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Guidelines for the General Clinical Research Centers Program (M01)

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Contact Information:

Division for Clinical Research Resources
National Center for Research Resources
National Institutes of Health

6701 Democracy Boulevard
Room 906
Bethesda, MD 20892-4874

Telephone: (301) 435-0790
Fax: (301) 480-3661
E-mail: CRADir@ncrr.nih.gov

Division for Clinical Research Resources Web page

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INTRODUCTION

INFORMATON ABOUT CHANGES IN THIS VERSION

These Guidelines for the General Clinical Research Centers Program, dated October 2005, differ from the previous GCRC Guidelines, dated September 2005, by: revision of Supplement I, entitled “Instructions for Preparing a GCRC Application” and inclusion of Supplement II, entitled “Review Criteria for Evaluation of GCRC Applications.”

GCRC applications submitted for the October 1, 2005 submission date are to be prepared in accordance with the April 2005 GCRC Guidelines; review of these applications will include a site visit.

All GCRC applications submitted in 2006 or thereafter are to be prepared in accordance with these October 2005 GCRC Guidelines; review of these applications will not include a site visit.

GUIDELINES FOR THE GENERAL CLINICAL RESEARCH CENTERS PROGRAM

GENERAL CLINICAL RESEARCH CENTER PROGRAM DESCRIPTION

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 devoted to medical research also may 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 host both funded studies and 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, core or other resource laboratories for radioimmunoassays, mass spectrometry, cell sorting, imaging, sleep studies, and more.

GCRC investigations 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 safety of participants in clinical research is of paramount importance, and the GCRC Program funds Research Subject Advocates (RSAs) in support of this goal.

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. Due to the nature of the GCRCs, no single group of investigators or categorical research area may dominate the utilization of the GCRC or use more than one third of the GCRC resources, except for acquired immunodeficiency syndrome (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 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 subject advocates, research bionutritionists, administrators, core laboratory staff, biostatisticians, and computer personnel. Funds for renovation and equipment also may be provided.

A. Inpatient Area:

The inpatient facility of a GCRC usually is located within a physically discrete unit that contains inpatient rooms and research beds. It also may 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. Research Subject Advocate:

The primary function of the RSA is to ensure that studies on the GCRC are designed and conducted safely and ethically with protection of human subjects accorded the highest priority. The RSA acts as a liaison with the institutional Offices of Human Protections (or equivalent), including the Institutional Review Boards (IRBs). The RSA develops and guides implementation of policies and procedures for timely and appropriate reporting of adverse events, development and adherence to the Data and Safety Monitoring (DSM) Plan, approval and recording of all protocol amendments and changes in informed consent documents, performance of regulatory responsibilities in a complete and timely manner, and conduct of the research as written in the most recently approved protocol. While the RSA cannot and should not take on the above responsibilities of others, he/she will monitor activities on the GCRC and recommend appropriate corrective action if deficiencies are found. The RSA should be informed of all issues related to human subject protection on the GCRC. In addition, the RSA should receive copies of all correspondence to and from the IRB, FDA, and the sponsor related to conduct, safety, clinical holds, removal of holds, changes, and other relevant information concerning

protocols on the GCRC. The RSA should provide educational and training opportunities for GCRC staff on human subject protection. The RSA should reflect the views of the research participants to GCRC staff when appropriate.

The RSA works closely with and keeps the Program Director (PD) and GAC informed of activities related to human subject safety and protection on the GCRC. However, the RSA reports to the Principal Investigator (PI) of the GCRC grant and not to the PD or GAC. This reporting structure ensures that the RSA has the appropriate independence from those involved in the design, approval, and conduct of studies, as well as the implementation of activities related to human subject protections.

D. 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. In addition, the laboratories may provide clinical research training for investigators.

Core Laboratory requirements vary widely. Some GCRCs may not need a full Core Laboratory; rather, only a small sample-processing area may be required. Laboratory equipment, supplies, and personnel supported through the GCRC grant 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; rather, they are 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. Cost sharing of Core Laboratory functions should be sought from funded investigators.

Core Laboratories may specialize in, but are not limited to, areas such as exercise physiology and body composition, mass spectrometry, magnetic resonance imaging, ultrasound, positron emission tomography, tissue culture, cell biology, molecular genetic analyses of DNA obtained from patient material, and cell and gene therapy.

Core Laboratories are encouraged to make their areas of specialized expertise available to other GCRCs. Records of such services and collaborations should be kept, as they may be helpful in justifying continued support of the laboratory. See information below regarding Program Income.

The GAC is responsible for reviewing the Core and other resource Laboratories to ensure 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.

