National Center for Research Resources
National Institutes of Health
Department of Health and Human Services

Division of Clinical Research

April 2001

An Administrative Document Issued by the
National Center for Research Resources (NCRR).

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CONTENTS

INTRODUCTION

The National Center for Research Resources (NCRR) is a "catalyst for discovery." Through NCRR, biomedical investigators supported by the disease-oriented institutes of the National Institutes for Health (NIH) can access the resources and technologies they need to conduct research that improves human health.

The diverse research centers and resources supported by NCRR throughout the nation include:

- clinical research and career development, including support for General Clinical Research Centers grants (MO1s), which include supplements for Clinical Associate Physician Awards; Mentored Patient-oriented Research Career Development Awards (K23); Midcareer Investigator Awards in Patient-oriented Research (K24); Small Business Grants (R41, R42, R43, and R44); and Cooperative Agreements (U13, U42);

- biomedical technologies and instrumentation;

- mammalian and nonmammalian models of human disease;

- research infrastructure, including science education, facility construction and renovation, and support to increase research competitiveness of minority institutions and states with limited NIH funding.

NCRR-supported research centers and resources are cost-effective. Each year tens of thousands of investigators share in their use. Moreover, while conducting research at these centers and resources, many investigators enter into collaborations with scientists from other disciplines who have complementary skills and projects. These partnerships not only extend research dollars, but also enhance scientific ideas.

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Guidelines for the General Clinical Research Centers Program (M01)

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GUIDELINES FOR CLINICAL RESEARCH PROGRAM
of the National Center for Research Resources, National Institutes of Health

I. DIVISION OF CLINICAL RESEARCH

The Division of Clinical Research (DCR) of the National Center for Research Resources (NCRR) includes three complementary sets of programs: 1) a national network of General Clinical Research Centers (GCRCs); 2) a portfolio of regional and national research resources to foster clinical research; and 3) a portfolio of programs to enhance career development in clinical research. The NCRR Division of Clinical Research has been assigned the number 93.333 in the Catalog of Federal Domestic Assistance. GCRC grants carry the activity code, "M01."

II. GENERAL CLINICAL RESEARCH CENTERS

Medical institutions with clinical investigators supported with peer-reviewed funds from NIH and other sources are eligible to compete for a GCRC award to facilitate patient-oriented research in a cost effective approach. Most institutions with NCRR-funded GCRCs are affiliated with medical schools but institutions of higher learning that are devoted to medical research may also apply. Inpatient and outpatient areas of the GCRC must be located in facilities either accredited by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) or certified to accept Medicare and/or Medicaid reimbursement. Academic institutions are encouraged to assign the GCRCs a central, leadership role for all of their patient-oriented research. GCRCs are encouraged to host qualified investigators from other nearby institutions that do not have such a facility.

The GCRCs may host pilot studies that may lead to future NIH or other sources of peer-reviewed clinical research grant support. GCRC configurations vary from site to site and reflect the research needs of investigators. An institutional GCRC may include inpatient and outpatient facilities, and core or other resource laboratories for radioimmunoassays, mass spectroscopy, cell sorting, imaging, sleep studies, and more. The investigations carried out in the GCRCs can include studies of normal and abnormal human physiology and studies of the cause, prevention, progression, control and cure of diseases that afflict individuals of all ages and ethnic backgrounds. Collaborations between basic and clinical scientists are encouraged. The GCRCs also provide a unique environment for mentored training of health professionals in issues related to patient-oriented research.

The essential feature that is common to all GCRCs is the broad range of patient-oriented scientific inquiry. Investigators from research disciplines including medical subspecialties, bioengineering, and the basic sciences are encouraged to take full advantage of research advances including the rich databases containing important new data on the human genome and novel imaging technologies. Because of the nature of the GCRCs, no single group of investigators or categoric research area may dominate the utilization of the GCRC or use more than one third of

the GCRC resources, except for AIDS studies. In unusual circumstances, a research discipline may temporarily exceed that limit.

Because each GCRC is designed to support the investigator-initiated, peer-reviewed, clinical research projects within the institution, the configuration and available resources of the respective GCRC vary according to the research needs of the investigators. Consequently, either the inpatient or the outpatient activities may predominate in a GCRC. All studies must adhere to the NIH policies regarding inclusion of women, minorities and children, federal regulations that relate to human subject research (45 CFR 46), and FDA regulations and policies. The priorities of the research to be performed at each GCRC are determined by the local GCRC Advisory Committee (GAC). This committee also anticipates future needs for clinical research within the institution and proposes new initiatives.

The GCRC Program allows flexibility in the design, accessibility, and scope of research. This facilitates rapid initiation of new and novel protocols and pilot studies. The GCRC Program provides financial support for the components essential to clinical research: operating expenditures, hospitalization and ancillary laboratory costs, and salaries of key personnel including nurses, research bionutritionists, administrators, core laboratory staff, biostatisticians and computer personnel. Funds for renovation and equipment may also be provided.

A. Inpatient Area:

The inpatient facility of a GCRC is usually located within a physically discrete unit that contains inpatient rooms and research beds. It may also include administrative offices, a laboratory, research bionutrition area, computerized data analysis facility, and other supporting services required to perform high quality clinical research. Ideally, the GCRC is in close proximity to other established patient care units. Supported inpatient research may also include studies conducted in other "scatter-bed" areas such as psychiatric wards or intensive care units.

B. Outpatient Area:

Clinical research that involves outpatients frequently complements or provides an alternative to inpatient investigations. This type of research may be performed in one of several locations on the inpatient unit, in a separate dedicated GCRC outpatient area, in a regular hospital outpatient clinic or in another discrete area assigned for GCRC use on a *pro rata* basis. Staffing and space allocations depend on the scope and complexity of the outpatient investigations.

C. Core Laboratories:

The primary functions of a Core Laboratory are to provide sophisticated support to ongoing GCRC protocols and to develop or validate new methods for this purpose. In addition, the laboratories may provide clinical research training for investigators, fellows, students, and technicians.

Core Laboratory requirements vary widely. Some GCRCs may not need a full Core Laboratory, rather only a small sample-processing area. In general, however, laboratory equipment, supplies, and personnel are supported through the GCRC grant when it has been documented that they will serve several investigative groups. Under special circumstances, a test for a single group of investigators may be supported if it is within the Core Laboratory's capabilities and is critical to conduct an investigation of high scientific merit and program relevance.

In general, routine tests, such as blood chemistries, hematologic determinations and urinalyses, that are available in the hospital's clinical chemistry laboratories or in another Medicare-approved clinical chemistry laboratory are not performed in the GCRC Core Laboratory, but rather supported through ancillary funds. However, such tests may be performed in the GCRC Core Laboratory when this is critically important for timeliness, when an extreme degree of accuracy is needed, or if patient safety is at stake. Whenever possible, cost sharing of Core Laboratory functions should be sought from the investigators.

Core Laboratories include laboratories performing radioimmunoassays, but may also include, depending on the needs of the GCRC, specialized laboratories for, for example, exercise physiology and body composition, mass spectroscopy, magnetic resonance imaging, ultrasound, positron emission tomography, tissue culture, cell biology, molecular genetic analyses of DNA obtained from patient material, and/or cell and gene therapy.

Core Laboratories are encouraged to share their specialized expertise with other GCRCs. Records of such services and collaborations should be kept, as they may be helpful in justifying continued support of the laboratory. See below (Section IV-G-11) regarding Program Income.

The GAC is responsible for reviewing the Core and other resource Laboratories to assure that the activities are serving the research needs of a wide array of investigators, that laboratory tests are not routine, and that priorities are set for the use of the Laboratory when concurrent demands exceed the Laboratory's capacity. In all cases, NIH-supported investigations are to be given the highest priority.

D. Informatics Core:

A clinical investigator must be able to publish his/her scientific findings. This requires that data be (1) collected accurately, (2) monitored appropriately, (3) secured, (4) managed effectively, and (5) accessible for analysis and reporting. The mission of the Informatics Core is to provide the information infrastructure necessary to accomplish this.

For a GCRC to be successful and efficient, information flow between the GCRC Cores must be both timely and accurate. The Informatics Core interacts with the other GCRC Cores, integrating the information needs of the Center. The Informatics Core should facilitate the secure and confidential sharing of scientific data between research centers. The Informatics Core should provide leadership in exploring and implementing new technologies to stimulate and promote

clinical research. The Informatics Core should provide education and training in the use of information technologies and research data management to the GCRC staff and research teams.

The requirements of the Informatics Core will depend both on the specific needs of the GCRC and the existing institutional resources. In all cases, each Informatics Core should have a file server to comply with current and anticipated NCRR bioinformatics goals to communicate within and between GCRCs. The file server should meet standards for the secure storage, archiving, management, and analysis of protocol data. A network should be in place to facilitate GCRC operations and investigations associated with all GAC approved studies. The Informatics Core should insure that GCRC network facilities are accessible to all GCRC Core components and promote the adherence to data management standards. The Informatics Core should also provide or facilitate ongoing training and education in the use of its resources.

The GAC is responsible for reviewing the Informatics Core activities to ensure that the research needs of a wide array of investigators are being served. The GAC will prioritize the use of the Informatics Core resources when concurrent demands exceed capacity, with NIH-supported investigations being given the highest priority. Initiatives which might have a substantive impact on the Informatics Core should be presented to the GAC for review and approval.

E. Bionutrition Research Area:

A GCRC Bionutrition Research Area is supported to provide the controlled dietary regimens for either GCRC inpatient or outpatient studies. However, not all GCRCs require a Bionutrition Research Area. A cost effective means to provide meals should be used, outsourcing when appropriate. The Bionutrition Research Area may function as an important resource to train medical and paramedical personnel.

F. Principal Investigator:

The Principal Investigator (PI) of a GCRC derives no salary support from the grant and is an individual whose authority transcends departmental lines--for example, the Dean of the medical school. Requests for an exception will be reviewed on a case-by-case basis. The PI has the ultimate responsibility for the administration and operation of the GCRC, and is the person with whom the NIH communicates on broad institutional matters relating to the GCRC grant. The GCRC Program Director, National Center for Research Resources (NCRR), should be notified immediately in writing when a change in PI is planned. The letter should include the curriculum vitae of the proposed individual. The PI appoints the Program Director (PD) and members of the GAC (see Section II-G) and is responsible for the development of the GCRC as an institutional resource. Should the PI determine that a new PD is needed for the GCRC, it is his/her responsibility to seek approval from the GCRC Program Director, NCRR, for such a change. This request should be accompanied by a current curriculum vitae, and information regarding existing sources of peer-reviewed research support. All requests are to be cosigned by the authorized institutional business official and the PI.

G. Institutional GCRC Advisory Committee (GAC):

The GAC usually consists of 8 to 12 members, appointed by the PI, on a rotating basis. This Committee is responsible to the PI. It should be composed of a cross-section of the faculty members who are familiar with the broad elements of the GCRC research activities. The GAC shall not be chaired by the PD or Associate/Assistant PD. Individuals in Program Directorship positions shall not be voting members of the GAC. The GAC supervises and reviews the operations of the GCRC, its Core Laboratories, and Informatics Core; sets general policies; delineates common needs of the GCRC investigators; establishes admission policies; and evaluates projects for GCRC use. Studies on the GCRC must have GAC approval prior to initiation, except when temporary approval has been given by the PD or his/her designee and the Institutional Review Board (IRB) for urgent studies created by an unexpected opportunity to study unusual research patients.

The GAC should prioritize projects for GCRC use prospectively to assist the PD in allocating resources. In all cases, NIH-funded clinical research must be given preference. The GAC is responsible for assuring implementation of existing NIH policy on the inclusion of women, minorities, and children as study subjects and the policy regarding approval of data and safety monitoring plans for Phase I and Phase II clinical trials. The GAC must also designate for each protocol, the category of inpatient research days and outpatient visits as Category A, B, or D (see Sections II-N and IV-G). For appropriate classification of industry-related projects, the GAC must review copies of the research agreement between the investigator and industry, an itemized budget, and other relevant correspondence, detailing the drug, or other therapeutics or devices supplied. All these reviews should be appropriately summarized in the minutes of the GAC meeting.

The GAC should periodically review GCRC operations to ensure that GCRC resources are used for the most scientifically justified and relevant projects. It should also encourage junior faculty members to perform clinical research and assist them in applying appropriate concepts and methods. Meetings of the full GAC should be held at least quarterly, and detailed records must be kept. The minutes of the GAC meetings are examined at the site visit when the GCRC grant application is reviewed. The GAC may form subcommittees to carry out some of its functions. These may include the review of biostatistical design of projects, ethical concerns, and the assignment of priority scores based on scientific merit as well as their need for GCRC resources.

The GAC should include a biostatistician both to assist with the review of project design and to optimize subsequent data analyses.

H. Institutional Review Board for Human Research:

All research projects conducted in the GCRC must be reviewed and approved by the IRB to ensure protection of the rights and welfare of research subjects (see 45 Code of Federal Regulations 46). 45 CFR 46.110 allows expedited review for certain kinds of research. The

Office for Human Research Protections is responsible for the oversight and implementation of 45 CFR 46. The composition of the IRB and its attendance records and minutes are examined at the site visit when the GCRC grant application is reviewed. All research projects must be approved by the IRB as well as by the GAC. The IRB is also responsible for the implementation of the NIH policies of inclusion of women, minorities and children in all protocols, where appropriate. The activities of the Data Safety and Monitoring Boards also need to be coordinated through the IRB. If the IRB becomes aware of information that would bear on the safety of a GCRC protocol, it is incumbent upon the IRB to re-review that protocol. Likewise, it is the investigator's duty to notify the IRB of any new information that is considered to be relevant to the safety or efficacy of a GCRC protocol for which he/she is responsible. Documentation of IRB approval of protocols, as well as copies of currently approved consent forms, must be maintained in the GCRC administrative files. "IRB approval" means full, final IRB approval including IND assignment from FDA if an IND is required.

I. Grant-Supported Personnel:

The personnel positions which may be supported by GCRC grants are listed below (see Section IV-B for allowable costs). The number of positions supported in each category depends upon the size and complexity of the GCRC as recommended by the NIH peer review system and set by program priorities. No portion of the salary of the PI may be supported by the GCRC grant.

1. Program Directorship: The PD is a senior physician-investigator and a medically licensed, full-time member of the institution's faculty who derives a portion of his or her salary from the GCRC grant for administration of the GCRC. The PD reports to the PI, and works closely with the GAC. Furthermore, the PD should be a productive clinical investigator who holds independent peer-reviewed research support and has active GCRC-based protocols. In the event that a PD loses all independent peer-reviewed research support, up to two years will be allowed for submission of grant applications and subsequent funding. If the PD still does not have independent peer-reviewed research support by the end of that time, the PI must nominate a new PD. "Independent peer-reviewed research support" as described herein, is not limited to NIH support; other sources of peer-reviewed support will satisfy this requirement.

The PD's activities include supervision of GCRC nursing, bionutrition, paramedical, and administrative staffs, and the organization and operation of the Core Laboratories, Informatics Core, and Bionutrition Research area. The PD must be familiar with all research projects conducted on the GCRC, and assure that the research is carried out as approved by the local IRB. Support for a PD from the GCRC grant is ordinarily limited to a maximum of 0.50 full time equivalent (FTE). Requests for an exception will be reviewed on a case-by-case basis. The PD should provide a focus through which clinical research skills are taught to medical students, house staff, fellows, Clinical Associate Physicians (CAPs), K23 awardees and other junior faculty members. In addition, the PD is expected to be an expert clinician who can command respect and instill the highest standards of clinical research and medical care in the GCRC staff and investigators.

Most GCRCs will require additional administrative oversight from Associate and/or Assistant Directors. The Associate PD should be a licensed physician and full-time faculty member who is currently conducting research on the GCRC and holds peer-reviewed research support. Support provided to an Associate PD from the GCRC grant may reach a maximum of 0.50 FTE, as long as the individual is either a principal investigator or co-investigator on a NIH grant or other significant source of peer-reviewed funding. If an Associate or Assistant PD loses all peer-reviewed grant support, that individual will be allowed two years to become a principal investigator or co-investigator of a peer-reviewed grant. If the individual is unsuccessful at the end of that time, either a new Associate PD shall be appointed, or the level of support from the GCRC grant reduced to 0.25 FTE or less. An Associate PD usually assists the PD in the administrative oversight of the Center; this includes the quality of inpatient and outpatient medical care, nursing, paramedical, Core Laboratory, and research bionutrition staffs. The Associate PD may supervise an inpatient or outpatient satellite facility apart from the main GCRC and commonly assists the PD in teaching clinical research methods to medical students, house staff, fellows, and faculty. The total level of Program Directorship reflects the level of GCRC research activity and its complexity.

2. Administrative Support: The Administrative Manager is a skilled specialist, responsible to the PD for the day-to-day management of GCRC administration, fiscal matters and records of GCRC activities. He or she maintains the statistical and financial data needed by the grantee institution and the NCRR Office of Grants Management and for Annual Reports to the GCRC Program, NCRR. In the interest of GCRC efficiency, the PD may delegate some administrative authority in non-scientific and non-health care delivery matters to the Administrative Manager.

If warranted by the size of the GCRC, a full- or part-time Administrative Assistant may be supported to perform duties related to GCRC operations such as maintaining GAC meeting records and consent forms. Administrative Assistants are not supported from GCRC funds to prepare renewal applications or to provide support for developing scientific publications for the Program Director or other investigators. In general, Facilities and Administrative (F&A) costs provided to an institution by the grant support clerical assistants who prepare grant applications and manuscripts for publication.

3. Core Laboratory:

a. <u>Core Laboratory Director</u>: A Core Laboratory Director may supervise the Core Laboratory operations if the scope and sophistication of the laboratory procedures justify such a position; otherwise, the laboratory is supervised by the PD or Associate PD, often through a senior laboratory technician. A Core Laboratory Director is an individual with an advanced degree who may also provide training in sophisticated laboratory techniques to GCRC-based investigators, their laboratory personnel, junior faculty or fellows. This position usually requires only a small fraction of an FTE. A larger portion of a Core Laboratory Director's time may be required in the initial establishment of complex laboratory procedures, with a smaller fraction of

the Laboratory Director's time being required for routine laboratory activities. When there are multiple Core Laboratories with different functions (e.g., radioimmunoassay core, mass spectrometry core), the GCRC grant may support a fraction of an FTE for the Director of each.

b. Core Laboratory Personnel: The Core Laboratory staff must possess the expertise needed to provide reliable and accurate analyses required by GCRC research activities.

c. Quality Control and Confidentiality: The GAC must assure that quality control and confidentiality are maintained in compliance with existing Federal and local requirements, such as the Clinical Laboratory Improvement Act.

4. Nursing:

a. Head Nurse/Nurse Manager: The Head Nurse/Nurse Manager is responsible for the administrative organization of the GCRC nursing staff (cost effective staff distribution), training, patient care delivery, and interaction with investigators to assure that research projects are carried out as approved by the IRB and the GAC. The Head Nurse/Nurse Manager should have a Bachelor of Science degree in Nursing, must be licensed within the state and have staff privileges within the hospital wherein the GCRC is located. GCRCs which have many complex projects or a large number of outpatient research visits may require an Associate Head Nurse/Nurse Manager to assist in providing the research patient care needs. That individual should have an educational background and nursing experience comparable to that of the Head Nurse/Nurse Manager of the GCRC.

b. Nursing Staff: The GCRC nursing staff should be trained to make complex research observations and perform precise collections of specimens, while providing exemplary patient care. The staff should be assigned exclusively to the GCRC and not be assigned to duties outside of the GCRC. For the same reason, nurses who are not regular members of the GCRC staff should be assigned to the GCRC only in emergencies. The professional level and number of nursing personnel required for a GCRC are determined by the size of the unit, the number of research inpatient days and outpatient visits, and the complexity of the research and medical care performed on the GCRC. All nurses must be licensed and have staff privileges either at the

hospital in which the GCRC is located or satellite or scatter bed unit. Except for the smallest centers, support of either a full-time or part-time Ward Clerk, Unit Manager or Unit Secretary is appropriate.

5. Bionutrition Research:

a. Bionutrition Research Manager: Those GCRCs that have metabolic or other protocols that demand sophisticated nutritional support may justify a position for a Bionutrition Research Manager. This person should have a Bachelor's degree and be a registered dietitian, R.D.. The Bionutrition Research Manager oversees the GCRC dietary staff and works closely

with both the nursing staff and physician-investigators. Up to 1.0 FTE may be supported.

b. Nutrition Staff: The preparation of controlled diets for research subjects requires special skills and meticulous attention to detail. To provide the research subjects and investigators with optimal service the bionutrition staff should be assigned exclusively to the GCRC. The staff number and professional level are determined by the nature of the research, the number of research patients requiring dietary control, and the complexity of the nutritional studies.

6. Informatics Core: The Informatics Core Manager is responsible for its overall operation. Due to the evolving nature of information technology, the Informatics Core Manager should work closely with the PD to ensure that current technologies are employed to meet the GCRC's goals. The Informatics Core Manager should be competent to assist in the organization and analysis of research data and be familiar with the broad array of basic methods of data analyses. He/She must ensure that the tasks necessary to achieve the goals of the Informatics Core are implemented, including:

a. Work with GCRC investigators to design and develop methodologies that meet accepted standards for research data management.

b. Instruct GCRC staff and investigators in the use of Informatics Core resources.

c. Facilitate the dissemination of information within and outside of the GCRC.

d. Work with the biostatistical staff on GCRC-approved protocols.

e. Ensure the proper operation and maintenance of GCRC computer hardware and software.

f. Develop and maintain a strategic plan for the Informatics Core.

The minimum qualifications for the Informatics Core Manager include a Master's degree or formal training in research methods and 2 years of experience in application development or computer/network management.

