BASE
Current Support
(as above)
Pending Support
(as above)

NON-CENTER-RELATED RESEARCH SUPPORT
Current Support
(as above)
Pending Support
(as above)

If co-investigator's name is used, put principal investigator's name in parentheses below.

ILLUSTRATION IV: (FOR COMPETING RENEWALS ONLY) COLLABORATIONS BETWEEN CENTER MEMBERS

	JONES	SMITH	ADAMS	CHU	EVERS	KNIGHT	OLSON	SANDS	TAYLOR	YOUNG	ZANE
JONES	X	*		*	*		*		*		*
SMITH	*	X			*		*				*
ADAMS			X	*			*	*	*		
CHU	*		*	X		*					
EVERS	*	*			X			*			
KNIGHT				*		X				*	
OLSON		*		*			X				*
SANDS			*		*			X		*	
TAYLOR	*		*						X		
YOUNG						*		*		X	
ZANE	*	*					*				X

*Indicates collaboration as evidence by joint publications, abstracts, or research grants or by joint research projects.

ILLUSTRATION V: USE OF CORE FACILITIES

CORE: NAME
Determination/Services Rendered

A.
B.

Users	Funded Projects with Identifying Number	Period of Performance	Determinations/ Services	Estimated Use and Comments
1.				
2.				
3.				

CORE: Transgenic Animals
Determination/Services Rendered

A.
B.
C.
D.

Users	Funded Projects with Identifying Number	Period of Performance	Determinations/ Services	Estimated Use and Comments
			A B C D E	
1. J. Doe	R01 DK00000-00	3/7/97-3/7/98	X X	5 per month for 12 months
				A.
C. 100 per month				
2. L. Smith	K08 DK00000-00	1/4/97-1/4/00		40 per week through 1/4/00
			X	
3. S. Jones	R01 GM00000-00	9/1/01-2/1/02	X	B. A. 16 per week for 6 months

EXAMPLE

ILLUSTRATION VI: PILOT & FEASABILITY (P&F) PROJECT OUTCOMES-FOR RENEWAL APPLICATIONS ONLY

Set up column headings:

P&F Project Number
Investigator (last name, first name)
Department
P&F Funding Dates (MM/YY to MM/YY)
Amount of P&F (direct costs for entire P&F project period)
P&F Project Title
Type of P&F Investigator (New, Established, or New to Diabetes)
Type of P&F Research (Basic, Clinical, Translational)
Publications (# of papers, # of abstracts)
Subsequent Grant Applications Funded (Yes, No, Pending)
Subsequent Grant Number (of the grant received most proximate in time to the P&F award, i.e. for investigators who received funding 5-10 years ago, this will usually not be current funding)
Subsequent Grant Project Period (MM/YY to MM/YY)
Amount of Subsequent Grant Award (Total Direct Costs for Duration of Award)
Still in Kidney Disease Research (Yes, No)

ILLUSTRATION VII: PUBLICATIONS CITING SUPPORT FROM THIS CENTER GRANT (FOR COMPETING RENEWALS ONLY)

Core Number or P&F P.I. Name	Publications	Core 1	Core 2	Core 3	Core 4
1. Doe, J	**Doe, J; Jones, S.; Smith, L. Albuminuria trends in a DCCT cohort AJKD, 2004**	**P**		**S**	
	Doe, J.; Jones, S.; Brown, P. Murine models of Diabetic Kidney Disease. Am J Physiol Renal Physiol, 2003	**P**	**S**		**S**
2. Jones, S.	**Jones, S.; Black, L. Treatment of glomerulonephridites Nature Medicine, 2004.**	**S**	**P**		**S**
	Smith, L.; Jones, S.; Defining FSGS phenotypes AJKD, 2003		**P**	**S**	

List each publication only once under the Core (or P&F Project PI name) most significantly contributing to the work. The Core most significantly contributing to the work should be signified by a P (primary). All other contributing Cores are designated by an S (secondary).