E. 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 GCRCs. 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 on both 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 ensure that GCRC network facilities are accessible to all GCRC Core components and promote the adherence to data management standards. The Informatics Core also should 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 that may have a substantive impact on the Informatics Core should be presented to the GAC for review and approval.

F. Bionutrition Core:

Not all GCRCs require a Bionutrition Core. When present, it facilitates and implements the nutrition components of GCRC protocols. It may be involved in one or more of the following functions: assisting investigators with nutrition aspects of research design, implementation, data collection and analysis; implementing controlled feeding studies (via meals prepared on site or outsourced as appropriate) and metabolic studies, as well as facilitating and monitoring subject nutrition compliance; performing nutrition and nutrient intake assessment; conducting anthropometric, body composition, calorimetry and other physiologic and metabolic measurements; providing personnel administration,

metabolic kitchen operations, food procurement, production and service; and educating and training professional and non-professional staff, study participants, students, and the public.

G. Principal Investigator:

The PI of a GCRC is required to commit at least one percent time effort to the M01 grant; however, he/she derives no salary support from the grant. He/she is an individual familiar with human subjects research 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 NIH communicates on broad institutional matters relating to the GCRC grant. The DCRR 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 PD and members of the GAC (see below) 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, he/she is responsible for seeking approval from 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; the request is to be cosigned by an authorized institutional business official and the PI.

H. Institutional GCRC Advisory Committee (GAC):

The GAC usually consists of 8-12 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 faculty members who are familiar with the broad range of the GCRC research activities. The GAC shall not be chaired by the PD or Associate/Assistant PD. Individuals receiving salary support from the GCRC grant shall not be voting members of the GAC.

The GAC supervises and reviews all operations of the GCRC, its Core Laboratories, Informatics Core, and other components; 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. This approval must be obtained prior to initiation, except when temporary approval has been given by the PD or his/her designee and the IRB for urgent studies created by an unexpected opportunity to study unusual research patients; these studies will be reviewed by the GAC at its earliest meeting.

The GAC should prospectively prioritize projects for GCRC use to assist the PD in allocating resources. In all cases, NIH-funded clinical research must be given preference. The GAC is responsible for ensuring implementation of existing NIH policy on the inclusion of women, minorities, and children as study subjects and for approval of DSM plans for all GCRC protocols. In addition, the GAC shall determine if a protocol involves significant risk and, if so, will evaluate and approve the required Data and Safety Monitoring Board (DSMB). The GAC must also designate for each protocol, the

category of inpatient research days and outpatient visits as Category A, B, or D. For appropriate classification of industry-related projects, the GAC may request additional materials. 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.

The GAC should review periodically all GCRC operations to ensure that GCRC resources are used for the most scientifically justified and relevant projects. Each year, a copy of the GCRC's Annual Progress Report shall be supplied to each GAC member and shall be reviewed at a subsequent GAC meeting. The GAC should 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, which may include the review of biostatistical design of projects, ethical concerns, or 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 analysis.

The GAC is to work closely with the PD to proactively address investigator resource needs, encourage GCRC use by investigators at the institution who are not currently using the resource, and provide outreach to investigators from institutions without a GCRC or comparable resources.

The GAC shall oversee the GCRC budget. All requests to NCRR for funds (competitive renewal, noncompetitive renewal, supplements) shall be endorsed by the GAC prior to submission of the request to NCRR. Once funds are awarded, all significant rebudgeting shall be endorsed by the GAC. During the grant year, the GCRC PD and Administrative Manager are to work closely with the GAC and provide systematic updates on financial matters including: comparison of projected expenditures with actual expenditures to date; and actual use to date of GCRC resources (inpatient days, outpatient visits, and ancillaries) by specific protocols. In addition, the GCRC PD and Administrative Manager are to report to the GAC on apparent unmet needs of investigators, career development and other related activities, and other topics relevant to the host institution.

The minutes of the GAC meetings shall document all reports to the GAC and all recommendations made by the GAC.

I. Institutional Review Board for Human Research:

All GCRC research projects must be reviewed and approved by an IRB to ensure protection of the rights and welfare of research subjects. (See 45 Code of Federal Regulations 46.) The IRB must have registered with the Office for Human Research Protections and have completed a Federalwide Assurance. All research projects must also

be approved by the GAC. 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. In addition, all GCRC protocols must comply with all applicable Federal and State regulations.