Additional Informatics Core staff may be employed when needed to fulfill the goals of the Informatics Core**.**

7. Biostatistician: The GCRC Biostatistician should hold a doctoral degree in biostatistics or statistics, or have comparable training and experience. The GCRC Biostatistician should have experience in the planning, design and evaluation of clinical research. The GCRC Biostatistician reviews all protocols and is a voting member of the GAC. The GCRC Biostatistician consults, and may collaborate, with investigators on study design, implementation,

analysis, interpretation and dissemination of results. He/She should develop new statistical methods as needed for specific projects and train clinical researchers in the principles of study design and analysis. Total support of up to 1.0 FTE will be provided to a GCRC for this individual or other biostatisticians working under his/her direction.

8. Clinical Associate Physician (CAP) and K23 Programs: See supplement II of these Guidelines regarding the CAP and K23 programs for mentored patient-oriented career development. Previously CAPs were funded as competitive supplements to the parent GCRC (M01) grant. The K23 mechanism has now replaced those supplements and funds new applicants directly.

9. Medical and Dental Students: The GCRC grant may provide support for a "Mentored Medical Student Clinical Research Program" whereby a medical student could take time off from medical school to engage in a mentored program of up to one year of supervised participation in clinical research, didactic coursework related to patient-oriented research, and/or acquisition of laboratory skills that can be applied to patient-oriented clinical research efforts. Support from the GCRC grant (to be phased in) may support up to five students per GCRC per year, at a salary of up to $20,000 each, plus up to $5,000 for other relevant expenses. Selection of the recipients should be based on a competitive review by the GAC or another committee constituted for this purpose. Information about the activities of students supported from these funds is required in the GCRC Annual Reports. The GCRC may rebudget, with institutional prior approval, unrestricted GCRC grant funds for this purpose. The GCRC may also request additional funds for this purpose. In the latter case , the GCRC site is to provide NCRR Division of Clinical Research its guidelines including: eligibility of students and mentors; as well as selection criteria of the student-mentor pair, and the student's plan for research, didactic coursework, and/or acquisition of laboratory skills. The evaluation plan of the local program is also to be provided. Subsequent support for this program will be reviewed as part of the competitive renewal of the parent GCRC grant.

10. Research Subject Ombudsman (RSO): The GCRC grant will include funding for a position which may be called "Research Subject Ombudsman" or "Data and Safety Monitor" or another similar title. The RSO will be directly responsible to the Principal Investigator of the GCRC grant. The RSO will be responsible for ensuring that the GAC-approved data and safety monitoring plan for Phase I and Phase II clinical trials is fully implemented, that the research carried out on the GCRC is in compliance with the IRB-approved protocol, and that serious adverse events are reported in a timely fashion to the IRB and appropriate Federal agencies. In addition, the RSO may serve as a source of information for patients or volunteers participating in GCRC studies. The PI of the GCRC may also request that the RSO monitor all GCRC-based research subjects.

The RSO is to have appropriate training and experience within the clinical research arena. The RSO may hold an M.D. degree, but appropriately trained Ph.D.s, pharmacists, or research nurses also qualify. Responsibility assigned to the RSO may be divided among two or more qualified

individuals, depending on the size of the research portfolio at the GCRC site, and its satellites. However, one individual must be designated as the Principal RSO. In addition, the GCRC grant may support a part-time Program Administrative Assistant to assist the RSO.

As this is a new program beginning in FY 2001, initially GCRCs may request support for this position through a request for an administrative supplement in a letter signed by the Principal Investigator and Business Official. Subsequently the request should be in the type 5 (non-competitive) or type 2 (competitive) renewal application.

J. Provisions for Medical Care:

1. General: All GCRC research subjects must receive optimal medical care. It is the responsibility of the principal investigator of the project to assure that appropriate medical care is provided to research subjects participating in his or her research proposals. This responsibility may be discharged either personally if the principal investigator is a physician, by a physician co-investigator, fellow, resident or other physician who possesses the requisite clinical expertise, admitting privileges, and is familiar with the protocol. This individual must be named in advance of implementing the protocol. Responsibility for protocol design, authorship, and like issues resides with the principal investigator; however, for reporting purposes, the physician who provides medical coverage should be identified on the protocol in new and competing GCRC grant applications and in the GCRC annual report. Arrangements for emergency and night care must be formalized. House officer coverage is desirable.

2. Intercurrent Illnesses: The appropriate disposition of a patient who develops an illness during the course of study depends on the severity of the illness and its relationship to the research. The patient may be treated on the GCRC when the illness is unrelated to the research but is anticipated to be of short duration. If the intercurrent illness requires termination of the studies or their interruption for a substantial period of time, other arrangements for the patient's care should be made.

K. Data and Safety Monitoring Plans:

In 1998, NIH issued a document entitled, "NIH Policy for Data and Safety Monitoring." It is available electronically at http://grants.nih.gov/grants/guide/notice-files/not98-084.html. It describes the NIH policy for data and safety monitoring of clinical trials.

In June, 2000, NIH issued a document entitled, "Further Guidance on a Data Safety and Monitoring For Phase I and Phase II Trials." It is available electronically at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html. This document indicates that for Phase I and Phase II clinical trials a data and safety monitoring plan "must be . . . reviewed and approved by the funding Institute and Center (IC) before the trial begins."

In considering this requirement for GCRCs, one should first note that as described in other NIH

documents located at http://crisp.cit.nih.gov/crisp_FAQ.html and http://www.nih.gov/news/crp/97report/execsum.htm, "clinical trials" are only a subset of "clinical research." Those GCRC projects which are clinical research (patient-oriented research) but are not clinical trials are not required by http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html to have a data and safety monitoring plan.

A definition of Phase I, II and III clinical trials is given by the Food and Drug Administration in the Code of Federal Regulations at 21 CFR 312.21. NIH definitions of Phase I and Phase II clinical trials are located at http://crisp.cit.nih.gov/crisp_FAQ.html and at http://clinicaltrials.gov/ct/gui/c...ServSessionIdcs_current=qpno7v4azh. Most clinical trials conducted on the GCRCs receive their primary funding from other NIH Institutes or Centers (ICs). In these cases, it will be the responsibility of that funding IC to approve the data and safety monitoring plan.

For that subset of GCRC projects which are clinical trials but which do not receive their primary funding from another NIH IC, NCRR has received a waiver from the NIH Office of the Director, whereby approval of the data and safety monitoring plan by NCRR is not required; rather, approval authority is delegated from NCRR to the institution receiving the GCRC grant, and the local Institutional Review Board and GCRC Advisory Committee replace the NCRR for approval of the data and safety monitoring plan.

The GCRC Advisory Committee is to maintain a log of the minutes that relate to their review of the data and safety monitoring plans for proposed Phase I and Phase II clinical trials, not sponsored by another NIH component, to be performed on the GCRC. Those minutes may be reviewed by NCRR or other NIH program staff who are responsible for oversight of specific clinical trials conducted on the GCRC. In addition, GCRC program staff or members of the site visit team may request access to the log during the competitive renewal process of the GCRC.

L. Reporting Serious Adverse Events (SAEs):

In the Code of Federal Regulations at 21 CFR 312.32, FDA defines the term "Serious Adverse Drug Experience" and requires that FDA be notified of "any adverse experience associated with the use of the drug that is both serious and unexpected." Some GCRC protocols are subject to this FDA mandate.

45 CFR 46 (the portion of the Code of Federal Regulations dealing with Protection of Human Subjects) - which is applicable to all studies on the GCRC - states that there shall be "prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head of any unanticipated problems involving risks to subjects or others."

Whenever a gene transfer protocol conducted on the GCRC results in a report to FDA of a serious unexpected adverse experience or a report to the IRB of an unanticipated problem involving risks to subjects or others, a copy of that report should be sent at the same time to: the

Office of Biotechnology Activities, NIH; the Division of Clinical Research, NCRR; and the categorical NIH Institute (e.g., NCI, NIAID) supporting the study. In all such SAE reports to NIH, no names or other patient identifiable material should be included.

M. Training and Career Development:

The training of health professionals in the methods of clinical investigation should be an integral part of the research effort on every GCRC. The GCRC should serve as the institutional focus for training in clinical research methodology, bioethics, biostatistics, clinical trial design, epidemiological studies and basic laboratory methods. Formal courses may be set up for this goal and include NRSA fellows and trainees as well as CAPs, K23 awardees, and junior faculty.

Regular rotation on the GCRC by research fellows, house officers, and medical, nursing, and dietary students is encouraged. Because GCRCs are expected to represent models of excellence in current clinical research techniques, they may also be used for other instructional purposes, including programs of continuing education for practicing physicians, nurses and dietitians. These activities, along with the use of the Core Laboratory for training in research methodology, are the responsibility of the PD but may be delegated to an Associate or Assistant PD.

Each student or postdoctoral fellow who participates in research on a GCRC must have a qualified mentor identified in GCRC records. This supervisor, typically the principal investigator of the protocol on which the trainee is working, is responsible for the medical and scientific quality of the work performed by the trainee.

N. Annual Reports:

Each grantee institution is required to submit an Annual Report of scientific progress and an annual Financial Status Report (FSR) within 90 days after completion of the grant year. These reports are reviewed by NIH staff and are used for planning and evaluation. Through these reports, the NIH staff is kept apprised of current research activities and accomplishments at each GCRC for Congressional reports and budget justifications and for other reports.

O. Credit on Publications:

All publications that result from utilization of any of the GCRC resources (e.g., inpatient area, outpatient area, Core Laboratory, Informatics Core) should cite the grant as a contributing source of support and indicate the GCRC grant number, including the prefix "M01RR." Publications crediting the GCRC grant should be approved by all listed co-authors. Each GCRC must maintain a current and complete bibliography of GCRC-related publications for inclusion in its Annual Report, and for program-wide inquiries of scientific accomplishments. It is recommended that GCRC scientific and administrative records be retained for at least five years.

P. Industry-Sponsored Research:

GCRCs are sometimes used for projects funded in whole or in part by for-profit organizations. Investigator-initiated projects which are partially supported by such an organization through a grant of unrestricted funds or by a donation of drugs or devices may be pursued on the GCRC in the usual manner, subject to the usual IRB and GAC review and approval. Funds from the proprietary organization which are budgeted for research patient care must be credited to the patient care category of the GCRC grant if the GCRC is used. Copies of the agreement with the drug company or other source must be maintained in the GCRC's administrative files. In addition, copies of other relevant correspondence, along with the Food and Drug Administration (FDA) letter assigning an Investigational New Drug (IND) number and approval for initiation of studies with any relevant experimental drug or device, are to be maintained in the GCRC's research project files.

Those projects which are designed by for-profit organizations will be considered industry initiated. That organization is expected to pay for the use of the GCRC facilities at the same rates that it would pay for any other hospital beds and ancillary charges at that institution. This can be accomplished by classifying research subjects in such projects as Category D patients (see Section IV-G). All Category D patient charges are to be paid to the hospital from funds provided by the commercial organization. In some cases, investigators may add additional research aims to the project. In that case, the GAC ascertains the relative resource needs to be contributed by the company, GCRC, and investigator's resources. All industry-initiated projects must be approved for use of the GCRC by the GAC. Industry-initiated projects should constitute only a small portion of total GCRC activity. In some cases, a commercial organization may provide clinical research funds for an investigator-initiated study. If investigator-initiated, the research project is appropriately classified as Category A or Category B rather than Category D. The funds provided by industry are to be credited to the patient care category of the GCRC grant.

The determination of whether a research project is industry-initiated or investigator-initiated is to be made by the GAC, using the above general principles after reviewing the appropriate documents. Deliberations are to be documented in the minutes of the GAC. Investigators who are receiving industry support for projects conducted on the GCRC must be free to publish or distribute data from such studies without restriction.

Q. Clinical Research Feasibility Funds (CReFF) Program:

GCRC grant funds may be used to support pilot studies. A GCRC may rebudget unrestricted GCRC grant funds for this purpose.

A GCRC may also request additional funds for a CREFF program. In such a case, the GCRC must establish and submit to NCRR, guidelines for: eligibility; selection criteria for candidate investigators and projects; and a plan for evaluating success. Eligibility would be limited to junior faculty - ranks equal to or less than assistant professor - or senior faculty only if they have a change in research career path. Recipients will be required to prepare a final report. Such

requests for CREFF additional funds should undergo review first by the local GCRC Advisory Committee and then by NCRR. The CREFF awards could be up to $20,000 for one-year renewable projects; each GCRC would be limited to $100,000 annually (to be phased in). Subsequent support of the CREFF program will be reviewed as part of the competitive renewal of the parent GCRC grant.

III. PHYSICAL FACILITIES

A. General:

The design of a GCRC must facilitate the proper conduct of patient-oriented investigations. Usually the GCRC is geographically discrete and adjacent to a routine hospital patient care area/unit. It should include adequate space that enables research operations to be performed in an optimal manner. While regular patient traffic routes should not traverse the GCRC, the GCRC should be located close to other patient care areas if possible, so that clinical services and emergency care are readily available. The GCRC must be in a facility accredited by the JCAHO or certified to accept Medicare or Medicaid reimbursement. All renovations of GCRCs financed by NIH grant funds must meet applicable federal guidelines. (Guidelines for Construction and Equipment of Hospital and Medical Facilities.)

GCRC relocation, within the current hospital or to a new hospital, or changes in the current space which differ from those recommended in the last peer review must be reviewed and approved by NCRR, prior to initiating the modifications. Detailed drawings of the floor plan along with a list indicating the use and number of square feet for each room, a narrative justification, and an estimate of cost for the revised GCRC site should be co-signed by either the PD or PI and the appropriate Business Official and submitted to NCRR. When such a proposed change in space would result in an increase in Routine Cost and/or Space Cost to be requested from NCRR in the future, NCRR may not fund the increased Routine Cost or Space Cost unless the planned change in space and estimated attendant increase in Routine Cost and/or Space Cost was approved in advance by NCRR; this advance approval by NCRR is required independent of the source of funds paying for the renovation/relocation/expansion.

B. Inpatient Area:

Space requirements for the inpatient area are dependent on local codes, JCAHO standards, research needs and federal guidelines. Space should be adequate both for patient comfort and for equipment used in bedside studies. It is preferable that at least half of the research beds are located in private rooms, to accommodate gender or age differences. Rooms that provide controlled environments such as those involving laminar air flow, special monitoring or isolation, may be supported if justified scientifically for patient or staff safety. The nurses' station should be large enough to accommodate the nursing and paramedical staffs. Ideally the office for Head Nurse/Nurse Manager, a doctors' writing area, and a patient lounge, which may also serve as a reception area for outpatient research studies, should be provided. A treatment or

procedure room is usually essential for research and patient care procedures. Adequate storage space and utility rooms, in keeping with JCAHO guidelines, must also be provided. Occasionally more than one inpatient facility may be required for a GCRC, such as when large numbers of both pediatric and adult patients are being seen simultaneously.

C. Outpatient Area:

A facility for outpatient research can be located in the GCRC inpatient area or in a unit that is geographically separate from the hospital outpatient department. A contiguous unit could share supporting facilities and paramedical staffs with the inpatient GCRC and is usually more cost-effective and provides greater flexibility for research. Space requirements of the outpatient area depend upon the scope of the outpatient activities. The inpatient reception area, patient lounge, and examining rooms can be utilized if they are of sufficient size. In some cases, patient beds on discrete GCRCs may be used for complex outpatient studies that require a visit lasting several hours. Additional offices and treatment rooms may be necessary. The area should be functionally designed specifically for outpatient studies; a doctor's consultation room may serve two or more examining rooms.

Renovations for ambulatory research operations need not be extensive or costly. Many existing GCRCs can handle outpatient visits with little modification of their physical structure. When the GCRC outpatient research must be carried out in a unit of the hospital outpatient department, efforts should be made to maintain the discrete nature of the outpatient research area with regard to both location and scheduling.

D. Core Laboratory:

Core Laboratory research facilities should be within the boundaries of the GCRC or in a nearby location. A specimen processing area is often an essential part of the GCRC even when no analytical Core Laboratory is required.

E. Bionutrition Research Facility:

A Bionutrition Research area, if justified for the proposed research program, should be located in or near the GCRC. Specially defined and routine diets can usually be served from the same kitchen. The size of the kitchen will depend on the number of subjects who will receive special and routine diets. An office for the Bionutrition Research Manager should be located near the kitchen.

F. Office and Conference Space:

Office space for the PD and the administrative staff should be provided on or near the GCRC. Offices for an Associate PD, Core Laboratory Director, or other personnel are sometimes justified. A conference room is often needed for meetings, research seminars and teaching

purposes, especially for large GCRCs.

The Informatics Core should be located in dedicated space on or adjacent to the GCRC. The physical facilities should include an Informatics Core Manager's office, a user/training room, and a secured room for the file server(s). The computer facilities should be configured for both local and remote access. Both hardware and software should be the focus of a rational renewal strategy to maintain information technologies that meet the evolving needs of the investigators.

IV. GRANT MANAGEMENT

A. General:

The award and administration of GCRC grant funds are subject to the laws, regulations, and policies indicated in the Notice of Grant Award, the Terms and Conditions therein, and these Guidelines. Awarded funds for patient care costs may not be transferred to other budget categories without prior approval from both the GCRC Program, NCRR, and the Office of Grants Management, NCRR. Awarded funds for nursing and bionutrition salaries and their related fringe benefits may be rebudgeted to other budget categories without NCRR prior approval in accordance with NIH rebudgeting policies. Rebudgeting between nonrestricted budget categories must be in compliance with NIH rebudgeting policies. As described below, Category A activities at a GCRC may be commingled with other patient-oriented research activities (such as Categories B and D activities), provided appropriate individual programmatic accounting is maintained. In addition, other patient-oriented research units may be co-located with a GCRC, provided appropriate fiscal accountability exists.

In accordance with NCRR policy, the recurring direct costs (direct costs excluding equipment and alterations and renovations) requested for the first year of a competitive renewal application cannot exceed the final noncompeting year's budget direct recurring costs budget by more than 20 percent. Where this policy may significantly limit the program scope of the proposed research, the applicant may request a waiver of the 20 percent ceiling. A letter, clearly justifying the request for a waiver must be submitted to the GCRC Program Director, NCRR, well in advance of the application receipt date. The waiver to the ceiling must be approved in writing by the GCRC Program Director, NCRR, before the center's competing renewal application is submitted and accepted.

B. Personnel Costs:

Salaries and wages of personnel may be charged to the grant in proportion to the time which they devote to GCRC activities. Salaries of personnel paid by the GCRC grant must not exceed the salaries of personnel in comparable positions elsewhere within the institution. Fringe benefits, if not included as an F&A cost, are allowable as a direct cost in proportion to the salaries charged to the grant, provided that such payments are made under institutional policies which are formally established and consistently applied. Charges must be in accord with applicable

institutional policies and records must be maintained to substantiate these charges. Sabbatical leave salaries for GCRC personnel are not allowable charges to the GCRC grant; however, sabbatical leave costs to the institution may be included in a composite fringe benefit rate or in the institution's F&A cost rate. An appropriate salary may be charged to the GCRC grant for the person performing the duties of the GCRC staff member who is on sabbatical.

C. Equipment:

Fixed or movable equipment for patient, laboratory, dietary, informatics and administrative areas may be purchased with grant funds if necessary for GCRC activities and not otherwise available to the GCRC from within the institution. Equipment not requested in initial, renewal, or supplemental applications may be purchased from unexpended grant funds, as permitted by institutional and *NIH Grants Policy Guidelines*. Requests for such purchases from funds available in patient care categories accompanied by a detailed justification, must be submitted to NCRR by the PD and co-signed by an authorized Business Official of the institution.

D. Consumable Supplies:

Consumable supplies for the Core Laboratory, Informatics Core, and the GCRC administrative office may be purchased with grant funds provided in the supply budget category. Routine hospital, drug, and raw food supplies are ordinarily provided for within the patient care cost budget categories and are not directly charged to the supply budget category of the grant.

E. Travel:

Domestic travel by the PD and other staff members which will provide direct benefit to the administration of the GCRC may be paid for by the grant. This may include meetings of the Program Directors, Informatics Core Managers, Biostatisticians, Administrative Managers, Nurse Managers, and Research Bionutritionists, and travel of GCRC personnel for consultation with the GCRC Program, NCRR. These travel/meeting costs are specifically indicated on the Notice of Grant Award. Funds for patient travel are not allowable charges to a GCRC grant, but may be reimbursable through other sources.

F. Other:

The Other category usually encompasses miscellaneous services directly related to the GCRC operations, such as software and hardware maintenance and training, equipment maintenance contracts, and duplicating services. Publications such as patient handbooks, annual reports for the lay public, and public information documents, are allowable as publication costs and may be included in the Other category. However, research publication costs (page charges, reprints, etc.) are an individual investigator’s expense and are not chargeable to the GCRC grant. Subscriptions to research publications are allowable only if they are of direct relevance to a significant number of GCRC staff members. Membership fees to scientific and professional

organizations are not allowable charges to a GCRC grant, nor are payments to research subjects for their participation in any protocols.

G. Patient Care Costs:

l. General: Research patient care costs incurred under GCRC grants must be computed using research patient care rates or amounts established by the regional office of the Division of Cost Allocation (DCA) of the Department of Health and Human Services (DHHS). Such rates must be used in all requests and claims for research patient care costs. The institution must submit patient care rate proposals annually to the DHHS Regional Office and reply promptly to inquiries from that Office. Inpatient utilization is based on midnight census.

2. Patient Categories: Each patient admitted to the GCRC shall be assigned to one of four categories: Research (Category A), Research Service (Category B), Industry-Initiated (Category D), and Non-Research (Category C). These assignments are to be made prospectively for each research project by the PD and GAC, in consultation with the involved investigator. The GAC evaluation of research projects for GCRC use is to be made exclusively on the basis of the scientific merit of the projects and their need for the GCRC, without regard to the assignment of patients to Category A or B. In all cases, NIH-funded clinical research has the highest priority status.

GCRC grant funds pay for research costs. They are not used to pay for established patient medical care or treatment during the course of research. When Category C and Category D patients are admitted to a GCRC, all costs for their care are charged to the patients or third parties rather than to the grant.

a. <u>Research Patients (Category A)</u>: These are research inpatient days or outpatient visits utilized solely for research purposes. All hospitalization costs associated with Category A research days or visits are the financial responsibility of the grant or the investigator's research funds. Persons who are hospitalized for research purposes only, but whose care is partly supported by non-GCRC funds, (e.g., other grants, industry) may also be classified as Category A. This category includes normal volunteers or control subjects and patients who may participate in research projects that include unproven forms of therapy or diagnostic techniques that may subsequently become standards of medical therapy or diagnosis. Even though a patient may have a third party carrier and have an underlying disease, the GCRC assumes all research costs related to patients in this category.

GCRC grant funds may be used to pay all costs, thereby encompassing the usual care costs, which are part of the research project, as well as research care costs. This financial responsibility is assumed for the entire period of hospitalization, research testing or provided services for patients who would not otherwise have been hospitalized or received such tests or services except for their participation in the research study. Any exceptions should be documented in GCRC administrative records.

These patients may include persons to whom no health advantages may be expected to accrue as a result of the hospitalization. Examples would be persons with genetic or other abnormalities of interest to the investigator, and those persons who although sick, would not have otherwise been brought to the hospital except for the research studies.

b. Research Service Patients (Category B): This category pertains to patients who require hospitalization or outpatient studies for diagnosis or treatment according to established standards of care. Although these patients also participate in GCRC-based research studies, the cost of established medical care, i.e., non-research care, for Category B patients is not charged to the grant. The patient or third party carrier is responsible for those costs. The institution is responsible for all billings and collections on these patients. A patient care credit, or offset, for each Category B inpatient day or outpatient visit is credited to the patient care category of the grant based on the patient care rate agreement for inpatient days or the rate developed by the GAC for outpatient visits (see Section IV-G-6). The cost of those ancillary services performed solely for research on Category B patients and not related to their routine medical care should be charged to the grant and not appear on the patient's hospital bill which is submitted to either the patient or the insurance carrier. Patients who meet the Category B classification criteria may not be classified as Category A simply because they lack applicable insurance.

c. Industry-Initiated Projects (Category D): This category includes inpatient days or outpatient visits utilized for an industry-initiated study. All charges are paid directly by industry through the responsible GCRC investigator. For each Category D inpatient day, a credit is provided to the patient care category of the grant based on the patient care rate agreement. In addition, the GCRC receives a credit for each outpatient visit and use of any other GCRC resources. The charge for each project is to be developed by the GAC and credited to the patient care category of the GCRC grant (see Section IV-G-6).

d. Non-Research Patients (Category C): Patients who are not participating in a research project may be admitted to the GCRC solely for the purposes of diagnosis or treatment according to established procedures, only when there is space and staffing available on the GCRC. The purpose of Category C inpatient admissions and outpatient visits is to decrease the cost of the operation of a discrete GCRC. As with Category B patients, the hospital is responsible for all billings and collections that involve Category C patients. Because Category C patients are not participating in research projects, no charges for their hospitalization or visits may be made to the grant. The requirements for providing credits to the grant are the same for Category C patients as for Categories B and D patients.

It is essential that the presence of Categories D and C patients not compromise other research activities involving Categories A and B patients on the GCRC. Admission of all Category C patients must therefore be at the discretion of the PD and the GAC. Dialysis patients, post-operative patients, intensive care patients, and other patients who require an extraordinary level of paramedical and nursing effort, should not be admitted as Category C patients.

3. Scatter-bed Inpatient Days:

a. Category A:

i. The cost of occasional, unexpected, temporary use of special facilities, such as an intensive care unit or other off-site area uniquely required to accommodate a research patient, may be charged to the GCRC grant provided that the care is required by the nature of the clinical research or by an illness resulting from the research; the care is provided in a specialized area (intensive care unit, coronary care unit, etc.); the occasional patient remains on the GCRC census under the scatter-bed classification while in the special care unit; and there is no duplication of payment for patient care. The GAC must review and approve this local activity.

ii. If the use of special facilities such as an intensive care unit or other off-site area is to be an established part of a GCRC research project and was not previously peer reviewed, prior written approval from the GCRC Program, NCRR, is required. The request is to be co-signed by the appropriate Business Official.

iii. If the cost of the proposed scatter-bed research activity combined with the support of the original peer-reviewed and recommended configuration of a GCRC exceeds the National Advisory Research Resources Council (NARRC) recommended funding level, then a competitive supplement may be submitted for peer-review of the request (see Part A).

b. Category B: As defined above for Category B inpatients on the unit, Category B scatter-bed patients require hospitalization for diagnosis or treatment according to established standards of care but are also research subjects. These off-site inpatients may require ancillary services solely for research purposes that may be charged to the grant. Scatter-bed B research inpatients with ancillary costs charged to the GCRC grant will be tracked as scatter-bed B days. If a GCRC research nurse is required, the nurse's time is tracked separately as "Scatter-bed Research Nurse Hours" (see below).

c. Category C and Category D: These categories are not classifications used for scatter-bed research days.

4. Scatter-bed Research Nurse Hours:

a. Category A and Category B: A GCRC research nurse may be required to perform the research component of a study on a Category B inpatient hospitalized off-site on an approved scatter-bed research project. Scatter-bed research nurse hours will be tracked by project for nurses who are paid directly by the GCRC grant. The hours tracked will reflect all the requisite time associated for each research project (for example, scheduling, preparation, direct patient research procedures, chart entry). Scatter-bed research nurse hours are entered in the Annual Report for each subproject by patient category (A, B or D). Total scatter-bed research nurse hours for all subprojects combined are computed by the Annual Report Program and

displayed at the end of Section 11 of the Annual Report. The scatter-bed research nurse hours associated with all off-site research inpatients should be recorded. If ancillary costs are not charged to the GCRC grant, no Category B scatter-bed inpatient days are recorded. Off-site "B" research inpatient projects that have no ancillary charges will require only scatter-bed nurse hours to be tracked. Category A scatter-bed days are recorded since either inpatient costs or ancillary costs (or both) are paid by the GCRC grant. Scatter-bed research nurse hours for Category A projects will only count the hours of nurses paid directly by the GCRC grant, not those nurses whose salaries are included in a *per diem* charge.

b. Category D: With the approval of the GAC, a Category D project with patients hospitalized off-site may have a scatter-bed research nurse assist in the study. Scatter-bed research nurse time for an off-site Category D research project should be tracked and appropriate financial credit should be made to the GCRC grant.

c. All scatter-bed research nurse activity must take place in a facility either accredited by JCAHO or certified to accept Medicare and/or Medicaid reimbursement.

5. Outpatient and Research Meal Visits: A GCRC research subject who is not hospitalized at midnight is considered to be an outpatient. Thus, an outpatient visit could be as short as a few minutes or as long as almost 24 hours. The visit may take place on the GCRC unit or at a remote site, as long as it is funded by the GCRC grant and/or involves a GCRC nurse. There is no category called "scatter outpatient visit."

When a research subject is on the unit to eat or pick up a research meal and has no contact with either GCRC nurses or investigators, the interaction is categorized as a research meal visit, not as an outpatient visit. The research meal visits should be tracked and reported in the Nutrition section of the Administrative Narratives in the Annual Progress Report and listed as "research meal visits."

6. Outpatient Visit Credits: Charges for Category D (industry-initiated) visits, Category C visits, and the non-research portion of Category B visits are to be credited to the GCRC grant. This activity must be reflected in the computations on the census page of the Annual Progress Report, and must be included as a credit in the patient care computation pages of the Annual Progress Report.

For each project, an appropriate credit, preferably based on an hourly rate, must be computed. In developing a rate, all components of the GCRC utilized are to be included, i.e., program directorship, administration, research bionutrition, nursing, core laboratory, computer, biostatistical services, space charges, as well as any other appropriate GCRC resource. A rate should be established and approved by the GAC.

7. Changes in Patient Category: A patient's category may change during the hospital stay on the GCRC. For example, a patient may be designated as Category B during the first part

of an admission, when the patient would have been hospitalized regardless of research participation, and subsequently as Category A after the completion of standard care because components of the research project have yet to be completed. Similarly, part of a research subject's hospital stay may be Category D and another portion Category A or B. The categorization is determined prospectively by the GAC.

8. GCRC Funding Methods: There are two general means for funding of GCRCs, the Discrete Method and the Per Diem Method. The method chosen depends on cost-effectiveness, unit size, and institutional constraints, and is determined by negotiations between the grantee institution and NCRR staff.

a. Discrete Unit Method: With this method, most often used for large or medium-sized GCRCs, the expected cost of all research inpatient days, nursing, dietary services, and other fixed expenses are funded in the grant award. When Research Service (Category B), Industry-Initiated (Category D), or Non-Research (Category C) inpatients are cared for on the GCRC, the grant is reimbursed by the hospital by means of a credit ("offset") to the grant based on the annual DHHS negotiated rate agreement. Category B, C and D patient credits may not be rebudgeted to nonrestricted budget categories by the grantee institution without prior approval from NCRR staff.

b. Per Diem Method: With this method, the expected cost of the Research Patient (Category A) inpatient days is provided in the grant award but the hospital is reimbursed only for the Category A days actually used. The payment for each day is based on an average routine per diem rate for Category A patients, adjusted for any items funded directly by the grant, such as some or all of the nursing. When the per diem rate includes hospital-provided nursing, the grant will usually support one or more additional Research Nurses.

c. Discrete vs. Per Diem Comparison: In comparing per diem versus discrete methods of funding, the following should be used as a guide:

	Per Diem	**Discrete**
Space Cost		N/A
Per Diem Cost		N/A
Routine Costs	N/A	
Nursing Salaries (FTEs)		
Bionutrition Salaries (FTEs)		
Service Patient Credits	N/A	

Description of Cost Items:

Space Costs -- On a per diem GCRC, space costs may be requested for administrative offices, laboratory space, computer space, and research bionutrition space. A detailed description of square feet per office/room should be provided. Cost should be based on the number of square feet applicable to these areas which is then calculated by multiplying the square feet by the square foot dollar rate for the hospital.

Per Diem -- The per diem cost is usually the Medicare rate for the hospital. This rate for a per diem center should be the Service Patient Credit rate for a discrete center. The per diem is calculated by applying this rate to the number of Category A days requested.

Routine Costs -- This is the cost for the total inpatient space of the GCRC.

Nursing -- On a per diem GCRC, research nursing salaries for a Nurse Manager and 1 or 2 additional nurses may be paid directly. The number of nurses depends on the level of outpatient activity and the intensity of nursing care required. In unusual circumstances, more than 2-3 nurses may be needed.

Bionutrition Research Salaries -- On a per diem GCRC, the dietary component must be justified based on the need for a bionutrition research component. Normal patient meals should be provided by the central hospital kitchen.

Service Patient Credits -- This is the Medicare rate applied to B, C and D patients on a discrete Center.

Ancillary costs are generally not affected by the method of funding, and thus are not considered in the above.

9. Scatter-bed Reimbursement: Some studies require that patients be cared for in beds not located on the GCRC. These are referred to as scatter-beds. If Category A scatter-bed days have been funded in the award statement, or prior approval has been obtained from the GCRC Program, NCRR, patient care costs will be provided using a negotiated inpatient routine per diem applicable to the area where the patient is housed. Scatter-bed patients often are Category B, in which case the only cost to the grant is for the ancillary costs associated with the research.

10. Ancillaries: All ancillary services provided to Category A patients and those provided to Category B patients which are not required for their routine medical care but are performed solely for research can be supported from GCRC grant funds. Ancillary services are defined as services routinely available through hospital departments for all patients in the hospital. This definition applies even when these services are purchased from sources outside the hospital for reasons of economy or efficiency. Tests needed by individual investigators for

their research are not proper charges to the GCRC grant if the tests are not routinely available to all patients in the hospital. Also, services provided either by the laboratory of a GCRC researcher or by a hospital laboratory or service which is directed by a GCRC researcher (even if that researcher has a contractual arrangement with the hospital to provide these services) may not be charged to the GCRC grant for any project for which that researcher is the principal investigator or a collaborator. Research ancillary charges must be reduced to cost based upon the Negotiated Rate Agreement between the hospital and DHHS.

11. Program Income: Program income is defined as the gross income earned by a grant recipient that is generated directly by an activity supported by the grant or earned as a result of the grant (see 45 CFR 74.2 and 74.24 for additional information). An example of program income is fees resulting from charges made for laboratory tests performed by the GCRC Core Laboratory. An estimate of the amount and source of program income expected to be generated as a result of the GCRC grant award must be included on the Checklist Page of all competing and noncompeting continuation applications. Net program income earned during a budget period must be reported on the long form FSR (except for program income earned as a result of inventions, to which special rules apply). Costs incident to the generation of program income may be deducted from gross income to determine program income, provided these costs have not been charged to the award.

Program Income earned during the project period shall be retained by the GCRC recipient and, in accordance with the terms and conditions of the award, used in the following way:

a. The first $25,000 earned during a budget period is added to funds committed to the project or program, and used to further the objectives of eligible projects or program;

b. Any amount over $25,000 earned during a budget period is to be deducted from the total project or program allowable costs in determining the net allowable costs on which the federal share of costs is based. NCRR may offset a future award by this amount or reauthorize it for expenditure on a future award.

H. Professional Fees:

1. Category A patients: Physicians' fees or other professional services may not be charged to the grant for Category A patients, except when included in the charge for a hospital service to a research patient AND that hospital department providing the service, such as radiology, pathology, and anesthesiology has a contractual agreements with the grantee institution or participating hospital. Administrative approval by the GCRC Program, NCRR, is required prior to implementing payment for those professional fees.

2. Category B patients: Physicians' fees may not be charged to the GCRC grant for Category B patients. However, physicians' fees may be charged directly to Category B patients or third parties. Budgetary records should be maintained to document this process. To avoid

apparent or real conflicts of interest, professional fees charged and collected by the hospital on behalf of GCRC investigators should be deposited directly into divisional or departmental accounts so that no investigator is the direct recipient of patient fees.

I. Consultant Fees:

Consultant fees to physicians are not allowable charges to a GCRC grant.

J. Alterations and Renovations:

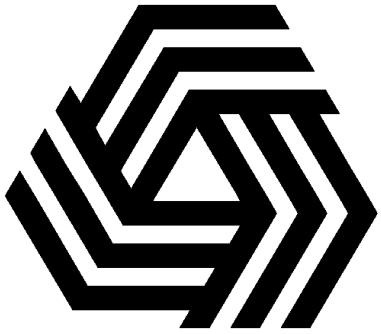
Approved renovations of an existing structure to provide facilities for a GCRC (see Physical Facilities section) may be paid by the grant. Funds may not be used for new construction or for completion of "shell space." All renovations of GCRCs financed by NIH grants must meet applicable federal guidelines (*Guidelines for Construction and Equipment of Hospital and Medical Facilities*, latest edition).

K. Facilities and Administrative Costs:

A special or off-campus F&A cost ("modified F&A") rate is normally required for all GCRC grants, since F&A costs such as depreciation, operations and maintenance, housekeeping, and space costs for the GCRC facilities are included in the direct component of patient care costs. Patient care costs also include F&A costs related to hospital-affiliated employees supported as a direct cost by the grant, regardless of the identity of the employer. Therefore, the base used to claim F&A cost must exclude all hospital-affiliated costs (salaries and fringe benefits for nurses, bionutritionists, ward clerks, social worker, etc., and patient care costs).

L. Overall GCRC Funding:

Funding for each GCRC each year is based on prior utilization and productivity and projected total (not just inpatient) patient-oriented research activity. This includes inpatient, scatter-bed, outpatient, nursing, research bionutrition, core laboratory, training, biostatistics, and computer analysis needs.



National Center for Research Resources
National Institutes of Health
Department of Health and Human Services

Division of Clinical Research

Guidelines for the General Clinical Research Centers (GCRC) Program

Supplement I: Instructions for Preparing a GCRC (M01) Application

April 2001

An Administrative Document Issued by the
National Center for Research Resources (NCRR).

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INSTRUCTIONS FOR PREPARING A GCRC APPLICATION

I. ELIGIBILITY FOR GRANT SUPPORT

Medical institutions or governmental agencies are eligible for General Clinical Research Centers (GCRC) Program support. The primary purpose for a GCRC is to provide the clinical research infrastructure to investigators who receive their primary research funding from the other components of the National Institutes of Health (NIH). While most grantee institutions of the GCRC Program are affiliated with medical schools, other institutions devoted to medical research may also apply. Inpatient and outpatient areas of a GCRC must be located in a facility accredited by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), or certified to accept Medicare and/or Medicaid reimbursement. GCRCs provide the infrastructure for high quality clinical research for physician-scientists currently funded by the federal agencies, private foundations, and other peer-reviewed sources. The resources of a GCRC may include inpatient and outpatient facilities, specialized personnel, Core Laboratory, and Informatics Core.

II. REVIEW OF APPLICATIONS

Each GCRC application submitted to the NIH is evaluated by three groups--first, by a site visit team composed of members of the GCRC Committee (Initial Review Group) and *ad hoc* consultants; next, by the GCRC Review Committee (National Center for Research Resources (NCRR)); and finally, by the National Advisory Research Resources Council (NARRC), which makes its recommendations to the Director of the NCRR. Criteria for evaluation of a new or competing renewal GCRC application include scientific merit of the proposed research, peer-reviewed research project support for GCRC investigators, program relevance, value as an institutional and regional resource, utilization by several medical disciplines, evidence of collaboration between basic and clinical scientists, availability of a sufficient research patient population, and the prospects for use of the GCRC as a clinical research training facility for medical students, house staff and subspecialty fellows.

New and competing continuation (renewal) applications, using Form PHS 398 are accepted and reviewed according to the following schedule:

Received By	Project Site Visit	GCRC Committee Review	Council Review	Earliest Possible Funding Date
October 1	Nov. - Jan.	February	June	July 1
February 1	March - May	June	September	December 1
June 1	July-Sep.	October	February	April 1

Form PHS 398 is available at most institutional offices of sponsored research and from the

Office of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, Room 6095, Bethesda, MD 20892-7910; phone: (301) 435-0714; fax: (301) 480-0525; e-mail: GrantsInfo@nih.gov. Forms are also available on the NIH Web site: http://www.nih.gov/grants/funding/phs398/phs398.html.

In accordance with NCRR policy, the recurring direct costs (direct costs excluding equipment) requested for the first year of a competitive renewal application cannot exceed the final noncompeting year's budget direct recurring costs budget by more than 20 percent. Where this policy may significantly limit the program scope of the proposed research, the applicant may request a waiver of the 20 percent ceiling. A letter, clearly justifying the request for a waiver must be submitted to the GCRC Program Director, NCRR, well in advance of the application receipt date. The waiver to the ceiling must be approved in writing by the GCRC Program Director, NCRR, before the center's competing renewal application is submitted and accepted.

Applications are recommended by the NARRC for project periods of varying length, up to a maximum of five years. Funding of approved initial or renewal applications depends on the availability of funds to the GCRC Program Director as well as the relative priority of the GCRC as assigned on the basis of the above criteria.

Requests for support above the level previously recommended by the NARRC, should be made by a competing supplemental (Type 3) grant application, using Form PHS 398. Program Directors are encouraged to consult with NCRR's GCRC Program staff before submitting a competing supplemental request. Supplemental requests exceeding $500,000 in direct costs for any year will not be accepted without prior consultation with and approval by the GCRC Program Director, NCRR. The format and review of supplemental grant applications are similar to those of new and renewal grant applications, except that the information to be included (projects, biographical sketches, tables, etc.) need be only the material required to justify support of the items requested in the supplemental application. The deadline receipt dates for supplemental applications are the same as those for new and renewal GCRC applications. Site visits are not usually required for supplemental applications unless they are very large or require additional assessment of GCRC resources.

Competing supplemental applications dealing only with research on acquired immunodeficiency syndrome (AIDS) may be given an expedited review. Such applications should meet the criteria given in the previous paragraph with the following modifications: (1) In order that the application be considered for expedited review, the submission dates are January 2, May 1, and September 1; and (2) All projects in the supplemental application must be AIDS-related. If a site visit is involved, expedited review may not be possible. Program Directors (PDs) are encouraged to consult with NCRR staff before submitting such an AIDS competing supplemental application.

SUGGESTED STEPS IN PLANNING A GCRC APPLICATION

A. Examine the Guidelines for the GCRCs.

B. Discuss the need for a GCRC with investigators from different departments at your institution. From these discussions and from meetings with institutional administrators, determine the following:

   1. Number of investigators with peer-reviewed sources of support who will utilize the GCRC for clinical research;

   2. Number and types of investigations that could effectively utilize GCRC resources, with encouragement of multidisciplinary use (resource needs of investigators);

   3. Number and category (A versus B, see below) of research inpatient days and outpatient visits required by the research project;

   4. Biostatistical, Informatics Core, Core Laboratory, bionutrition research and administrative support required;

   5. Optimal location for the GCRC within the institution.

C. Plan a visit to one or more established GCRCs to learn about GCRC administration and scientific oversight.

D. Make a preliminary sketch of the proposed GCRC. If necessary, obtain cost estimates for alterations and renovations.

E. Indicate whether the hospital has a currently effective Department of Health and Human Services' (DHHS) negotiated hospitalization rate agreement for inpatients; if not, determine the basis to be used for calculating patient care costs.

F. Outline a draft proposal and discuss it with the staff of the GCRC Program Director, NCRR.

III. SPECIFIC APPLICATION INSTRUCTIONS

Form PHS 398 should be used for all new and competing GCRC applications and supplemental applications. These specific instructions supplement the instructions attached to Form PHS 398. Follow Form PHS 398 instructions except where they differ from the specific instructions below.

Page limitations specified in Form PHS 398 instructions do not apply to GCRC applications; they have been modified as described below.

Submit a signed, original typewritten application with the Checklist, and two single-sided,

unbound, signed photocopies, in one package to: Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 1040, Bethesda, MD 20892-7710 or for express/courier service use Bethesda, MD 20817-7710. In addition, send three single-sided copies to: Office of Review, National Center for Research Resources, 6705 Rockledge Drive, Room 6018, Bethesda, MD 20892-7965; or for express/courier service use Bethesda, MD 20817.