J. Grant-Supported Personnel:

The personnel positions that may be supported by GCRC grants are listed below. (See below for allowable costs.) The number of positions supported in each category depends upon the size and complexity of the GCRC, recommendations of the NIH peer-review system, and NCRR 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 GCRC research projects and ensure that the research is carried out as approved by the local IRB. Support for a PD from the GCRC grant ordinarily is 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, K12 and 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 PI or co-investigator on either an NIH grant or another 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 PI or co-investigator

of a peer-reviewed grant. If the individual is unsuccessful at the end of that time, either a new Associate/Assistant PD shall be appointed, or the level of support from the GCRC grant will be 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 Director/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, the NCRR Office of Grants Management (OGM), and for inclusion in Annual Reports to NCRR. In the interest of GCRC efficiency, the PD may delegate some administrative authority in non-scientific and non-healthcare delivery matters to the Administrative Director/Manager. A GCRC may use the title "Administrative Director" or "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 PD 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. **Core Laboratory Director:** 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., body composition core, mass spectrometry core), the GCRC grant may support a fraction of an FTE for the Director of each core.

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 ensure 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 where the GCRC is located. GCRCs that 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 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 at the hospital where the GCRC is located, at a satellite, or at a scatter-bed unit. Except for the smallest Centers, support of either a full- 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 at least a Bachelor's degree and be a registered dietitian. The Bionutrition Research Manager oversees the GCRC dietary staff and works closely with both the nursing staff and GCRC investigators. Up to 1.0 FTE may be supported.

b. Nutrition Staff: Nutritional assessments and the preparation of controlled diets for research subjects require 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 further patient-oriented research.

   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. Supervise network and data security to ensure the proper operation and maintenance of GCRC computer hardware and software.

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

   g. 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 advises the GAC prior to the GAC approval of the protocol. 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. **Research Subject Advocate (RSA):** The GCRC shall include funding for a position called "Research Subject Advocate" or similar title. The RSA works closely with the PD and the GAC; however, the RSA shall be directly responsible and report to the PI of the GCRC grant or his/her designee. The designee must be a high ranking official in the institution with an understanding of clinical research and free from conflicts with the independent role of the RSA. Examples of conflicting roles include the PD, Assistant or Associate PDs, chair of the IRB, or official with overall responsibility for the institution's Human Subjects Protection Office. The RSA is to have appropriate training and experience within the clinical research arena. The RSA may hold an M.D. degree, but appropriately trained Ph.D.s, pharmacists, research nurses, or others also qualify; however, appropriate expertise in clinical research and human subjects protection is necessary. Depending on the needs at the GCRC site and its satellites, more than one FTE may be required for these activities. The RSA duties may be divided among two or more qualified individuals. However, one individual must be designated the Principal RSA. In addition, the GCRC grant may support a Program Administrative Assistant to assist the RSA with effort reflecting the GCRC activity. The effort of the RSA—funded through the GCRC grant—must be dedicated exclusively to the GCRC activities.

   The primary function of the RSA is to ensure that all studies conducted on the GCRC, including all research types, categories, and sites, are designed and conducted safely and ethically with protection of human subjects accorded the highest priority. The RSA assists GCRC investigators, nurses, and other GCRC staff in the safe and ethical conduct of GCRC studies through education, consultation, and enhanced communication and coordination among all members of the team. In addition, the RSA develops and implements policies and procedures to facilitate protection of GCRC human subjects. The RSA provides monitoring and oversight, which includes, but is not limited to, assuring timely and appropriate reporting of adverse events to all required parties, full implementation and adherence to the protocol DSM plan, and that the research is carried out in compliance with the most recently IRB-approved protocol. If deficiencies are found, the RSA recommends or implements corrective action as appropriate.

   The RSA assures that all GCRC protocols have GAC-approved DSM plans that are commensurate with the risks to human subjects. The RSA may provide input to the investigator on the design and content of the DSM plan and review proposed DSM plans of all protocols prior to the presentation for approval by the GAC. For those protocols that are of significant risk to be performed on the GCRC, the RSA ensures that the required Data and Safety Monitoring Board (DSMB) is constituted and approved by the GAC prior to start of activities related to this protocol. The RSA may establish and manage but not sit on a DSMB for these studies, but this is not required. The PI of the protocol is charged with the responsibility for establishing a DSMB in cases where no appropriate DSMB is available.

   The RSA assists research participants in understanding clinical research and what role they play; however, protocol-specific questions require the participation of the

investigator and research team. In addition, the RSA reflects the views of research participants on GCRCs as appropriate.

9. **Clinical Associate Physician (CAP) and Minority Clinical Associate Physician (MCAP) Programs:** Previously, CAPs and MCAPs were funded as competitive supplements to a GCRC (M01) grant. The K23 mechanism has replaced those supplements; K23s are funded directly, not as supplements to an M01 grant.

10. **Medical and Dental Students:** The GCRC grant may provide support 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 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 may cover up to $20,000 in salary for each awardee, 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 GAC and 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 the DCRR its guidelines including: eligibility of students and mentors; 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.