When submitting a revised (-A1) application, summarize in an "Introduction" section substantial additions, deletions and changes that have been made in all sections including all projects. Highlight these changes within the text of the "Research Plan" section by appropriate bracketing, indenting, or changing of typography. Do not underline or shade changes. Include any work done since the previous version was submitted. A revised application will be returned if it does not address criticisms in the previous summary statement and/or an "Introduction" is not included and/or substantial revisions are not clearly apparent.

Amended (-A1) applications may be reviewed at a site visit at the applicant institution, or may be reviewed at an "applicant interview." The NCRR Office of Review will make that decision and will notify the applicant institution, and include the agenda for the applicant interview. -A2 applications will generally not have a site visit. The NIH Policy on Submission of Revised (Amended) Applications which can be found at http://www.nih.gov/grants/policy/amendedapps.htm states that "the National Institutes of Health (NIH) will no longer consider any A3 or higher amendments to an application and, regardless of the number of amendments, the NIH will not accept a revised (amended) application that is submitted later than two years beyond the date of the receipt of the initial, unamended application. The new policy applies to all mechanisms."

All applications are due on or before the established deadline date. No request for a waiver will be considered prior to receipt of the application, and there is no guarantee that the waiver will be granted by the Center for Scientific Review (CSR). NCRR staff cannot grant a waiver. To request a waiver, include an explanatory letter with the signed, completed application.

Do not send any supplementary or corrective material pertinent to an application after the receipt date without specific solicitation and agreement by the Scientific Review Administrator (SRA) of the GCRC Review Committee or the site visit SRA. There is no guarantee that the reviewers will consider late material.

Pay close attention to type size specifications and limitations outlined on page 10 of the Form PHS 398 Kit.

Page 1
(Form PHS 398)

ITEM 1. TITLE OF PROJECT: General Clinical Research Center

ITEM 2a. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM

ANNOUNCEMENT: No

ITEM 3. See instructions for Form PHS 398.

ITEM 3. a. NAME OF PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: Name of Principal Investigator. Only the Principal Investigator's name and not the Program Director's name should be entered on this line. If Program Director's name is entered here the review of the application may be unduly delayed. Only one name per application is recognized in the NIH computer system.

ITEM 3. b, c, d, e, f, g, h. See instructions for Form PHS 398.

ITEM 5. [If projects include use of vertebrate animals, further information, as described in of the Form PHS 398 Kit, must be provided.] The information in Items 5a and 5b and the signatures on the Face Page fulfill the requirement for verification of IACUC approval. To insure against delays in the review of the application, IACUC review is best completed prior to submission of the application. However, if the IACUC review is unavoidably delayed beyond the submission of the application, enter "pending" at Item 5. A follow-up verification of IACUC approval from an official signing for the applicant organization must then be sent to and received by the SRA of the GCRC Review Committee within 60 days after the receipt date for which the application is submitted. Any modifications in the Research Plan section of the application required by the IACUC must be submitted with the follow-up verification. Occasionally PHS initial review may be scheduled to occur before the end of the 60-day grace period. In these special cases of accelerated review, the follow-up verification will be requested earlier. Otherwise, it is the responsibility of the applicant organization to submit the follow-up verification. The PHS does not guarantee that it will remind the applicant organization or the Principal Investigator/Program Director to provide this missing information. If verification of IACUC approval is not received prior to the scheduled PHS initial review date, the application will be considered incomplete and deferred to the next review cycle.

If a follow-up verification of IACUC approval has to be sent to the SRA of the GCRC Review Committee, an appropriately completed and signed letter, prepared according to the example in the PHS Policy on Humane Care and Use of Laboratory Animals, continues to meet the requirements for verification. In lieu of this preferred method, a revised Face Page is acceptable, provided that all of the following information is included: application number, title of project, name of investigator and institution, Animal Welfare Assurance number, date of IACUC approval, and appropriate signatures. An attached page should contain any changes or modifications required by the IACUC, and if none, a statement to that effect.

ITEM 6. DATES OF PROPOSED PERIOD OF SUPPORT

The entire proposed project period may not exceed five years. Applications can not be funded until the NARRC has completed its review. The project period end date of supplemental applications may not extend beyond the funded project period end date of the Center grant. Refer to the most recent Notice of Grant Award.

ITEM 7 through 16. See instructions for Form PHS 398.

Page 2
(Form PHS 398)

DESCRIPTION

Describe the major areas of investigation to be undertaken on the GCRC.

KEY PERSONNEL

Include only the Principal Investigator, Program Director(s) and other professionals (e.g., biostatistician, core laboratory director) for whom salary is requested. Do not include the names of the investigators of the individual projects.

Page 3
(Form PHS 398)

TABLE OF CONTENTS

Structure the application according to the format below. Number pages consecutively from the beginning to the end of the application without ancillary numbering systems. Applications which do not conform to this format may be returned.

PART I. BUDGET

A. Detailed Budget for Initial Budget Period (12 months or less)
B. Budget for Entire Proposed Project Period (up to 5 years)
C. Budgets Pertaining to Consortium/Contractual Arrangements and Budget Justification

PART II. BIOGRAPHICAL SKETCHES: provide an index in alphabetical order, with a page number for each individual. Biographical sketches are to be no more than two pages per individual.

A. Biographical Sketches
B. Other Support

PART III. RESOURCES AND ENVIRONMENT

A. Background and Introductory Statement
B. Organizational Framework
C. Administration
D. Patient Care
E. Training and Career Development
F. Core Laboratories
G. Biostatistical Support
H. Informatics Core
I. Physical Resources and Utilization
J. Other Existing or Planned Resources for Clinical Research
K. Data and Safety Monitoring Plan
L. Clinical Research Feasibility Funds

PART IV. RESEARCH PLAN

A. Accomplishments
B. Center Bibliography (for competing renewal applications)
C. Research Projects: listed by project principal investigator in alphabetical order. Provide page index for all research projects at the beginning of Section IV-C, along with title of the proposal and name of protocol principal investigator.

PART V. TABLES

A. Faculty Member Research Participation
B. Training
C. Utilization of the Center, Last Three Years (for competing renewal applications)
D. Principal Users of the Center, Last Three Years (for competing renewal applications)
E. Proposed Scientific Agenda for the Site Visit and Abstract Package

PART VI. SITE VISIT INFORMATION

Pages 4+5
(Form PHS 398)

PART I. BUDGET

A. Detailed Budget for the Initial Budget Period: For a new Center, the first period of requested support should be from the requested start date through November 30 of that calendar year. (The common budget period for all funded GCRCs is December 1 through November 30). For competing continuation (renewal) applications, the first budget period should be 12 months.

Itemize specific needs for the first budget period as follows:

1. Personnel: Follow instructions carefully in the Form PHS 398 Kit. In the justification, briefly describe the function of each position, and whether support is requested. List the holder of each position by name if the position is filled and indicate whether employed by the university or hospital. All salaries requested must be consistent with institutional standards, applied regardless of the source of funds. If any support is requested for an employee of the Department of Veterans Affairs (VA), see NIH Guide for Grants and Contracts, Vol. 18, No. 27, August 11, 1989.

   For nursing and research bionutrition personnel requested, indicate the shift coverage the nursing and research bionutrition staffs will provide. Describe any unusual nursing and research bionutrition duties such as staffing for extended outpatient studies. If research bionutrition staffing is proposed, provide the following table:

Meals	% Current*	% Proposed
Planned, calculated, or modified		
Prepared or cooked		
Served		

* renewal applications only

2. Equipment: List separately each item of fixed and movable equipment costing more than $5,000 requested. Provide a separate narrative justification for each equipment item requested and indicate which of the investigators and projects require the equipment and projected utilization by projects.

3, 4, 5, 6. Supplies, Travel, Alterations and Renovations, and Other Expenses: See Guidelines for the GCRC Program for details on which items may be requested. Funds requested for the CReFF program should be requested under "Other."

7. Patient Care Costs: The patient care costs requested in the application for inpatients and outpatients should be supported by computations provided within the following pages.

PATIENT CARE COMPUTATION: (Figures to be rounded to the nearest dollar)

INPATIENT

RATE USED

1. If proposed rate is used, show date filed with HHS:
   MO _____ DAY _____ YEAR _____

2. If rate has been published by HHS, show date of agreement:
   MO _____ DAY _____ YEAR _____

3. Show 12-month period of rate: _____ through _____

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4. A. Routine Cost (or Space Cost for per diem method, if applicable): $_____
   B. Per Diem Method:
   __*__ Category A days x $_____ = $_____
   C. Scatter Beds:
   __*__ Category A days x $_____ = $_____

   Total (4A and 4C or 4B and 4C) $_____

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5. Service Patient Credit (routine method)
   __*__ Category B days x $_____ = $_____
   __*__ Category C days x $_____ = $_____
   __*__ Category D days x $_____ = $_____
   All Other Inpatient Credits
   (Specify: grants, contracts, industry, etc.) $_____

   Total Credits ($_____)

---

6. Inpatient Ancillaries Required Solely for Research Purposes, Adjusted to Cost (Schedule 1)

   __*__ Category A days x $_____ = $_____
   __*__ Category B days x $_____ = $_____

   Scatter Beds:
   __*__ Category A days x $_____ = $_____
   _____ Category B days x $_____ = $_____

   Total Inpatient Ancillaries $_____

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7. Other Costs (Specify: drugs, raw food, special diets, outside laboratories, etc. Provide justification) $_____

8. TOTAL INPATIENT REQUEST

(Boxes 4, 6, and 7, less box 5) $_____

OUTPATIENT

9. Space Charge (If not included with inpatient routine costs) $_____

10. Outpatient Ancillaries Required Solely for Research Purposes, Adjusted to Cost (Schedule 2)

__*__ Category A visits x $_____ = $_____
__*__ Category B visits x $_____ = $_____

Total Outpatient Ancillaries $_____

11. Other Costs (Specify: drugs, raw food, special diets, outside laboratories, etc. Provide justification) $_____

12. Credits

__*__ Category B visits x $_____ = $_____
__*__ Category C visits x $_____ = $_____
__*__ Category D visits x $_____ = $_____
All Other Inpatient Credits
(Specify: grants, contracts, industry, etc.) $_____

Total Credits ($_____)

13. TOTAL OUTPATIENT REQUEST
(Lines 9, 10, and 11, less line 12) $_____

TOTAL PATIENT CARE REQUEST (Lines 8 and 13) $_____

* list total annual projected number of days and visits in each category including those which require no ancillaries

Schedule 1 — Category A Inpatient Projects*

Investigator Name	SPID Number	Project Title	Number Days Per Year	Annual Cost** For Tests: Hospital Ancillaries	Annual Cost** For Tests: Outside Ancillaries
		Total			

(Total ancillary costs for A days divided by A days equals average research ancillary cost per A day)

* List all projects including those for which no ancillary support is requested.
** Charges adjusted to cost by category per Patient Care Rate Agreement.

Schedule 2 Category B Inpatient Projects*

Investigator Name	SPID Number	Project Title	Number Days Per Year	Annual Cost** For Tests: Hospital Ancillaries	Annual Cost** For Tests: Outside Ancillaries
		Total			

(Total ancillary costs for B days divided by B days equals average research ancillary cost per B day)

* List all projects including those for which no ancillary support is requested.
** Charges adjusted to cost by category per Patient Care Rate Agreement.

Schedule 3 Category A Inpatient Scatter-bed Projects*

Investigator Name	SPID Number	Project Title	Number Days Per Year	Annual Cost** For Tests: Hospital Ancillaries	Annual Cost** For Tests: Outside Ancillaries	Annual*** Scatter-bed Research Nurse Hours
		Total				

(Total ancillary costs for A scatter-bed days divided by A scatter-bed days equals average research ancillary cost per A scatter-bed day)

* List all projects including those for which no ancillary support is requested.
** Charges adjusted to cost by category per Patient Care Rate Agreement.
*** Only include hours of nurses paid directly by the GCRC grant, not nurses included in a per diem charge.

Schedule 4 Category B Inpatient Scatter-bed Projects*

Investigator Name	SPID Number	Project Title	Number Days Per Year	Annual Cost** For Tests: Hospital Ancillaries	Annual Cost** For Tests: Outside Ancillaries	Annual*** Scatter-bed Research Nurse Hours
		Total				

(Total ancillary costs for B scatter-bed days divided by B scatter-bed days equals average research ancillary cost per B scatter-bed day)

* Include in this Schedule both those projects which involve scatter-bed B days (with entries to be made in all columns), and those scatter-bed B projects where there are no ancillary costs charged to the GCRC grant (with no entries to be made for days and ancillaries, but entries to be made for the other columns).

** Charges adjusted to cost by category per Patient Care Rate Agreement.

*** Only count hours of those nurses paid directly by the GCRC grant.

Schedule 5 Category A Outpatient Projects*

Investigator Name	SPID Number	Project Title	Average Duration of Visit	Number Visits Per Year	Annual Cost For Tests** Hospital Ancillaries	Annual Cost For Tests** Outside Ancillaries
			Total			

(Total ancillary costs for A visits divided by A visits equals average research ancillary cost per A visit)

* List all projects including those for which no ancillary support is requested.
** Charges adjusted to cost by category per Patient Care Rate Agreement.

Schedule 6 Category B Outpatient Projects*

Investigator Name	SPID Number	Project Title	Average Duration of Visit	Number Visits Per Year	Annual Cost For Tests** Hospital Ancillaries	Annual Cost For Tests** Outside Ancillaries
				Total		

(Total ancillary costs for B visits divided by B visits equals average research ancillary cost per B visit)

* List all projects including those for which no ancillary support is requested.
** Charges adjusted to cost by category per Patient Care Rate Agreement.

Schedule 7 Category D Inpatient Projects

Investigator Name	SPID Number	Project Title	Number Days Per Year	Industrial Sponsor

Total

Schedule 8 — Category D Outpatient Projects

Investigator Name	SPID Number	Project Title	Average Duration Of Visit	Number Visits Per Year	Industrial Sponsor	Dollars Projected To Be Credited To The Grant
					Total	

[Note that in the tables on the preceding six pages, numbers of days and visits required annually for each project in the application are to be entered. Later in the application, this information is requested again when each project is described, and again in Table E for those projects to be presented at the site visit. Make sure that the numbers are consistent for a given project at each place in the application.]

B. Budget for Entire Proposed Period of Support: Provide a justification for any changes, as explained in Form PHS 398.

Additional Pages
(Form PHS 398)

PART II. BIOGRAPHICAL SKETCHES

A. Arrange the biographical sketches in alphabetical order. Provide biographic sketches for the Principal Investigator, the Program Director, Associate and Assistant Program Director, all professionals for whom salary support is requested, and the principal investigator and co-investigators of each project in the application. Restrict the list of publications in each sketch to those of the last five years (although indicating the total number of lifetime publications) and limit the entire sketch to two pages.

B. Other Support: This information should be submitted for all professional staff for whom salary support is requested from the GCRC grant and all principal investigators and co-investigators of all submitted protocols. Follow instructions in Form PHS 398. Note that if any of these individuals is the principal investigator or a co-investigator of a project to be presented at the site visit, this information is requested again in Table E. Make sure the information is consistent at both places in the application Provide the full grant number (e.g., 2 R01 HL51618-04) but a discussion of scientific overlap is not required.

PART III. RESOURCES AND ENVIRONMENT

A. Background and Introductory Statement

This section describes the institutional environment for research, both current and historical. Relevant information may include the following:

1. Briefly describe the origin of the institution and its past contributions to research, especially clinical research. Describe the interaction between basic and clinical departments.

2. Components or affiliates of the institution relevant to the proposed clinical research effort: graduate schools, medical and dental schools, schools of allied health science, hospitals, research laboratories, and government institutions.

3. Current assets for research: number of full-time faculty members involved with research, current annual grant and contract support, major endowment funds, funded Centers, etc.

4. Patient resources available for research: population and catchment area and number of admissions, inpatient days, and outpatient visits provided by the hospital or medical center.

5. Institutional assets for research training: number of medical and dental students, allied health science students, house officers, and postdoctoral fellows; nature of institutional funds for training.

B. Organizational Framework

The organizational structure of the institution should be defined as it relates to the GCRC, including the chain of professional and administrative responsibility. If these relationships involve another corporate entity (hospital, medical school, research institute, local government, etc.), describe the lines of authority and submit a letter of agreement signed by the responsible officer of each organization which supports the grant stating that the research area will be available on a continuing basis.

C. Administration

Describe the administrative structure under which the GCRC will operate, including the responsibilities of the Program Director(s), the local GCRC Advisory Committee (GAC) and its Subcommittees, and any other Committees with advisory roles on specific aspects of the GCRC's clinical research projects, such as the Institutional Review Board for Human Experimentation (IRB). Provide a membership list, with academic titles, for each committee. Describe the administrative relationship among the Principal Investigator, Program Director, and local GAC.

Indicate the procedures for coordination among Principal Investigator, Program Director, GAC, and individual investigators regarding patient care responsibilities and review and approval of submitted research projects. Describe the process for peer review or audit of the classification of research patients as Category A, B and/or D. Describe the process by which the GAC reviews and designates industry-related research patients as Category A, B and/or D.

D. Patient Care

Delineate responsibilities for medical care delivery by investigators and Program Director's oversight of medical care and research projects. Describe existing mechanisms to assure compliance with IRB-approved projects and witnessing of informed consent. Describe role of interns, residents and fellows in patient care and emergency coverage.

E. Training and Career Development

Describe the role of the GCRC as an institutional resource in the clinical research training and career development of medical students, house officers, research fellows, and paramedical personnel. In competing renewal applications, summarize previous work by CAPs and MCAPs and K23 awardees that used the GCRC (whether funded by NCRR or another NIH Institute), as well as their current academic positions, research support, and percent of effort devoted to basic and clinical research, teaching, patient care, and administration. If funds are requested for a "Mentored Medical Student Clinical Research Program" (whereby a medical or dental student could take time off from medical school to engage in a mentored program of up to one year, including supervised participation in clinical research, didactic coursework related to patient-oriented research, and/or acquisition of laboratory skills that can be applied to patient-oriented clinical research efforts), the following information should be provided: selection method (by the GAC or another committee constituted for this purpose); selection guidelines including eligibility of students and mentors, and the student's plan for research, didactic coursework, and/or acquisition of laboratory skills; evaluation plan; results over the past five years including number of students funded each of these years, name of student and mentor, what was accomplished, and their current activities.

F. Core Laboratories

The primary functions of a Core Laboratory are to provide sophisticated support to ongoing GCRC protocols and to develop or validate new methods for this purpose. In addition, the Laboratories may provide clinical research training for investigators, fellows, students, and technicians. Core Laboratory requirements vary widely. Some GCRCs may not need a full Core Laboratory, rather only a small sample-processing area.

In general, routine tests, such as blood chemistries, hematologic determinations and urinalyses that are available in the hospital's clinical chemistry laboratories or in another Medicare-approved clinical chemistry laboratory, are not performed in the GCRC Core Laboratory, but rather supported through ancillary funds. However, such tests may be performed in the GCRC Core Laboratory when this is critical for timeliness, when an extreme degree of accuracy is needed, or if patient safety is at stake. Whenever possible, cost sharing of Core Laboratory functions should be sought from the investigators.

The GAC is responsible for reviewing the Core Laboratory to assure that its activities are serving the research needs of a wide array of investigators, that laboratory tests are not routine, and that priorities are set for the use of the Laboratory when concurrent demands exceed the Laboratory's capacity. In all cases, NIH-supported investigations are to be given the highest priority.

The application should justify the requested Core Laboratory resources in terms of the

collective future resource needs of the investigators. Examples of requested Core Laboratories include those used for mass spectrometry determinations, magnetic resonance imaging, body composition determinations, and others. To allow an adequate evaluation of the Core Laboratory request, the following information must be provided, either for the most recent, complete 12-month period in a competing renewal application, or as projected in a new application:

1. The number and size of rooms used as Core Laboratories;

2. Type and number of laboratory analyses performed and proposed for the Core Laboratory, and an analysis for each test according to the percentages which have been and are proposed to be performed for each investigator or investigator group. In existing units, laboratory log books may be examined at the site visit;

3. Description of the criteria for deciding the types of analysis to be performed in the Core Laboratory. Role of GAC in this process. The number of investigative groups for whom specialized studies will be run;

4. Relationship to the laboratories of the Program Director and the Associate/Assistant Program Directors;

5. Future changes in research direction or expected GCRC activity which will alter Core Laboratory requirements;

6. Role and qualifications of Core Laboratory Director and, if requested, justification for level of support requested for that position. See Guidelines for additional information as to level of support permitted;

7. Role and qualifications of Core Laboratory support staff;

8. If the core has undergone a certifying review, the dates and results of that review should be described;

9. Means employed to protect patient privacy.

G. Biostatistical Support

Provide a brief description of project review by the GAC and provisions for review of biostatistical design and subsequent data analysis. Tell how much support for a biostatistician is requested, provide qualifications of the individual, the mechanisms by which the biostatistician will interact with investigators and the role to be assumed in research project design and analysis.

H. Informatics Core

The application should justify the requested Informatics Core resources in terms of the collective future resource needs of the investigators. The Informatics Core is to meet database management, special applications and analysis needs of GCRC-based investigators. Careful consideration should be given to the system configuration to facilitate investigator access to the software systems. To allow an adequate evaluation of the Informatics Core request, the following information must be provided, either for the most recent complete 12-month period in a competing renewal application, or as projected in a new application:

1. Provide a narrative justification for the space required to accommodate all functions of the Informatics Core.

2. Provide a narrative justification for the equipment selected and upgrades that are needed. The narrative justification for the system should reflect both the resource need and scientific merit of the GCRC-based research projects conducted by investigators who receive primary research funding from NIH and other peer-reviewed awards. The multi-user resource must reflect multidisciplinary and multicategorical clinical research.

3. Provide brief narrative summaries of those scientific studies which will use the Informatics Core and indicate how the Informatics Core will facilitate the progress of the research projects. All studies utilizing Informatics Core resources must have GAC approval. In instances where investigators conducting off-center clinical research request access to the Informatics Core, the proposals need to be reviewed for scientific merit and the GAC needs to assign priority for access to the Informatics Core. In all cases, NIH-funded clinical research receives the highest priority.

4. Describe the future changes in research direction or expected GCRC activity which will impact Informatics Core resource requirements.

5. Describe the selection process and qualifications of the Informatics Core Manager and justify the level of support which is requested for the position.

6. Provide a description of methods employed to protect the privacy of patients' data.

7. Describe the duties of the Informatics Core Manager which should include:

a) close interface with the GCRC-supported Biostatistician to assure adequate data management and analysis support to GCRC-based investigators;

b) close interaction with Administrative Manager to prepare the administrative components of reports required by NCRR and NIH;

c) ensuring adequate hardware and software maintenance and upgrades through interactions with informatics specialists and vendors, including negotiation and maintenance of hardware and software contracts;

d) maintaining security of the physical facility, equipment, data files, and file backups and storage;

e) instruction of and assistance to clinical investigators in the use of Informatics Core resources. However, the Informatics Core Manager is not required to carry out routine data analyses for investigators or the GCRC Biostatistician;

f) administering the resources for the Informatics Core, including ordering of supplies and upgraded equipment. Charges to Informatics Core users are not allowable for Category A and B research. Prorated fees for Category D research and off-center clinical research, are to be collected and credited to the patient care category of the GCRC grant.

I. Physical Resources and Utilization

Describe the GCRC facility in sufficient detail to identify each physical component. Include schematic line drawings, reduced to the size of the continuation pages, and identify the size and use of each room. Indicate the present room arrangement and use if renovation is proposed.

If space charges are proposed as a separate cost or as part of the routine cost, include a list detailing use and square feet of each room/area to be on the GCRC. If there are GCRC areas that will not be charged to the grant, indicate which areas. In addition, provide a tabular list of rooms to be used for inpatient and outpatient studies. Whether the outpatient area is separate from inpatient area or if inpatient rooms are also used for outpatient visits, indicate which rooms, projected number of visits, length of visits and average number of hours per day and days per week.

J. Other Existing or Planned Resources for Clinical Research

Attach a brief description of all available or projected facilities for clinical research at the institution and affiliated institutions; for example, GCRCs, categorical Clinical Research Centers, privately funded research wards, etc.. Describe the location and number of beds in these facilities and explain their projected relationship to the GCRC requested in this application.

K. Data and Safety Monitoring Plan

Provide a description of the GCRC's Data and Safety Monitoring Plan. At a minimum, the Plan must state that each phase I and II clinical trial to be conducted on the GCRC, funded by

an NIH categorical Institute, must have the DSM plan approved by that Institute prior to initiation of the trial. Phase I and II clinical trials that are to be conducted on the GCRC, without funding by an NIH Institute, are not required to have NCRR approval of the DSM plan. However, in this instance, the DSM plan must be approved by the IRB and GAC prior to initiation. In addition, this section of the application, should contain information regarding the role of the Research Subject Ombudsman and others, in overseeing the DSM plans and other aspects of human subjects protection.

L. Clinical Research Feasibility Funds (CREFF)

If funds are requested for a CREFF program, provide information on guidelines for eligibility, selection criteria and an evaluation plan. Also provide for each recipient of CREFF funds over the past five years: name and faculty rank; title of project; dates of funding; funds received; and accomplishments.

Section 2
(Form PHS 398)

PART IV. RESEARCH PLAN

A. Accomplishments

In competing continuation applications, or in applications for support of a GCRC which has previously been funded from other sources, summarize scientific accomplishments from use of the GCRC since the last review. Accomplishments selected should represent advances or achievements that led to the prevention of disease, provided a better understanding of a disease process or of a physiologic mechanism, provided a new or better therapeutic approach, or resulted in a new methodology either for the early detection or diagnosis of disease. Describe outcomes of clinical trials. Describe contributions to multicenter trials. The narrative should clearly describe each accomplishment, its originality, and significance in terms of the above categories. For each accomplishment, provide the relevant publication reference(s). If the accomplishment has found application in the health care system, point this out. Describe any findings which result in more cost-effective approaches to diagnosis or therapy. The Accomplishments section should not exceed five pages.

B. Center Bibliography (Competing Continuation Applications Only)

For Center renewal applications, cite only published papers. Include scientific articles which resulted in whole or in part from investigations undertaken with GCRC resources since the last funded application. Omit publications which are in press or have been submitted but not yet accepted, and papers in preparation. Include names of all authors in the same order as they appear in the journals, as well as titles of articles, volume numbers, inclusive pages and year of publication. Asterisk those papers which cited the GCRC, i.e., either mentioned use

of the GCRC in the text, or cited the GCRC (M01) grant number.

Review articles, books, and abstracts may be cited, but should be listed separately. If research reported in an article was aided by GCRC support but did not use inpatient or outpatient facilities (e.g., Informatics Core resources), indicate this in a footnote.

C. Research Projects

Include each research project proposed for use of the GCRC including projects already under way at the time of the application. List them by project principal investigator, in alphabetical order. Exclude completed or inactive projects. All projects to be presented at the site visit must be included, even if they are awaiting approval by the GAC or the IRB at the time of submission of the application. Indicate by a footnote those projects not yet approved at the time the application is submitted.

The total page limitation of the application specified in the instructions of Form PHS 398 do not apply to GCRC applications. The length of projects selected for presentation at the site visit may not exceed 25 pages, and the length of non-presented projects may not exceed 5 pages. These page limitations are inclusive of Specific Aims, Background and Significance, Progress Report and Preliminary Studies, and Research Design and Methods sections. For literature citation follow instructions in the Form PHS 398 Kit. Each project should include a clearly identifiable hypothesis, brief background information, and an in-depth narrative of the methodology to be employed. Provide details of biostatistical design and analysis for each project. Address each of the six points listed under Human Subjects in the Form PHS 398 Kit for each project.

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects unless a clear and compelling rationale and justification is provided documenting that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy is based on the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43) and is available electronically at http://www.nih.gov/grants/guide/1994/94.03.18/. It is further discussed in documents entitled, "Outreach Notebook for the NIH Guidelines on Inclusion of Women and Minorities as Subjects in Clinical Research, August 1994," and "Questions and Answers Concerning the 1994 NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, September 7, 1994." To comply with this policy, the following "three table" format with text between table 2 and table 3 may be used. The first table should give the national demographics of the disease under study. For example, if rheumatoid arthritis were being studied, the first table would be as follows:

National Demographics for Citizens Afflicted with Rheumatoid Arthritis (%)

	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Other or Unknown	Total
Female	0.3	0.7	15.3	1.9	51.3	4.1	73.6
Male	0.1	0.2	3.0	0.4	21.0	1.7	26.4

The numbers presented in the first table should represent percentages of the total number of rheumatoid arthritis patients in the United States who fall into the listed demographic categories. For example, of those with rheumatoid arthritis in the United States, 51.3% are white females and 3.0% are black males. Following the table, a reference listing the source of the information should be identified in full.

The second table should indicate the patient distribution that would be anticipated in the protocol if no special recruiting efforts were to be made. These data can reflect either numbers of research subjects or percentages thereof and represent: a) the patients recruited into this protocol to date, b) the recruitment into a forerunner of this protocol, c) the demographic distribution of all rheumatoid arthritis patients seen at the hospital, or d) the demographic distribution of all rheumatoid arthritis patients in the city or State. It should be indicated whether the data are characterized as a, b, c or d.

Table 2 should then be compared to Table 1. If the numbers listed in Table 2 are substantially lower in minorities overall or in women, then a plan should be described that will appropriately increase the participation of the relevant groups.

Table 3 should present numbers of research subjects, not percentages. The total number should be that which the investigator's power calculation indicated as the final number of subjects to be recruited into this protocol. The numbers within Table 3 should reflect the anticipated result of the plan for gender and minority recruitment and, when totaled, equal the final number of subjects. If Table 2 for this protocol is close to or surpasses the National demographics in terms of overall minorities and women, then the Table 3 data can be adapted from Table 2. However, if the data in Table 2 are far below the National demographics in terms of minorities overall and women, then the Table 3 should reflect the outreach plan to recruit the appropriate patients. Protocols specifically designed and approved to study only one minority group(s) or one gender are excepted from this guideline.

The NIH recently announced a policy that children, defined as individuals under the age of 21, must be included in all human subjects research conducted or supported by the NIH. Adherence to this guideline is mandatory unless there are scientific or ethical reasons to exclude children from a specific study. The policy is available electronically at:

http//www.nih.gov/grants/guide/notice-files/not98-024.html. In contrast to the Women and Minorities Policy, which applies to all applications, the Inclusion of Children Policy applies only to initial (type 1) applications.

In addition, for each project, provide a justification for utilization of GCRC resources, along with an estimate of the number of research patients to be studied and the number of research inpatient days and outpatient visits (categories A, B and D) and other GCRC resources (e.g., Core Laboratory, Informatics Core , etc.) to be used annually. Provide a summary of anticipated charges by inpatient day and/or by outpatient visit for ancillary costs for each project. Additionally, provide a summary of other research needs to be provided by the individual investigator's laboratory or outside laboratories. Federal and non-federal grants, contracts, or other support held by investigators conducting the proposed study should be identified by project together with a indication of whether they relate directly to the proposed study. Indicate the grant/contract number, source of support, and inclusive period of support.

Patients studied in industry-initiated projects are classified as Category D (see Guidelines). All charges of those protocols are to be paid directly to the institution (hospital). No charges are provided by the GCRC, but discrete GCRCs receive patient care offsets determined for inpatient days by the Patient Care Agreement developed by the regional HHS office.

Each project narrative should be followed by a current bibliography supporting the hypothesis, background, and methodology, including references to papers and abstracts which have resulted from previous work by the investigator submitting the project and references to the work of others. This bibliography is essential for an adequate review.

Each project in the application to be presented at the site visit must be accompanied by a brief (one-half to one page) abstract or summary of the project. The abstract will serve as the basis for the description of the proposal which will be incorporated into the Site Visit Report reviewed subsequently by the GCRC Review Committee, and the Summary Statement reviewed subsequently by the NARRC. The summaries should be appended to the site visit schedule which is sent at the same time the proposal is submitted to the NCRR.

PART V. TABLES

TABLE A. Faculty Member Research Participation (Instructors and above). List the number of faculty members in each Department and their percent of effort devoted to research.

Example
TABLE A
Faculty Member Research Participation

Number of Faculty Members			Number of Faculty Members Devoting the Indicated Percent of Effort to Research	
DEPARTMENT	FULL-TIME	*PART-TIME	5 - 50	Above 50
Medicine				
Surgery				
Ob-Gyn				
Pediatrics				
Other Clinical Departments				
Pre-Clinical Departments				
TOTALS				

*Salaried

TABLE B. Training. Complete Table B, below. Do not include house officers (interns and residents).

Example
TABLE B
Fellows in Training

DEPARTMENTS	Number of Post-Doctoral Fellows	
	M.D.	Ph.D. or equivalent
Medicine		
Surgery		
Pediatrics		
Ob-Gyn		
Other Clinical Departments		
Pre-Clinical Departments		

1. Provide a list of all funded institutional training grants, by department or division, including grant numbers, Principal Investigators, funding sources, and inclusive dates of support.

2. For competing continuation applications, provide the name(s) of all CAPs and MCAPs supported at the GCRC at present and in the past, inclusive dates of support, specialty, and a description of their current professional activities and academic affiliations. If possible, provide information as to whether those individuals are currently funded as Principal Investigators or Co-Investigators of research grants.

3. Provide a description of the opportunities for medical students to work with GCRC-based investigators and their projects. Provide a summary of medical students supported by GCRC-based investigators. Separately provide a detailed list of medical students (by name and year), supported totally or in part by GCRC resources since the time of previous GCRC review.

TABLE C-1. Utilization of the Center, Last Three Years (for competing continuation applications and applications from Centers previously funded from other sources). Indicate the number of Category A and Category B days on the Center, scatter-bed days off the Center, and outpatient visits for each of the last three years of the grant. Provide the average length of patient stay. Centers with separate adult and pediatric units subsumed under one grant must submit separate tables for each unit.

Example
TABLE C-1
Utilization of the Center, Last Three Years
INPATIENT DAYS

Year	Category A	Category B	Scatter Bed A	Scatter Bed B	Category D	Category C	Average Length of Inpatient Stay
1997-1998							
used:	1,100	1,200	25	300	400	0	4.5 days
awarded:	1,090	1,220	25	100	400	0	
1998-1999							
used:	etc.						
awarded:							
1999-2000							
used:	etc.						
awarded:							

Indicate number of days for all categories.
Category A: Research patients or normal controls.
Category B: Patients receiving established medical care and participating in a research project. All research costs are paid by the GCRC or from the investigator's research support.
Category D: Industry-initiated research project. All charges paid by industry directly to institution.
Category C: Non-research patients who are boarders on discrete Centers.

Example
TABLE C-2
Utilization of the Center, Last Three Years

OUTPATIENT VISITS

Year		Outpatient Visits A	B	D
1997-1998	< 1 hour	500	500	500
	1 - 3 hours	500	500	500
	3 - 6 hours	75	75	75
	6 -10 hours	75	75	75
	>10 hours	75	75	75
	TOTAL (USED)	1,225	1,225	1,225
	AWARDED	1,000	1,000	1,000
1998-1999	< 1 hour	500	500	500
	1 - 3 hours	500	500	500
	3 - 6 hours	75	75	75
	6 -10 hours	75	75	75
	>10 hours	75	75	75
	TOTAL (USED)	1,225	1,225	1,225
	AWARDED	1,000	1,000	1,000
1999-2000	< 1 hour	500	500	500
	1 - 3 hours	500	500	500
	3 - 6 hours	75	75	75
	6 -10 hours	75	75	75
	>10 hours	75	75	75
	TOTAL (USED)	1,225	1,225	1,225
	AWARDED	1,000	1,000	1,000

M01-RR-_____ Principal Investigator/Program Director:_____

TABLE D-1. Principal Users of the Center (for competing continuation applications and for applications from GCRCs previously funded from other sources). List approximately ten investigators who have used the most research inpatient days and outpatient visits by grant year for the last three grant years. Provide Category A, B, and D days and outpatient visits separately. If investigators have left the institution, footnote the year of departure.

Example
TABLE D-1
Principal Users of the Center

INPATIENT DAYS

		1997-1998					1998-1999					1999-2000				
Investigator	Department	Category			Scatter-bed		Category			Scatter-bed		Category			Scatter-bed	
		A	B	D	A	B	A	B	D	A	B	A	B	D	A	B

Example
TABLE D-2
Principal Users of the Center

OUTPATIENT VISITS

Investigator	Department	1997-1998 Category A	B	D	1998-1999 Category A	B	D	1999-2000 Category A	B	D

TABLE E. Proposed Scientific Agenda for the Site Visit and Abstract Package.

For each project to be presented at the site visit, provide the following information.

1) The title of the project and the page number at which it begins in the application.

2) The name, degree (M.D. or Ph.D.) and title of the principal investigator and all co-investigators, and the page numbers at which their biographical sketches begin in the application.

3) All sources of support for each investigator and co-investigator along with percent effort, with inclusive dates and approximate current annual dollar amounts, supporting the work of these investigators, regardless of whether the funding is related to the project to be presented at the site visit. Asterisk those sources of funding which directly support at least some aspects of the research project. Include support from portions of Program Project and Center grants. For each source of support cited, provide all information as required in the Form PHS 398 including the name of the principal investigator of that grant.

4) List the resources required annually from the GCRC (inpatient days and outpatient visits by category, Informatics Core, Core Laboratory, biostatistician, and bionutrition research).

5) Provide a ½ to 1 page abstract of the project.

EXAMPLE
Proposed Scientific Agenda for the Project Site Visit

1. Clinical Studies of the Mechanism of Spherical Missile Transfer. (Protocol p. 372)

Joseph B. Tinker, M.D., Professor of Surgery (C.V. p. 119)

John S. Evers, M.D., Ph.D., Associate Professor of Anesthesiology (C.V. p. 44)

Frank L. Chance, M.D., Assistant Professor of Medicine (C.V. p. 29)

NICHD Program Project P01 CA67182, $25,000, Dr. Chance 15% effort

(P.I. of Program Project, Harry M. Steinfeldt, M.D.)
(Jan. 1, 1998 to Dec. 31, 2002; annual budget $250,000)

Resources required:	130 Category A inpatient days
(annually)	75 Category B inpatient days
	10 Category A scatter-bed days
	50 Category A outpatient visits (1-2 hours)

10 Category A outpatient visits (10-12 hours)
50 Category B outpatient visits
Informatics Core (SAS, Ingres, PROPHET, etc.)
Core Laboratory (200 insulin determinations)
Biostatistician
Bionutrition Research

Abstract of project.

Section 3
(Form PHS 398)
Appendix

Do not include substantive materials in appendices.

SITE VISIT INFORMATION

I. SITE VISIT DATE

The Scientific Review Administrator (SRA) of the GCRC Review Committee is responsible for determining the need for a site visit. In general, new and renewal GCRC applications will be site visited. Occasionally, if needed, a complex supplementary application may be site visited. In some cases, an "applicant interview" (reverse site visit) may be held. Site visit dates are scheduled by the assigned site visit SRA usually months prior to submission of the grant application. Site visits will take place between 30 and 80 days after submission of the application; Program Directors should alert investigators who will be presenting at the site visit of this time-frame.

II. ADVANCE MATERIAL

Additional information is required to supplement the application and to allow for the preparation of the site visit. The following information should be sent directly to the site visit SRA: a copy of the proposed site visit agenda and abstract package, containing the project information from Table E of the application, arranged according to the schedule described below, and a diskette containing the abstracts of the protocols to be presented at the site visit. Alternatively, this information may be submitted electronically. Indicate building, room number and address where site visit will be held. (Applicants should examine Supplement III to the GCRC Guidelines, "Information and Instructions for Site Visitors on a GCRC Site Visit," so that they will be aware of the kind of information reviewers will be seeking.)

III. SITE VISIT AGENDA for most GCRCs.

The following is a suggested site visit schedule.

DAY 1:	7:45 a.m.	Preliminary executive session of site visitors.
8:15 - 9:00 a.m.		Brief outline by the Principal Investigator and Program Director of GCRC activities since the last review (renewals only) and proposed future utilization. Overview of resources which impact GCRC.
9:00 - 9:30 a.m.		Core Laboratory Presentation (if applicable)
9:30 - 10:00 a.m.		Informatics Core Presentation and justification and role of Biostatistician (if applicable)
10:00 - 10:15 a.m.		Break
10:15 a.m.		Administrative meeting of administrative reviewer with institutional officials (concurrent with scientific presentations).
10:15 - 10:45 a.m.		Scientific Presentation #1
10:45 - 11:15 a.m.		Scientific Presentation #2
11:15 - 11:45 a.m.		Scientific Presentation #3
11:45 - 12:15 p.m.		Scientific Presentation #4
12:15 - 1:00 p.m.		Lunch
1:00 - 1:45 p.m.		Tour of Facilities
1:45 - 2:15 p.m.		Scientific Presentation #5
2:15 - 2:45 p.m.		Scientific Presentation #6
2:45 - 3:15 p.m.		Scientific Presentation #7
3:15 - 3:45 p.m.		Scientific Presentation #8
3:45 - 4:00 p.m.		Break
4:00 - 6:30 p.m.		Executive Session
DAY 2:		
7:30 - 11:30 a.m.		Executive Session

Questions arising during the executive session may require a meeting with the Program Director, who should remain available until the site visit team leaves the institution.

IV. SCIENTIFIC CONTENT

Eight scientific presentations are suggested for most Centers. Projects which will account for extensive utilization of the GCRC resources are those to be selected for presentation. The projects presented should account for a significant fraction of requested inpatient days and outpatient visits and also reflect requests for other resources (Informatics Core, Core Laboratory, bionutrition, etc.). Industry-initiated projects shall not be presented at the site visit; multicenter trials may be presented only if the investigator at your institution originated the trial or has added unique features to the project, not being conducted at other Centers, and only after discussion with the site visit SRA.

A. Project presentations are to be hypothesis-oriented investigations requiring a significant number of inpatient days, outpatient visits, or Core Laboratory facilities.

B. Scientific presentations should be limited to 15 minutes, with 15 additional minutes for discussion between site visitors and investigators.

C. Presentations may begin with a brief review of previous work (no more than five minutes) but should proceed rapidly to a clear statement of the questions proposed for future investigation. The experimental project should be described in some detail. Each presentation should consist of a description of how the GCRC will be used for the research project and a justification for requested resources (e.g., number of research inpatient days or outpatient visits by category, Informatics Core, etc.), and preliminary data.

V. ADMINISTRATIVE REVIEW

During the site visit, the consulting administrator (sometimes accompanied by an NCRR staff representative) will meet with hospital and university officials to discuss budgetary and management procedures, physical facilities, staffing, personnel functions, and other operations pertinent to the unit; they will also discuss GCRC operations with the Head Nurse, Research Bionutritionist and Administrative Manager. These discussions will be held separately from the scientific meetings. Architects and plant management personnel should be present when changes in the physical facility are requested.

VI. ADDITIONAL SITE VISIT MATERIAL

To aid reviewers, it would be helpful if the following information is made available for examination during the site visit.

A. Consent forms for all projects in the application that have IRB approval.

In addition to all consent forms required to be available for examination at the site visit, two copies of all consent forms that have IRB approval will be requested to be sent to the NCRR Office of Review (OR) shortly after the application has been received, and the consent forms will then be sent out to the site visitors for their review prior to the site visit. If the title of a

consent form is not identical to the title of the corresponding protocol, or if there is more than one consent form for a given protocol, or more than one protocol for a given consent form, this must be clearly indicated when the consent forms are submitted to OR. In addition, if there is a recent proposed addition to a protocol and the revised consent form incorporating that addition has not yet been IRB approved, this must be clearly indicated when the consent forms are submitted to OR. Indicate the IRB number and protocol number on the consent form. Provide a master list index of all consent forms indicating the date of initial IRB approval and the date of the most recent annual IRB re-approval of the protocol.

B. Copies of scientific protocols, contracts, and budgets of all industry-related projects which currently use or anticipate utilization of GCRC resources, including Informatics Core-only or Core Laboratory-only projects. Documents are to be available for both investigator-initiated and industry-initiated projects.

C. IRB records, including minutes. Site visitors are representatives of the Department of Health and Human Services, and as such are authorized to inspect and copy IRB records at reasonable times and in a reasonable manner. It is essential that the representatives be given sufficient access to records to assure themselves that IRB activities are being carried out in accordance with the Federal Regulations for the Protection of Human Subjects, as described in 45 CFR 46.

D. GAC minutes.

E. If GCRC funds are used for animal-related research activities (e.g., antibody generation, harvesting cells or other tissues), at least one of the site visitors will visit the institution's animal facilities during the course of the site visit.

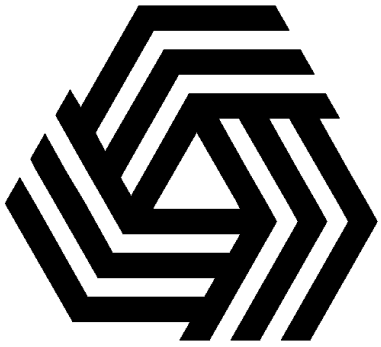
F. Tabular summary of research funding, by grant or contract, to investigators for projects presented at the site visit, as well as a separate table for those investigators with projects not presented at the site visit. The format requested in Form PHS 398 is to be provided.

G. Tabular summary of requested annual Categories A, B, and D research inpatient days and Categories A, B, and D outpatient visits by project for those presented at the site visit, as well as a separate table for those projects not presented. Indicate whether the Core Laboratory or Informatics Core resources are requested for each project.

H. Inpatient occupancy and outpatient statistics for the months since Table C was prepared.

I. One copy of the institution's catalog.

J. Biographical sketches of all major investigators not listed in the application, such as new arrivals.



National Center for Research Resources
National Institutes of Health
Department of Health and Human Services

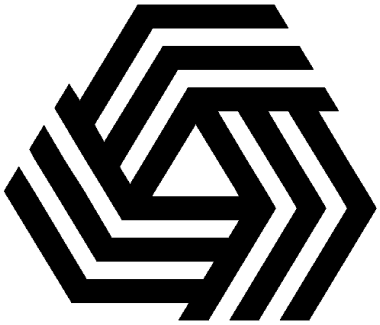
Division of Clinical Research

Supplement II: Clinical Associate Physician (CAP) and K23 Awards For Mentored Patient-Oriented Research Career Development

April 2001

The Clinical Associate Physician (CAP) Program began in 1974. The Minority Clinical Associate Physician (MCAP) Program began in 1991. CAPs and MCAPs were funded as competitive supplements to the parent GCRC (M01) grant. Starting in April, 2000, no new CAP or MCAP awards are being made. Instead, new awards for mentored patient-oriented research career development are being made under the K23 mechanism. CAPs and MCAPs that were funded prior to April 2000, may continue such funding in accordance with http://www.ncrr.nih.gov/clinical/crguide/crsup299.pdf and http://grants.nih.gov/grants/guide/notice-files/not99-143.html.

The Guidelines for the K23 program are found at: http://grants.nih.gov/grants/guide/pa-files/PA-00-004.html. Additional information regarding eligibility and assignment of K23 applications to NCRR is as follows: Candidates must have a clinical degree i.e., M.D., D.D.S., or an equivalent degree. Individuals holding the Ph.D. degree only, without an M.D. or D.D.S. degree, or a comparable medical or dental degree from a foreign country, are not eligible for an NCRR K23 award. The candidate must have an academic appointment at an institution hosting a General Clinical Research Center (GCRC). The individual must have approval of the GCRC Principal Investigator and Program Director (letters in support of the application are required) to use GCRC resources to accomplish the research goals outlined in the proposal. The candidate must also have a mentor who is an active GCRC-based investigator. The candidate must have an interest in pursuing career development in patient-oriented research towards becoming an independent clinical investigator. The applicant may also wish to pursue didactic course work and/or learn sophisticated research techniques, and should address these needs in the application. Applicants fulfilling these eligibility criteria should indicate their desire to have primary or secondary assignment to NCRR in a cover letter to the NIH Center for Scientific Review (CSR) that should be submitted with the K23 application.



National Center for Research Resources
National Institutes of Health
Department of Health and Human Services

Division of Clinical Research

Guidelines for the General Clinical Research Centers (GCRC) Program

Supplement III: Information and Instruction for GCRC Site Visitors

April 2001

An Administrative Document Issued by the
National Center for Research Resources (NCRR).

Contact Information:

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http://www.ncrr.nih.gov/clinical.htm

INFORMATION AND INSTRUCTION FOR GCRC SITE VISITORS

I. INTRODUCTION

A project site visit to the applicant institution is part of the evaluation of an application for a General Clinical Research Center (GCRC) grant. Written critiques from site visit teams and their recommendations are incorporated into a report which is presented to the next meeting of the GCRC Review Committee. This site visit report is essential to the GCRC Review Committee's evaluation of the application and serves as the basis for its recommendation (Summary Statement) to the National Advisory Research Resources Council (NARRC). Following GCRC Review Committee action, the Summary Statement with its priority score is sent to the Principal Investigator (PI). It is the policy of the National Institutes of Health (NIH) to treat applications and their supporting materials in confidence, unless a request is made for them under provisions of the Freedom of Information Act after the grant has been funded. Deliberations of review committees are considered confidential.

II. FACTORS IN THE EVALUATION

Factors considered by project site visitors include: l) scientific merit and biostatistical design of the clinical research proposals; 2) peer-reviewed funding held by participating investigators; 3) diversity of scientific areas and interaction between basic and clinical departments; 4) opportunities for junior investigators to gain expertise enabling them to become independent investigators; 5) the collective impact of the individual proposals on clinical research at the institution; 6) the budget; 7) the administration of the GCRC; 8) the physical facilities of the GCRC; and 9) the opportunities for medical students, house staff and fellows for research exposure on the GCRC and participation in research projects. Certain specific areas should be considered in evaluating these elements.

A. Specific Research-Related Factors:

1. Quality: whether the research projects are hypothesis-oriented, incorporate adequate biostatistical design, and are likely to provide new scientific information.

2. Peer-reviewed funding of investigators: whether a significant number of investigators have independent grant support, especially from the NIH or other peer-reviewed funding sources.

3. Breadth: the extent to which utilization of the GCRC will be multidepartmental and multicategorical, and whether there is interaction among investigators from multiple disciplines, including basic and clinical departments.

4. Impact of the Award:

a. Need - whether the GCRC is necessary for the proposed studies, or whether they could be done as well elsewhere in the institution.

b. Importance - significant new research contributions by GCRC-based investigators and evidence of bidirectional translation of basic and clinical research activities.

c. Resources - the number of research inpatient days and outpatient visits to be provided for scientifically meritorious projects. Assessment of GCRC resources requested for support, and the number, breadth, and quality of projects utilizing the Core Laboratory, Informatics Core, and biostatisticians, and research bionutrition resources.

d. Productivity and Accomplishments - the number and quality of publications of proposed or current GCRC investigators over the previous five years.

e. Junior Investigators - opportunity for junior physician-investigators to gain the expertise to develop into independent investigators capable of successfully competing for independent research funding. Quality of research proposals submitted by Clinical Associate Physicians (CAPs), Minority Clinical Associate Physicians (MCAPs) and K23 applicants, and the current research activities and research support of previous CAP, MCAP and K23 awardees.

f. Training and Career Development - the extent to which the GCRC is or will be utilized as a research training environment for medical students, house staff, fellows, technicians, nurses, social workers, and bionutritionists.

g. Industry - relative balance of investigator-initiated as compared with industry-initiated research projects utilizing the GCRC and appropriate categorization of research projects by the local GCRC Advisory Committee (GAC).

B. Physical Facility:

Reviewers will evaluate whether the inpatient and outpatient research areas are suitable for the nature of patient research in the age groups (e.g., infants, adolescents, the aged) and research complexity required for the proposals. In some cases, specialized facilities within the GCRC may be required for patient safety or for specialized studies. Unless otherwise justified, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO)-approved unit should be discrete, and be within the main patient care area of the hospital, close to the administrative offices of the Program Director (PD) and Administrative Manager. The Informatics Core area should be convenient and efficient, with terminals readily accessible to investigators. The Core Laboratory should be an appropriate size for its proposed function. Bionutrition research facilities, if required, should be within one discrete facility or immediately juxtaposed to the patient research area.

C. Administration:

l. Principal Investigator: individual with authority which transcends departmental boundaries, and is usually the Dean of the medical school to which the GCRC is awarded. The PI appoints the PD and members of the GAC, including its chairman. The PI derives no salary support from the GCRC award.

2. Financial Management: includes a determination of whether the local GAC has classified inpatient days appropriately as Categories A, B, C, or D, and appropriately classified research subjects as inpatients or outpatients. These classifications are important because an appropriate use of Categories B, C, and D patients conserves program funds and makes the GCRC operation more cost-effective. Other factors to be considered, primarily by the administrative reviewer, include the quality of the operational relationships between GCRC and institutional staff, the qualifications of the Administrative Manager, and the capacity of the institution to provide adequate cost-accounting data.

3. Program Directorship: The PD should be an individual with relevant knowledge, scientific expertise, and evidence of administrative skills. In addition, the PD should be involved in the conduct of GCRC-based research, and be a recipient of independent peer-reviewed research funding. If there are Associate or Assistant PDs, their qualifications, research activities on the GCRC, sources of research support and their administrative functions are also reviewed. Associate and Assistant PDs are active investigators at the GCRC and recipients of peer-reviewed funding as Principal Investigator or Co-investigator. The PD is ultimately responsible for the day-to-day oversight of GCRC activities.

4. GCRC Advisory Committee: The composition and functions of the GAC and the content of its minutes are reviewed. The GAC is directly responsible to the PI and works closely with the PD. The GAC assesses the utilization of GCRC resources--such as inpatient days, outpatient visits, Core Laboratory, Informatics Core, bionutrition research--by investigators and reviews financial management. In addition, the GAC should make a genuine effort to improve the scientific merit of the projects, review biostatistical design, address ethical concerns, oversee data and safety monitoring plans, evaluate projects for proper gender, minority and children inclusion, and classify all patients as appropriate for Categories A, B, C, or D.

5. Institutional Review Board: Membership, attendance records, and minutes of the IRB are also examined by reviewers. The minutes should document significant issues discussed and not simply state "approved," "deferred" or "rejected."

6. Patient Care: quality of professional medical and nursing coverage of patients hospitalized in the GCRC or participating in outpatient research. Patient charts should have adequately detailed histories and physical examinations along with progress notes. The project principal investigator or his/her designee should have appropriate notes on the patient chart in addition to house staff and fellows' notes. A signed informed consent statement should be on

each patient's chart and/or copies maintained in the GCRC administrative office. All projects should have received full approval from the IRB and GAC. Reviewers should examine informed consent statements.

7. Animal Care: If GCRC funds support animal related research activities, reviewers should determine whether the proposed use of the animals is justified, and at least one of the site visitors will visit the animal care facility.

D. Budget:

The requested budget is organized into the following categories: Personnel, Consultant Costs, Equipment, Supplies, Travel, Patient Care Costs, Alterations and Renovations, and Other Expenses. In general, it is the responsibility of the site visitors to determine whether budgetary items are justified by worthwhile scientific projects in the application, not simply whether the costs are properly estimated. For example, the review process should determine how much support for program directorship is justified and how many nurses are required by the projects approved. Reviewers should also determine whether equipment requests are justified, not simply the equipment costs, and how many inpatient days and outpatient visits are necessary. Ordinarily, no more than 50 percent of the PD's time is supported for the administrative oversight of the GCRC; exceptions are considered on a case-by-case basis. Associate and Assistant PDs may also be supported for administrative oversight, not usually in excess of 25 percent of time for each individual unless unique GCRC needs require support up to 50 percent of time of an established, funded investigator as an Associate Director. In general, support for total program directorship of a GCRC does not exceed l.0 full-time equivalent (FTE), although this may be exceeded for very large or complex GCRCs. The level of support for laboratory supplies depends on the nature of the technology in the Core Laboratory. Routine chemistries (such as CBC, urinalyses, SMA 24, liver function tests) are not to be supported in the Core Laboratory, but rather to be paid as patient research ancillaries or by third parties if the patient category is B, C, or D. Alterations and renovations are also sometimes the subject of cost recommendations by site visitors. Using advice from expert consultants, these recommendations are based on scientific merit of GCRC-based research, need for the alterations and cost-effectiveness.

Site visitors are asked to make a recommendation on each request in the application. Decisions should be deferred only if key information which is needed by reviewers is not available but can be provided by the applicant in a reasonable period of time. A failure of the applicant to provide adequate justification for budget items may result in disapproval, not deferral.

III. SITE VISIT CONDUCT

A. Nature and Purpose:

The site visitors function as a fact-finding team and group of expert consultants for the Initial

Review Group, the GCRC Review Committee. Usually two or more members of the GCRC Review Committee are among the site visitors, and one of them serves as Chairperson. The remainder of the site visitors are scientists with specific expertise for particular areas of research described in the application, and an administrative reviewer. The Chairperson serves as moderator, conducts the executive sessions, and is primarily responsible for presenting the application and the report of the site visit team to the next meeting of the GCRC Review Committee.

A member of the NCRR Office of Review (OR) attends all site visits as Scientific Review Administrator (SRA), and provides necessary administrative information to the site visit team, communicates between GCRC personnel and the site visit team, instructs the visitors in their duties, monitors the process and conduct of the review, interprets review and program policy, collects review materials generated by members of the site visit team, and formulates the site visit report for the GCRC Review Committee. An NCRR Grants Management Specialist may also be present at the site visit to provide assistance to reviewers. In addition, a member of the GCRC Program staff usually attends the site visit and serves as an information resource on interpretation of program policies for the members of the site visit team.

At an executive session at the beginning of the site visit, the team discusses the agenda, addresses potential concerns raised in preliminary review of the submitted application, and may ask the SRA to request specific documents (e.g., patient consent forms, correspondence and other documents which relate to industry-related research).

B. Site Visit Agenda:

The following is a typical site visit agenda for most GCRCs The schedule is sometimes modified to suit very large GCRCs.

DAY 1:	7:45 a.m.	Preliminary executive session of site visitors.
	8:15 - 9:00 a.m.	Brief outline by the Principal Investigator and Program Director of GCRC activities since the last review (renewals only) and proposed future utilization. Overview of resources which impact GCRC.
	9:00 - 9:30 a.m.	Core Laboratory Presentation (if applicable)
	9:30 - 10:00 a.m.	Informatics Core Presentation and justification and role of Biostatistician (if applicable)
	10:00 - 10:15 a.m.	Break
	10:15 a.m.	Administrative meeting of administrative reviewer with institutional officials (concurrent with scientific presentations).

10:15 - 10:45 a.m.	Scientific Presentation #1
10:45 - 11:15 a.m.	Scientific Presentation #2
11:15 - 11:45 a.m.	Scientific Presentation #3
11:45 - 12:15 p.m.	Scientific Presentation #4
12:15 - 1:00 p.m.	Lunch
1:00 - 1:45 p.m.	Tour of Facilities
1:45 - 2:15 p.m.	Scientific Presentation #5
2:15 - 2:45 p.m.	Scientific Presentation #6
2:45 - 3:15 p.m.	Scientific Presentation #7
3:15 - 3:45 p.m.	Scientific Presentation #8
3:45 - 4:00 p.m.	Break
4:00 - 6:30 p.m.	Executive Session

DAY 2:

7:30 - 11:30 a.m.	Executive Session

Questions arising during the final executive session may require a meeting with the PD, other administrative staff as well as investigators, who may or may not have presented on the preceding day; all should remain available until the site visit team leaves.

C. Scientific Content:

1. Project presentations are to be hypothesis-oriented and include justifications for GCRC resources requested for carrying out the studies.

2. Scientific presentations are limited to 15 minutes, with l5 additional minutes for discussion between site visitors and investigators.

3. Presentations may begin with a brief review of previous work (no more than three-to-five minutes) but should proceed rapidly to a clear statement of the questions proposed for future investigation. The experimental protocol should be described in some detail. Each presentation should consist of a description of how the GCRC will be used for the research project and a justification for requested resources (e.g., number of research patient days or visits by category, Informatics Core, etc.), and preliminary data.

4. For each presentation, reviewers will evaluate the scientific merit of the project and its inpatient day, outpatient visit, laboratory, Informatics Core, bionutrition research, nursing, and any other GCRC resource needs. In addition to asking questions about projects that are presented, reviewers may question investigators about projects described in the application but not presented.

During the scientific presentations, the administrative consultant will meet with institutional representatives, the GCRC Administrative Manager, Nurse Manager, and Bionutrition Research Manager, and any other relevant GCRC staff.

D. Executive Sessions:

During this time, the administrative consultants will present a summary of GCRC administration and fiscal management to the site visit team. The primary reviewers of presented projects and specific GCRC resources (e.g., Informatics Core, Biostatistics, Core Laboratories) will present their critiques, including their evaluations of scientific merit and need for the GCRC resources. Following these presentations and discussion, reviewers will individually score (in a closed ballot, using the numerical ranges described below) each of the presented projects, both for "Scientific Evaluation" and "Center Resource Needs," and will then collectively make their recommendations on each of the items requested in the budget: inpatient days and outpatient visits (Categories A and B), grant-supported positions, equipment, supplies, renovations, etc. In addition, site visitors will be assigned projects to review that are not presented at the site visit to assess their scientific merit, need for Center resources, inclusion of women, minorities and children, and whether any human subject concerns exist. Written comments for the projects not presented are only requested if there are safety and/or women/minority/children inclusion issues. The PD should be available to address any questions raised during the executive session.

IV. RESPONSIBILITIES OF THE SITE VISIT CHAIRPERSON

The Chairperson of the site visit team, usually a member of the chartered GCRC Review Committee, should be a senior clinical investigator experienced in the review of complex multidisciplinary applications and generally knowledgeable in the scientific areas to be reviewed. When there is to be no subsequent review by the chartered GCRC Review Committee, due to conflict of interest or other reasons, the site visit team will also constitute a Special Emphasis Panel (SEP) and the site visit Chairperson becomes the Chairperson of that Panel. It is expected that the Chairperson is to become thoroughly familiar with the entire application prior to coming to the site visit.

At the site visit, at the beginning of each of the executive sessions of the site visitors, the site visit SRA together with the Chairperson, brief the site visitors on each of their responsibilities and answer questions from the site visitors. The Chairperson may find it necessary to request additional information from the PD. This is done through the site visit SRA.

During the presentations at the open sessions of the site visit, the Chairperson moderates the flow of the presentations, makes sure that the presenters keep to the predetermined schedule, and assures that the presenters leave adequate time for questions. At the end of each presentation, the Chairperson invites the members of the site visit team to address questions to the presenter on issues that need further clarification. The site visitors should be thorough in their efforts to obtain all information necessary for adequate evaluation of the proposal, but the questions asked are to be relevant to the presentations, and the Chairperson must remain alert not to allow the discussion to develop into a confrontation. The Chairperson is to assure that, at all times, the site visit remains a friendly, non-adversarial, fact-finding mission. The reviewers are asked to rate every administrative or scientific section according to a scale provided by the SRA.

During the concluding executive session of the site visit, the Chairperson moderates the discussion on the scientific presentations and on various programmatic issues and decides when to cut off discussion on each topic and proceed to scoring or voting. The Chairperson leads the discussion on the budget with the assistance of the site visit SRA and other NCRR staff, assuring that recommended deletions from the requested budget are justified.

V. PREPARATION OF REVIEWS OF SCIENTIFIC PRESENTATIONS

Reviews of all projects presented at the site visit at a GCRC should be written in a uniform format. Additionally, each project receives two priority scores. The first priority score reflects the scientific merit and the second, the need for GCRC resources. The projects presented at the site visit should reflect a significant portion of the resources requested within the GCRC's application.

Each project will be individually reviewed, and the assigned primary reviewer(s) will read his/her critique of the project with suggested recommendations to the entire site visit team. If, after discussion among the site visitors, a majority of the members of the site visit team disagree with the critique, the level of enthusiasm for scientific merit, or GCRC resource needs expressed by the primary reviewer(s), then the written critique will be changed to reflect the view of the majority. A detailed written summary, in the format provided below, will have been completed and given to the SRA at the close of the site visit. It is strongly recommended that primary reviewers prepare their reports ahead of time, typewritten, double-spaced. The reports should be edited and modified as necessary at the time of the site visit to reflect the site visit team's evaluation and recommendations.

FORMAT FOR SCIENTIFIC PROJECT REVIEW

A. Protocol Title:

B. Investigator Name(s):

C. Summary of Investigator Credentials: Describe the professional background and training of

investigator(s), publications in peer-reviewed journals, and current research grant support. Is the investigator appropriately trained and well suited to carry out this protocol? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?

D. Summary of Proposal: You need not supply a summary of the proposal, as this will be taken from the abstract supplied by the investigator in the grant application. However, if there are major changes in the project as presented at the site visit compared to that in the grant application, the reviewer should add text indicating the changes.

E. Critique: Do not include descriptive information in this section. Please address in five individual sections each of the criteria listed below. Under each criterion are sample questions. These are examples only, and you need not feel constrained to address each query. For competing continuation (renewal) applications, include an evaluation of progress over the past project period. For amended application, evaluate progress, changes, and responses to the critique in the summary statement from the previous review. Indicate whether the application is improved, the same as, or worse than the previous submission.

(1) Significance
Does this protocol address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that move this field forward?

(2) Approach
Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the protocol? Does the applicant acknowledge potential problem areas and consider alternative tactics?

(3) Innovation
Does the protocol employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

(4) Investigator
(Described in C above)

(5) Environment
Does the scientific environment in which the protocol will be performed contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

(6) Overall Evaluation
Briefly summarize the strengths and weaknesses of the protocol and recommend an overall level of merit, weighting the above criteria as you feel appropriate. A protocol does not need to be strong in all categories to be judged likely to have a major scientific impact. For example, an investigator may propose to carry out important work, that by its nature is not innovative, but is essential to move a field forward.

Provide a detailed narrative based upon the written proposal and the additional information obtained at the site visit. Do not include questions in your critique; any questions you have should be asked during the site visit and your evaluation of the answers made part of your write-up. In preparing your evaluation, please be concise, address all issues in the third person; state what is missing, what remains unclear; and avoid any use of pejorative language. If in your preliminary evaluation you have noted deficiencies in the proposal or issues requiring clarification which are adequately dealt with during the site visit, this portion of your review should be modified or deleted.

F. Scientific Recommendation: The scientific merit of the proposal is the major determinant in the assignment of a score. The record of the investigator, while an important factor, does not justify a high level of enthusiasm for projects with serious scientific deficiencies. The recommendation should be a numerical score ranging between 1.0 and 5.0 (1.0 being the best) or, if the proposal does not have substantial and significant merit, a motion may be entertained for "not recommended for further consideration."

G. Center Resource Needs: Here use one of the descriptors listed below in your recommendation.

Descriptor	Numerical Range
Cannot be carried out without Center resources	(1.0 - 1.5)
Unlikely to be carried out without Center resources	(1.6 - 2.5)
Could possibly be conducted off-Center, but Center resources would facilitate study	(2.6 - 3.5)
Minimal need for Center resources	(3.6 - 5.0)
No apparent need for Center resources	(No Score)

H. Human Subjects Issues: Indicate whether any additional restrictions or clarifications for patient enrollment in the proposed study should be considered, and whether ethical issues exist. If none, state so specifically. Reviewers should examine consent forms. A recent NIH redefinition of a Human Subject Concern is "Any potential or actual unacceptable risk, or inadequate protection against risk(s), to human subjects as described in any portion of the application or proposal."

I. Inclusion of Women, Minorities and Children: Indicate whether inclusion of women, minorities and children is properly addressed in the project, and provide the appropriate code.

GENDER CODE	MINORITY CODE	CHILDREN CODE
First Character: G	First Character: M	First Character: C
Second Character	Second Character	Second Character
1=both genders 2=only women 3=only men 4=gender unknown	1=minority and nonminority 2=only minority 3=only nonminority 4=minority representation unknown	1=both children and adults 2=only children 3=no children included 4=representation of children unknown
Third Character	Third Character	Third Character
A=scientifically acceptable U=scientifically unacceptable	A=scientifically acceptable U=scientifically unacceptable	A=acceptable U=unacceptable

J. Animal Use Issues: If animals are involved, state whether their use and care are appropriate for the proposed studies.

K. Summary of Resources Requested and Recommended: Provide a summary of the resources requested by the investigator (category A and/or B inpatient days and/or outpatient visits, Core Laboratory usage, etc.), and your judgment of what is needed. For industry-related projects, state whether the study is investigator-initiated or industry-initiated.

Important Note: At the site visit, you should modify the review you wrote prior to coming to the site visit to take into account additional information presented at the site visit, as well as the discussion and consensus of the site visit team. Please edit your written review accordingly and give it to the SRA by the close of the meeting. Provide the SRA a "hard copy" of the critique and on a disc in WP6.1 or MSWord.

VI. PREPARATION OF REVIEWS OF ADMINISTRATION AND INFRASTRUCTURE

The administrative reviewer of the GCRC site visit team should use the following format to prepare the written critique for the site visit. You are requested to write up the following sections: A. BACKGROUND; B. ORGANIZATION AND ADMINISTRATION; C. NURSING; D. BIONUTRITION RESEARCH; and E. PHYSICAL FACILITY. Other members of the site visit team will provide evaluation of: F. PROGRAM DIRECTORSHIP; G. ACCOMPLISHMENTS; H. GAC; I. IRB; J. PATIENT CARE; K. TRAINING AND CAREER DEVELOPMENT; L. CORE LABORATORY; M. BIOSTATISTICS; N. INFORMATICS CORE; O. DATA AND SAFETY MONITORING PLAN; and P. CLINICAL RESEARCH FEASIBILITY FUNDS. Each of these categories is reviewed according to the instructions given below and given a verbal descriptor. The list of descriptors and corresponding priority scores is:

Descriptor Numerical Range

Outstanding	(1.0 - 1.5)
Excellent	(1.5 - 2.0)
Very good	(2.0 - 2.5)
Good	(2.5 - 3.5)
Acceptable	(3.5 - 5.0)

A. BACKGROUND (Need not be more than a half a page, single spaced).

This section should briefly, but accurately, describe the following: organizational structure of the institution (hospital); 2) the relationship of the medical school to the state or local government (if appropriate), or its relationship to any other entity; 3) institutional chain of command; 4) the different types of health-related professional schools; 5) the approximate size of the faculty; 6) the types of degrees the medical school offers (M.D., Ph.D., M.D./Ph.D., etc.); 7) the number of students, fellows, interns, etc., being trained; 8) the number of beds and bed occupancy of the hospital(s); 9) the administrative and financial structure of the institution; and 10) the administrative lines of responsibility, as related to the administration of the GCRC grant. Describe the financial structure: Medicare, Medicaid, private patient income, etc.

Describe briefly the history of the GCRC. Mention administrative changes (P.I., Program Director, etc.) since the last review of the GCRC and particularly note changes made in response to critiques of the previous review.

B. ORGANIZATION AND ADMINISTRATION

Administration and Financial Management: Briefly describe the lines of responsibility within the Institution and GCRC concerning administrative matters. If there are separate units, such as

separated inpatient and outpatient units, list these and give name and rank of persons in charge. Discuss financial management within the Institution and GCRC: 1) office responsible for the preparation of the proposed patient care rates; 2) office responsible for the preparation of the financial status reports; 3) persons responsible for the authorization of grant expenditures and verification of the charges to the grant; 4) patient bills; 5) costs by project; 6) verification and control of charges to grant; 7) involvement in budget preparation for application; 8) review of routine cost stepdown in patient care rates; 9) census data records by category: A, B, C, D inpatient days, outpatient visits, scatter-bed days; 10) records for annual and expenditure report requirements; and 11) classification of inpatient days and outpatient visits along with the appropriate designation of patients to categories.

C. NURSING

Evaluate whether the requested number of nursing personnel is justified on the basis of the number and intensity of research projects. Your evaluation should include the following: 1) relationship between and hospital nursing administration and the GCRC nursing staff; 2) evaluation of the Head Nurse/Nurse Manager; 3) stability of the staff; 4) involvement of nurses in practical aspects of project planning and in nursing research; 5) staffing patterns; 6) extent of weekend research activity on the GCRC; 7) source of staff coverage for leave and holidays; 8) nursing student training; 9) number of nurses required for outpatient or scatter-bed activities; 10) nursing care required by research subjects and category C and D patients, severity of patient illness, and extent of special nursing problems: children, transplant subjects, acutely ill subjects, patients in isolation, etc.; and 11) adequacy of current number and qualifications of nursing staff and recommendation for any requested increments in nursing positions.

D. BIONUTRITION RESEARCH

Evaluate past utilization of bionutrition research and the future needs, and determine if the request is justified on basis of the projects. Your evaluation should include the following: 1) interaction between hospital dietary staff and GCRC bionutrition research staff; 2) evaluation of bionutrition research manager; 3) stability of staff (rate of turnover); 4) dietary student training; 5) bionutritionist involvement in practical aspects of project development and in bionutrition research; 6) staffing pattern (weekdays and weekends); 7) number of hours the research bionutrition area is open; 8) meals planned, modified, prepared on unit and served - number of formula diets - number of meals served to outpatients; 9) number of meals prepared for category C patients in diet kitchen; and 10) adequacy of current bionutrition research staffing and recommendations for any requested increments of bionutrition research positions.

E. PHYSICAL FACILITY

Evaluate the configuration of the space on the GCRC needed to implement the scope of research activities recommended. Your evaluation must include considerations for outpatient use as well as inpatient use, computing facilities, and all other space on the GCRC.

Note changes that were made in the physical facility of the GCRC since the last review, and describe the general appearance of the GCRC and ways in which its configuration or maintenance needs to be improved.

Assess the most cost-effective configuration on the GCRC *vis a vis* the site visit recommendation for inpatient research days and outpatient visits, taking into account the complexity of the proposed research for proposals of high scientific merit and the level of illness of research patients. Review the list in the application detailing use and square feet of each room/area proposed for the GCRC and areas that will not be charged to the grant. Review the proposed list of rooms to be used for inpatient and for outpatient studies. Assess cost effectiveness of configuration *vis a vis* the projected number of visits, length of visits, average number of hours per day and days per week. If the proposed configuration is disparate with the resource needs projected by the site visit team recommendation for inpatient research days and outpatient visits, provide an alternative configuration during the executive session of the site visit.

If alterations and renovations are requested, provide an explanation for these and make recommendations to the site visit team whether or not the alterations and renovations are justified in terms of the needs of the GCRC.

Review all requests for equipment and for supplies; provide recommendations of the site visit team, and justification for the recommendations.

F. PROGRAM DIRECTORSHIP

The site visitor assigned primary responsibility for reviewing Program Directorship should describe the professional background of the Program Director, Associate Director(s) and/or Assistant Director(s); training, publications in peer-reviewed journals, current research funding, history of demonstrated scientific and administrative leadership, and the extent to which GCRC resources are used. For each individual, detail administrative functions on the GCRC and evaluate the appropriateness of the proposed effort (fraction of FTE).

G. ACCOMPLISHMENTS

This section is only written for GCRC renewals and not for new GCRCs. Highlight major scientific accomplishments of the GCRC since the last competitive renewal. Accomplishments selected should represent advances or achievements that led to the prevention of disease, provided a better understanding of a disease process or of a physiologic mechanism, provided a new or better therapeutic approach, or resulted in a new methodology for the early detection or diagnosis of disease. The narrative should make clear the nature of each accomplishment, its originality, and its significance. If the accomplishment has found application in the health care system, point this out. Describe any findings which result in more cost-effective approaches to diagnosis or therapy. Did the Bibliography section of the application properly indicate those publication which cited the GCRC grant?

H. GAC

Describe the makeup and functioning of the GAC. At the site visit, review minutes of recent GAC meetings. Are minutes complete and informative? Are meetings held regularly? Is attendance adequate? Is the GAC operating properly (i.e., approving projects before they begin; classifying projects as category A, B or D, especially industry-related projects; assuring implementation of the NIH policy on the inclusion of women, minorities and children as study subjects; approving data and safety monitoring plans; overseeing the Core Laboratory; setting Center policies)?

I. IRB

Describe the makeup and functioning of the IRB. At the site visit, review minutes of recent IRB meetings and consent forms. Are minutes complete and informative? Are meetings held regularly? Is attendance adequate? Is the IRB often requiring changes in proposed protocols and/or consent forms submitted for its review? Are the consent forms adequate?

J. PATIENT CARE

Delineate responsibilities for medical care delivery by investigators and Program Director's oversight of medical care. Describe the role of interns, residents and fellows in patient care and emergency coverage. At the site visit, inspect some patient charts and comment on adequacy of chart entries including records of histories and physical examinations.

K. TRAINING AND CAREER DEVELOPMENT

The training of health professionals in the methods of clinical investigation should be an integral part of the research effort on every GCRC. The GCRC should provide a major local institutional focus for training in clinical research methodology, bioethics, biostatistics, clinical trial design, epidemiological studies, and other methods, including basic laboratory methods. Formal courses may be set up for this goal and include NRSA fellows and trainees as well as CAPs K23 awardees, and junior faculty. Regular rotation on the GCRC by research fellows, house officers, and medical, nursing, and dietary students is encouraged. Because GCRCs are expected to represent models of excellence in contemporary clinical research techniques, they may also be used for other instructional purposes, including programs of continuing education for practicing physicians, nurses and dietitians. If the institution has received a K30 award, describe how the GCRC is involved.

Describe the accomplishments and plans of the GCRC as a training resource for CAPs, K23s, medical students, house officers, fellows, faculty, nurses and dietitians.

L. CORE LABORATORIES

The Guidelines for the GCRC Program state that the primary functions of a Core Laboratory are the support of ongoing GCRC clinical research and the development or validation of new methods for this purpose; it may also include clinical research training of investigators, fellows, students, and technicians. Not all GCRCs need a Core Laboratory. Sometimes the only requirement is for a small sample-processing area.

In general, routine blood chemistries, hematologic determinations and urinalyses, available in the hospital's clinical chemistry laboratories or in another Medicare-approved clinical chemistry laboratory, are not supported in the GCRC Core Laboratory, but rather paid as ancillaries. However, such tests may be supported in the GCRC Core Laboratory when this is important for patient safety, timeliness or accuracy which will affect the scientific quality of the results.

Prepare your critique of the Core Laboratory addressing the following issues:

1. The justification for a Core Laboratory in terms of collective needs and cost.

2. The scientific merit of projects and availability of peer-reviewed funding of investigators using or requesting core laboratory function and activities.

3. The types of laboratory determinations to be performed. How decisions are made as to which analyses will be performed?

4. The role, qualifications, and full-time equivalents requested for the Core Laboratory Director and technical staff. Justification for level of effort in terms of Core Laboratory function and complexity.

5. The utility of the Core Laboratory as a resource for a wide spectrum of clinical research by GCRC users. Number of investigators using the GCRC and number using the Core Laboratory. Is there inappropriate dominance of Core Laboratory usage by only one or two investigators or groups?

6. The performance of the Core Laboratory to date and its proposed future direction as influenced by expected changes in GCRC activity. Its use for training of clinical investigators, students, fellows, and technicians.

7. The adequacy and appropriateness of space and equipment to carry out the work.

8. The cost of the Core Laboratory operation including personnel, equipment to be purchased, and consumable supplies.

9. The adequacy of record keeping**,** confidentiality and quality control procedures. Is the laboratory CLIA certified?

10. Is there any intermingling of personnel, space, or equipment of the Core Laboratory with other laboratories such as the GCRC Program Director's research laboratory or the hospital's clinical chemistry laboratory? Can those activities be identified and appropriate charges made?

11. Is there appropriate reimbursement to the GCRC grant for those tests for which investigators are provided support through their peer-reviewed funding? (Reimbursement is transferred to the patient care category of the GCRC grant).

12. Cost effectiveness, *per se***,** does not provide justification of a Core Laboratory or any of its separate functions and components.

M. BIOSTATISTICS

Is there a biostatistician (with proper qualifications) funded by the GCRC grant? Is he/she a member of the GAC and does he/she review all projects before they are approved to begin on the GCRC? Do the projects in the application (both those presented at the site visit and those not presented) document proper statistical design including appropriate power calculations, sample sizes and stratifications?

N. INFORMATICS CORE

1. Evaluate the scientific merit of GCRC projects using Informatics Core and evidence of peer-reviewed funding of investigators.

2. Evaluate the reasonableness of proposed hardware configuration in light of GCRC size and anticipated investigator use and the plans to accommodate growth or extend usefulness, e.g., local area network within GCRC or institution. Is it/will it be cost-effective?

3. Comment on location of the resource. Include comments on access to Informatics Core by staff and to the Informatics Core Manager for help on technical problems.

4. Comment whether appropriate quality control of data acquisition and data maintenance are employed. Is data security in place?

5. For a renewal application, evaluate information on past use.

    a. Evaluate evidence of appropriate utilization of system and rationale for requested changes. Is data storage and analysis appropriate?

b. Is there review and oversight by the GAC for utilization of the Informatics Core resource? Is there evidence that the Informatics Core Manager and the Biostatistician have input into project review for needs assessment (statistical analyses; requisite software)?

c. Identity and number of investigators or individuals with hands-on experience.

d. Comment on utilization for collaborative investigations or registries.

e. Evaluate the extent to which the Informatics Core is used for non-GCRC based studies and whether these studies are related to ongoing or proposed research projects at the GCRC.

6. Role/expertise of Informatics Core Manager in implementing/supporting systems at GCRC site.

O. DATA AND SAFETY MONITORING PLAN

Evaluate the overall Data and Safety Monitoring Plan of the GCRC. Will there be an approved DSM plan for each Phase I and II clinical trial protocol before the protocol begins? What is the role described in the application of the IRB, GAC and Research Subject Ombudsman? Is the overall DSM Plan adequate?

P. CLINICAL RESEARCH FEASIBILITY FUNDS

Is there a request for a CREFF Program? If so, comment on the guidelines for eligibility, selection criteria and evaluation of the program. If the CREFF Program has been in existence, comment on its accomplishments to date.

VII. STRENGTHS AND WEAKNESSES

A summary listing of the GCRC application's strengths and weaknesses will be compiled by the Chairman of the site visit team, and discussed near the conclusion of the site visit meeting.

A. Typical strengths of an excellent GCRC application may include the following:

Hypothesis-oriented projects of high scientific merit and good biostatistical design, with demonstrated need for the GCRC, a substantial number of investigators receiving peer-reviewed grants from Federal agencies; publication of research findings in high quality, peer-reviewed journals; evidence of multidisciplinary research among both basic and clinical departments; a balance of senior and junior investigators; effective efforts to encourage and promote career development of young clinical investigators; scientifically and administratively strong Program Director; good institutional support to the GCRC, Core Laboratory and Informatics Core used by a large number of investigators and projects; well-trained and effective nurses and bionutrition

research staff; functional and attractive physical facility; unique patient populations; positive response to weaknesses in past review.

B. Typical weaknesses of a GCRC application may include the following:

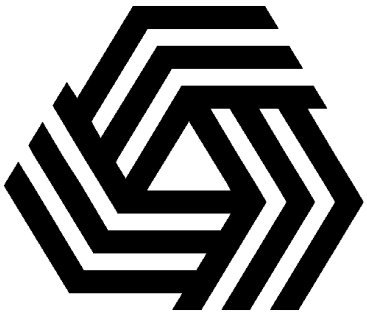
Minimal peer-reviewed grant support to GCRC investigators; several projects with serious flaws in biostatistical design; several projects with no real need for the GCRC; many papers by investigators proposing to use the GCRC published in journals not subjected to critical peer-review; domination of the GCRC by one research group; many projects are descriptive rather than hypothesis-testing; poor utilization of outpatient facility and research beds; inadequate correction of weaknesses cited at the previous review; few investigative groups active in research; institution not supportive of the GCRC; deficiencies in physical facility; lack of supervision of younger physician-investigators; application or site visit not well prepared; Program Director not actively involved in research and not independently funded; inadequately functioning local GAC and/or IRB; GCRC not used well for training; inadequate inclusion of women, minorities and children in projects.

VIII. SUMMARY AND RECOMMENDATIONS

The Chair will entertain a motion for not recommending the application for further consideration. In the absence of such a motion, the Chair will entertain a motion for the number of years recommended for support. The majority vote carries. If the site visit team is also a Special Emphasis Panel (SEP), all of the reviewers record a final priority score for the GCRC.

The team will then discuss the budgetary recommendation for the GCRC. Reviewers should provide an explanation for any reduction or deletion in the requested budget. Should there be a difference of opinion, the majority vote carries.

For a SEP, if there is a split vote (two or more votes of dissent) with regard to not recommending the application for further consideration, a minority report shall be prepared.



National Center for Research Resources
National Institutes of Health
Department of Health and Human Services

Division of Clinical Research

National Gene Vector Laboratories (U42)

Policy and Procedures Manual

To access the latest (November 24, 1997) version of the Policy and Procedures Manual for the National Gene Vector Laboratories go to http://www.ncrr.nih.gov/clinical/crguide/crtoc.htm and click either on the Policy and Procedure Manual (PPM) or the Appendices to the PPM.

The NGVL Policy and Procedures Manual is an Administrative Document Issued November 24, l997 by the NGVL Steering Committee.

Contact Information:

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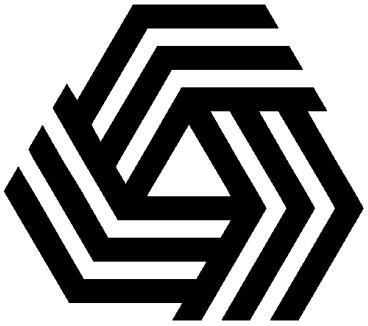
Indiana NGVL Web site:
http://www.uipui.edu/~iucc/ngvl/



National Center for Research Resources
National Institutes of Health
Department of Health and Human Services

Division of Clinical Research

Other Grant Programs

- **Midcareer Investigator Award in Patient-Oriented Research** (K24)
- **Small Business Grants** (R41, R42, R43, R44)
- **Cooperative Agreements** (U13, U42)

April 2001

An Administrative Document Issued by the
National Center for Research Resources (NCRR).

Contact Information:

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Division of Clinical Research Web site:
http://www.ncrr.nih.gov/clinical.htm

Contents

MIDCAREER INVESTIGATOR AWARD IN PATIENT-ORIENTED RESEARCH (K24)

I. PURPOSE

The purpose of the Midcareer Investigator Award in Patient-Oriented Research (K24) is to provide support for clinicians to allow them protected time to devote to patient-oriented research and to act as mentors for beginning clinical investigators. The target candidates are outstanding clinical scientists engaged in patient-oriented research who are within 15 years of their specialty training, who can demonstrate the need for a period of intensive research focus as a means of enhancing their clinical research careers, and who are committed to mentoring the next generation of clinical investigators focussing on patient-oriented research. The award is intended to further the research and mentoring endeavors of outstanding patient-oriented investigators, enable them to expand their potential to make significant contributions to their field of patient-oriented research, and to act as mentors for beginning clinicians.

For the purposes of this award, patient-oriented research is defined as research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator directly interacts with human subjects. This area of research includes: (1) mechanisms of human disease; (2) therapeutic interventions; (3) clinical trials; and (4) the development of new technologies.

The National Institutes of Health (NIH) is especially interested in increasing the number of scientists trained to conduct high-quality clinical research. Accordingly, this award forms an important part of the NIH initiative to attract and retain talented individuals to the challenges of patient-oriented research. With a view towards stabilizing clinical research settings and preventing an interruption in trainee mentoring, the NIH has chosen to establish the Midcareer Investigator Award in Patient-oriented Research. This award is intended to relieve clinical investigators from patient care duties and administrative responsibilities, thereby increasing the opportunities for clinicians in midcareer to be well grounded in patient-oriented research. This initiative is consistent with the recommendations of the NIH Director's Panel on Clinical Research (http://www.nih.gov/news/crp/index.html) and the recommendations from the Institute of Medicine Committee on Addressing Career Paths for Clinical Research.

The objectives of the Midcareer Investigator Award in Patient-Oriented Research are to:

- # encourage midcareer clinicians to devote more time to patient-oriented research and enhance their clinical research skills in order to conduct meritorious patient-oriented research and mentor beginning clinical investigators; and

- # increase the pool of clinical researchers who can conduct patient-oriented studies, capitalizing on the discoveries of biomedical research and translating them to clinical settings.

This award will enable candidates holding clinical degrees to undertake up to five years (a minimum of three years is required) of patient-oriented research, thereby further developing their research skills, devoting time to patient-oriented research, and acting as a mentor and role model for beginning clinical researchers. (See III. Eligibility Requirements below.)

The prospective candidate for the Midcareer Investigator Award in Patient-Oriented Research should propose a period of patient-oriented research consistent with his/her research and clinical experience and further development of research skills. All programs should be carefully tailored to meet the individual needs of the candidate and must include a description of a research project that meets the definition of patient-oriented research. In addition, the candidate should have a demonstrated record of conducting meritorious patient-oriented research and have experience in mentoring (or demonstrate mentoring capabilities) and describe mentoring activities that will involve beginning clinicians with little or no research experience. The applicant must have independent research support at the time of application for this program. This award is intended to enable the candidate to devote a greater percent effort to patient-oriented research.

II. HEALTHY PEOPLE 2000

The Public Health Service is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program Announcement, Midcareer Investigator Award in Patient-Oriented Research, is related to the priority area of human resource development. Potential candidates may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) from the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, phone (202) 512-1800 or electronically at http://odphp.osophs.dhhs.gov/pubs/hp2000.

III. ELIGIBILITY REQUIREMENTS

Candidates for this award must have a clinical degree or its equivalent, including the M.D., D.O., D.D.S., D.M.D., O.D., D.C., N.D. (Doctor of Naturopathy), and doctorally prepared nurses. In addition, individuals holding the Ph.D. degree may apply for the award if they have been certified to perform clinical duties, such as a clinical psychologist, clinical geneticist, etc. Candidates must have completed their specialty training within 15 years of submitting the application, and there is no age limit for candidates. In exceptional circumstances, the period of eligibility may be extended if it can be demonstrated that candidates had an interruption in their career progression due to family or personal circumstances.

Candidates must be working in a research environment, conducting patient-oriented research, and have independent research support. Candidates must be willing to spend up to 50 percent effort (at least 25 percent) conducting patient-oriented research and mentoring. All programs should be carefully tailored to meet individual needs and capabilities of candidates.

Applications may be submitted on behalf of candidates by domestic, non-Federal organizations, public or private, such as medical, dental, or nursing schools or other institutions of higher education. Minorities, women and individuals with disabilities are encouraged to apply. At the time of award, candidates must be citizens or noncitizen nationals of the United States, or must have been lawfully admitted to the United States for permanent residence (i.e., in possession of a currently valid Alien Registration Receipt Card I- 551, or other legal verification of such status). Noncitizen nationals are generally persons born in outlying possessions of the United States (i.e., American Samoa and Swains Island). Individuals on temporary visas are not eligible.

A candidate for the Midcareer Investigator Award in Patient-oriented Research may not concurrently apply for any other PHS award that duplicates the provisions of this award. Recipients of this award are required to hold independent research support, either Federal or private, during the period of this award. However, they may not receive additional compensation on another federal award that exceeds the maximum allowable salary compensation (currently $125,000 per year.)

IV. MECHANISM OF SUPPORT

Awards in response to this program announcement will use the K24 mechanism. Planning, direction, and, execution of the program will be the responsibility of the candidate on behalf of the applicant institution. The project period may be for up to five years(at least three years are required) . Awards are renewable for one additional five year period if the candidate still meets the stated requirements. Specific K24 application instructions have been modified to reflect "Just in Time" streamlining efforts being examined by the NIH. "Just in Time" postpones the collection of certain information that currently must be included in all competing applications when submitted. The "Just in Time" concept allows applicants to submit certain information only when there is a possibility for an award. It is anticipated that these changes will reduce the administrative burden for the applicants, applicant institutions, reviewers, and NIH staff.

V. AWARDS AVAILABLE

The overall goal of the NIH is to support between 60 and 80 awards in Fiscal Year (FY) 1999 and in each succeeding year through FY 2003. The actual number of awards to be made by each Institute or Center will vary yearly and will be dependent upon the number and quality of applications submitted and funds available.

VI. RESEARCH OBJECTIVES

A. Environment:

The institution must have a well-established research and clinical career development program. The institution must be able to demonstrate a commitment to the candidate as a productive,

independent investigator. The candidate and institution must be able to describe a career program that will utilize the relevant research and educational resources and the institution must certify that the candidate will be released from other duties and be able to devote up to 50 percent effort (at least 25 percent effort) to a patient-oriented research program. The Institution must demonstrate the availability of beginning clinical investigators to be mentored.

B. Program:

The award provides up to five consecutive 12-month awards. Up to 50 percent of the investigator's effort (at least 25 percent) must be devoted to the patient-oriented research program and mentoring. The remainder may be devoted to other clinical, teaching, or research pursuits consonant with the objectives of the award. The research phase of an award period must be devoted to patient-oriented research in scientific areas relevant to the career goals of the candidate.

C. Allowable Costs:

1. Salary: The NIH will provide salary for the award recipient of up to $62,500 per year plus commensurate fringe benefits for up to 50 percent effort. At least 25 percent effort is required. The institution may supplement the NIH contribution up to a level that is consistent with the institution's salary scale. Institutional supplementation of salary must not require extra duties or responsibilities that would interfere with the purpose of the award.

Recipients of this award may derive additional compensation from other Federal sources or awards provided the total salary derived from all federal sources does not exceed $125,000 per year and their total percent effort does not exceed 100 percent. Direct salary is exclusive of fringe benefits and facilities and administrative costs.

The total salary requested must be based on a full-time, 12-month staff appointment. It must be consistent both with the established salary structure at the institution and with salaries actually provided by the institution from its own funds to other staff members of equivalent qualifications, rank, and responsibilities in the department concerned. If full-time, 12-month salaries are not currently paid to comparable staff members, the salary proposed must be appropriately related to the existing salary structure.

2. Research Development Support: The NIH will provide generally up to $25,000 per year for the following expenses: (a) research expenses, such as supplies, equipment and technical personnel for the principal investigator and his/her mentored clinical investigators; (b) travel to research meetings or training; (c) statistical services including personnel and computer time.

3. Ancillary Personnel Support: Salary for secretarial and administrative assistance, for example, is not allowed.

4. Facilities and Administrative Costs: These costs will be reimbursed at 8 percent of modified total direct costs.

D. Evaluation:

In carrying out its stewardship of human resource related programs, the NIH may request information essential to an assessment of the effectiveness of this program. Accordingly, recipients are hereby notified that they may be contacted after the completion of this award for periodic updates on various aspects of their employment history, publications, support from research grants or contracts, honors and awards, professional activities, and other information helpful in evaluating the impact of the program.

E. Special Leave:

Leave to another institution, including a foreign laboratory, may be permitted if directly related to the purpose of the award. Only local, institutional approval is required if such leave does not exceed 3 months. For longer periods, prior written approval of the NIH funding component is required. To obtain prior approval, the award recipient must submit a letter to the NIH describing the plan, countersigned by his or her department head and the appropriate institutional official. A copy of a letter or other evidence from the institution where the leave is to be taken must be submitted to assure that satisfactory arrangements have been made. Support from the career award will continue during such leave.

Leave without award support may not exceed 12 months. Such leave requires the prior written approval of the NIH funding component and will be granted only in unusual situations. Support from other sources is permissible during the period of leave. Such leave does not reduce the total number of months of program support for which an individual is eligible. Parental leave will be granted consistent with the policies of the NIH and the grantee institution.

F. Termination or Change of Institution:

When a grantee institution plans to terminate an award, the NIH funding component must be notified in writing at the earliest possible time so that appropriate instructions can be given for termination. If the individual is moving to another eligible institution, career award support may be continued provided:

A new career award application is submitted by the new institution;

All conditions of the award are met at the new institution;

The period of support requested is no more than the time remaining within the existing award period; and

The new application is submitted far enough in advance of the requested effective date to allow the necessary time for review.

The funding component may require a review by an initial review group and/or the appropriate National Advisory Council or Board. Alternatively, review may be carried out by staff within the NIH funding component depending upon the circumstances.

The NIH may discontinue an award upon determination that the purpose or terms of the award are not being fulfilled. In the event an award is terminated, the Director of the NIH shall notify the grantee institution and career award recipient in writing of this determination, the reasons therefore, the effective date, and the right to appeal the decision.

A final progress report, invention statement, and Financial Status Report are required upon either termination of an award or relinquishment of an award in a change of institution situation.

Inclusion of Women and Minorities in Research Involving Human Subjects

For research projects involving human subjects, it is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43). All investigators proposing research involving human subjects should read the "NIH Guidelines For Inclusion of Women and Minorities as Subjects in Clinical Research," which has been published in the Federal Register of March 28,1994 (FR 59 14508-14513), and in the NIH Guide For Grants And Contracts of March 18,1994, Volume 23, Number 11. It is also available electronically at http://www.nih.gov/grants/guide/1994/94.03.18/.

Investigators may obtain copies from these sources or from the program staff or contact person listed below. Program staff may also provide additional relevant information concerning the policy.

NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects

It is the policy of NIH that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by NIH, unless there are scientific and ethical reasons not to include them. This policy applies to all applications submitted in response to this Program Announcement. All investigators proposing research involving human subjects should

read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" that was published in the *NIH Guide for Grants and Contracts*, March 6, 1998 and is available at the following URL:
http://www.nih.gov/grants/guide/notice-files/not98-024.html

As part of the scientific and technical merit evaluation of the research plan, reviewers will be instructed to address "the adequacy of plans for including children as appropriate for the scientific goals of the research, or justification for exclusion.

VII. APPLICATION PROCEDURES

The Midcareer Investigator Award in Patient-Oriented Research is an NIH-wide program. All candidates are strongly encouraged to contact the staff person in the relevant NIH institute or center. The NCRR staff person is listed under "Inquiries" on page 16. Such contact should occur early in the planning phase of application preparation. Such contact will help ensure that applications are responsive to the goals and policies of the individual institute or center.

Applicants to NCRR should be using the General Clinical Research Center (GCRC). They are requested to include a letter from either the GCRC Program Director (PD) or the Principal Investigator (PI) with the application.

Applications are to be submitted on the grant application form PHS 398 and will be accepted on or before the receipt dates indicated in the application kit. Forms are available at most institutional offices of sponsored research or from: Office of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, Room 6095, Bethesda, MD 20892-7910; phone (301) 435-0714; fax: (301) 480-0525; e-mail: asknih@od.nih.gov. Forms are also available at the NIH Web site: http://www.nih.gov/grants/funding/phs398/phs398.html.

To identify the application as a response to this program announcement, check "YES" on item 2 of page 1 of the application and enter "PA-98-053, Midcareer Investigator Award in Patient-Oriented Research."

Submit a signed, typewritten original of the application with five signed photocopies, in one package to:

Center for Scientific Review (CSR), National Institutes of Health, 6701 Rockledge Drive, Room 1040, Bethesda, MD 20892-7710--or for express/courier service use Bethesda, MD 20817. (CRS was formerly the Division of Research Grants.)

The application must contain the following information:

Candidate

A description of the candidate's commitment to a career in patient-oriented research.

Evidence of the candidate's ability to conduct high quality patient-oriented research.

A description of immediate and long-term career objectives, explaining how the award will contribute to their attainment.

A description of how the award will contribute to a patient-oriented research program and how it will relieve the candidate from other patient care or administrative duties.

Research Plan

A commitment of up to 50 percent effort (at least 25 percent effort) to the patient-oriented research program.

A description of the ongoing patient-oriented research. The research plan should briefly describe the specific aims, the background and significance of the studies, and the research design and methods. Additional research may be proposed as a basis for this award.

Documentation that appropriate and adequate resources, both in terms of support and facilities, are available to the candidate to conduct the research program. This must include a description of other monetary support that will be utilized to conduct the research program.

Mentoring Plan

A demonstrated record of mentoring or training clinical investigators or a demonstration of the capability to provide mentoring to beginning clinical investigators.

A description of plans for providing mentoring opportunities to beginning clinical investigators, including a description of the type of clinical investigators that could be mentored, plans for recruiting and selecting such individuals, and the type of training and educational experiences to be provided.

Environment and Institutional Commitment

The sponsoring institution must document a strong, well-established patient-oriented research and training program related to the candidate's area of interest including a high-quality research environment with staff capable of productive collaboration with the candidate.

The sponsoring institution also must provide a statement of commitment to enhancing the candidate's ability as a productive, independent investigator.

The sponsoring institution must provide documentation that the candidate will be relieved from other duties, patient care, administrative, etc., to allow him/her to devote time to the patient-oriented research program.

Budget Instructions

The total direct costs must be requested in accordance with the K24 program guidelines, following the budget instructions described below.

Face Page - As a reminder, Item 7 should be completed to indicate direct costs requested and Item 8 should reflect total costs (direct plus Facilities and Administrative)

Detailed Budget for Initial Budget Period - Do not complete form page 4 of the PHS 398. It is not required nor will it be accepted at the time of application. In some cases it may be requested prior to award.

Budget for Entire Proposed Period of Support - Do not complete the categorical budget table on form page 5 in the PHS 398. Only the requested total direct costs for each year and total direct costs for the entire proposed period of support should be shown.

Begin the budget justification in the space provided, using continuation pages as needed.

List the name, role on project and percent effort for all project personnel (salaried or unsalaried) and provide a narrative justification for each person based on his/her role on the project and proposed level of effort.

Identify all consultants by name and organizational affiliation and describe the services to be performed.

Provide a narrative justification for any major budget items, other than personnel, that are requested for the conduct of the project that would be considered unusual for the scope of research. No specific costs for items or categories should be shown.

Facilities and Administrative costs will be calculated at the time of the award using the 8% rate. Applicants will be asked to identify the exclusions prior to award.

If consortium/contractual costs are requested, provide the percentage of the subcontract total costs (direct plus Facilities and Administrative) relative to the total direct costs of the overall project. The subcontract budget justification should be prepared following the instructions provided above.

Biographical Sketch

A biographical sketch is required for all key personnel, following the modified instructions below. Do not exceed the two-page limit for each person.

Complete the education block at the top of the form page.

List current position(s) and those previous positions directly relevant to the application.

List selected peer-reviewed publications directly relevant to the proposed project, with full citation.

Provide information on research projects completed and/or research grants participated in during the last five years that are relevant to the proposed project. Title, principal investigator, funding source, and role on project must be provided.

Other Support

Do not complete the other support page (form page 7 of the PHS 398). Information on active support for key personnel will be requested prior to award. A completed checklist will be required prior to award.

VIII. REVIEW CONSIDERATIONS

Applications will be reviewed for completeness by the Center for Scientific Review and for responsiveness to this program announcement by the appropriate institute or center staff. Incomplete or non-responsive applications will be returned to the applicant without further consideration. Applications that are complete and responsive to the program announcement will be evaluated for scientific and technical merit by a peer review group convened by the appropriate NIH Institute or Center in accordance with the standard NIH peer review procedures. As part of the initial merit review, all applications will receive a written critique and undergo a process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed, assigned a priority score, and receive a second level review by the appropriate national advisory council or board.

The following review criteria will be applied:

Candidate

Quality of the candidate's academic and clinical record, including capabilities and commitment to serve as a mentor;

Evidence of ongoing high quality patient-oriented research and the relationship of that research to this program;

Potential to conduct quality patient-oriented research;

Commitment to a patient-oriented research career;

Appropriateness of the content and duration of the proposed research program; and

Evidence of monetary support for patient-oriented research.

Research Plan

Although it is understood that K24 applications do not require the level of detail necessary in regular research grant applications, a fundamentally sound research plan must be provided. In general, less detail is expected with regard to research planned for the later years of the award, but the application should outline the general goals for these years.

Appropriateness of the research plan as a vehicle for demonstrating skills and capabilities in patient-oriented research;

Scientific and technical merit of the proposed research;

Relevance of the proposed research to the candidate's career objectives;

Availability of adequate resources to conduct the research program;

Demonstration that the proposed program will relieve the candidate from other patient care or administrative duties and allow him/her to devote time to patient-oriented research;

Adequacy of the plan's attention to gender and minority issues associated with projects involving human subjects; and

Adequacy of plans for including children as appropriate for the scientific goals of the research, or justification for exclusion.

Mentoring Plan

Experience and potential to serve as a mentor; and

Adequacy of the plans for mentoring or supervising beginning clinicians in patient-oriented research.

Environment and Institutional Commitment

Applicant institution's commitment to the scientific development of the candidate and assurances that the institution intends the candidate to be an integral part of its research program;

Adequacy of research facilities and the availability of appropriate educational opportunities;

Quality and relevance of the environment for scientific and professional development of the candidate and others pursuing patient-oriented research; and

Applicant institution's commitment to provide adequate time for conduct of the research program.

IX. AWARD CRITERIA

The institute or center will notify the applicant of the board or council's action shortly after its meeting. Funding decisions will be made based on the recommendations of the initial review group and council/board, the need for research personnel in specific program areas, and the availability of funds. The NIH policy on submission of revised (amended) applications limits the number of such applications to two.

X. INQUIRIES

Inquiries concerning this program announcement are strongly encouraged especially during the planning phase of the application. Direct inquiries regarding programmatic issues to:

Division of Clinical Research
National Center for Research Resources
6705 Rockledge Drive, Room 6120
Bethesda, MD 20892-7965
phone: (301) 435-0790
fax: (301) 480-3661

SMALL BUSINESS GRANTS

The NCRR Division of Clinical Research actively participates in federal set-aside programs designed to support innovative research conducted by small business that has commercial potential. The Division of Clinical Research awards the majority of its funds for grants, but occasionally it may solicit contracts. These are detailed in solicitations published each year and can be obtained in hard copy from:

PHS SBIR/STTR Solicitation Office
13685 Baltimore Avenue
Laurel, MD 20707-5096
phone: (301) 206-9385
fax: (301) 206-9722
e-mail: a2y@cu.nih.gov

or in electronic form at http://www.nih.gov/grants/funding/sbir.htm.

Innovation and the potential for commercialization are important factors stressed in the review criteria included in these solicitations. The Division of Clinical Research is particularly interested in the application of clinical technology, instruments, devices and related methodologies that may have broad application to clinical research, especially as it pertains to enhancing the ability to do clinical research. These include but are not limited to: development of systems or devices which enhance patient monitoring of physiologic or biochemical parameters; applications of biotechnologies, sensors, and imaging technologies to enhance patient management; miniaturization of existing biomedical technologies for adaptation to pediatric use; development of artificial tissues and organs for medical use; development or improvement of technologies for securing storage and transmission of confidential medical data. The Division of Clinical Research also supports the development of vectors for gene therapy to: (1) target specific cells and/or tissues; (2) improve transduction and expression efficiency; (3) optimize the method of delivery to patients; and/or 4) develop methodologies to enhance production and purification.

Inquiries should be directed to:

Geoffrey Cheung, Ph.D.
Division of Clinical Research
National Center for Research Resources
6705 Rockledge Drive, Room 6130
Bethesda, Maryland 20892-7965
phone: (301) 435-0790
fax: (301) 480-3661

Before submitting small business applications under the fast-track initiative, applicants are strongly encouraged to consult with the NIH small business program staff representative for NCRR:

Dr. Louise E. Ramm

National Center for Research Resources
Building 31, Room 3B11
Bethesda, MD 20892-5662
phone: (301) 496-6023
fax: (301) 402-0006
e-mail: louiser@nccr.nih.gov

Applicants are reminded that in the cover letter addressed to the CSR Referral Officer it may be helpful to suggest one or two secondary NIH institutes or centers (ICs) as well as a primary IC as potential funding sources. In addition, the applicant can name the fields of expertise needed to review the grant application and if he/she observes that this expertise is found in a particular study section, can request that the grant be reviewed by that study section. A list of study sections and their scientific areas and rosters can be found at http://www.drg.nih.gov/review/irgdesc.htm. The cover letter should be firmly attached to the grant application.

I. SMALL BUSINESS INNOVATION RESEARCH (SBIR) GRANT (R43; R44)

The SBIR program is intended to support small business innovative research in the United States that results in commercial products or services that benefit the public. Normally the award period for Phase I is for six months for an amount up to $100,000. Normally, Phase II is for two years and for up to $750,000. This total includes direct costs, F & A costs, and fixed fees. Applicants may propose longer periods of time and greater amounts of funds if justified.

The small business grant is awarded to the small business concern. Academic investigators may be named as consultants or facilities at research institutions may be included under subcontracts but these are not required. The total amount of all consultant and contractual costs normally may not exceed 33% of the total costs requested for Phase I and 50% on Phase II.

Receipt deadlines for SBIR applications are: April 15, August 15, and December 15.

II. SMALL BUSINESS TECHNOLOGY TRANSFER (STTR) GRANT (R41; R42)

The STTR Program is intended to support small business innovative research in the United States that results in commercial products or services that benefit the public. However, in the STTR program the research is conducted cooperatively by a small business concern and a research institution.

Normally, the award period for Phase I is for one year for an amount up to $100,000. Normally, Phase II is for two years and for up to $500,000. This total includes direct costs, F & A costs, and fixed fees. Applicants may propose longer periods of time and greater amounts of funds, if justified.

At least 40 percent of the STTR research project is to be conducted by the small business concern and at least 30 percent of the work is to be conducted by the single "partnering" research institution.

Receipt deadlines for STTR applications are: April 1st, August 1st, and December 1st.

COOPERATIVE AGREEMENTS

Cooperative agreement mechanisms are used to complement grant supported activities. Contract and cooperative agreement proposals are solicited as an initiative of the Program and intended to support projects with highly specific aims.