K. Provisions for Medical Care:

1. **General:** All GCRC research subjects must receive optimal medical care. It is the responsibility of each PI to ensure that appropriate care is provided to patients participating in his or her research protocols. This responsibility may be discharged either personally, if the PI is a physician or dentist with the requisite expertise, or by a physician co-investigator, fellow, or resident who possesses the requisite clinical expertise and admitting privileges. The qualifications and expertise of physicians or dentists who provide clinical care for research participants must meet institutional and applicable local guidelines and bylaws. GAC review of protocols must include a determination that medical coverage for research subjects will be optimal. Plans for emergency coverage by licensed M.D.s and, where appropriate, for night care, must be formalized for each protocol, or for the entire GCRC.

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, other arrangements for the patient's care should be made.

L. Data and Safety Monitoring Plans:

In 1998 and 2000, NIH issued policies on Data and Safety Monitoring for Clinical Trials. These policies, NIH Policy for Data and Safety Monitoring and Further Guidance on a Data Safety and Monitoring For Phase I and Phase II Trials, provide NIH requirements for data and safety monitoring of clinical trials supported by NIH funds.

In addition, NCRR requires that all GCRC protocols, not just clinical trials, must have a DSM plan that has been approved by the GAC. Based on an exemption from the Office of the Director of NIH, GAC-approved protocols do not require additional approval by NCRR staff. However, GAC approval does not supplant the required approval by staff at other NIH Institutes and Centers that support the research.

Further, NCRR requires that all protocols that place participants at significant risk must have an independent DSMB. The determination of significant risk is to be made by the local GAC. The charter (or list of the responsibilities, meeting frequency, etc.) and membership of any DSMB, as detailed in the NIH Guidances on Data and Safety Monitoring referenced above, must be included in the DSM plan of any protocol that includes a DSMB.

The GAC is to document in its minutes its approval of the DSM plans. 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.

M. Reporting Serious Adverse Events (SAEs):

Federal regulations (45 CFR Part 46, Subpart A, i.e., the "Common Rule"), which are applicable to all GCRC studies, require reporting of "unanticipated problems" involving risks to participants to the IRB, the appropriate institutional officials, and the Federal Department or Agency head. In addition, for those studies regulated by the FDA (21 CFR 312.32), sponsors must notify the FDA and participating investigators of any adverse event associated with the use of the test article that is "both serious and unexpected." In addition, NIH has issued several policies and guidances related to adverse event reporting and serious adverse event reporting. These include:

NIH Policy for Data and Safety Monitoring;

Further Guidance on a Data Safety and Monitoring for Phase I and Phase II Trials;

Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials;

Notice to NIH Grantees/Contractors Regarding Letters or Notices from the Food and Drug Administration (FDA).

In addition, whenever a gene transfer protocol conducted on the GCRC results in a report to the FDA of a serious unexpected adverse event 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; NCRR's DCRR; and the categorical NIH Institute (e.g., NCI, NIAID) supporting the study. In all such SAE reports to NIH, names or other patient-identifiable material should **not** be included.

N. Training and Career Development:

The training of health professionals in the methods of clinical investigation should be an integral part of the research effort of 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 National Research Service Award (NRSA) fellows and trainees, K12 and 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 also may 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 they 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 PI of the protocol on which the trainee is working, is responsible for the medical and scientific quality of the work performed by the trainee.

O. 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 GCRC research activities and accomplishments for Congressional reports and budget justifications and for other reports.

P. 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 coauthors. Each GCRC must maintain a current and complete bibliography of publications that resulted from studies that used GCRC resources for inclusion in its Annual Report. It is recommended that GCRC scientific and administrative records be retained for at least five years.

Q. Industry-Sponsored Research:

GCRCs are sometimes used for projects funded in whole or in part by for-profit organizations. Investigator-initiated projects that 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 that 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 appropriate regulatory documents and other relevant correspondence are to be maintained in the GCRC's research project files. This includes, but is not limited to, FDA-required documents and relative correspondence.

Those projects 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 below.) 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. All industry-initiated projects must be approved for use of the GCRC by the GAC and include a DSM plan. 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 meetings. 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.

R. Clinical Research Feasibility Funds (CReFF) Program:

GCRC grant funds may be used to support pilot studies subject to review and approval by the GAC. A GCRC may rebudget unrestricted GCRC grant funds for this purpose.

A GCRC also may 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. The CReFF awards could be up to $20,000 for one-year renewable projects; each GCRC would be limited to $100,000 annually. The CReFF program will be reviewed as part of the competitive renewal of the GCRC grant.

S. **Availability of GCRC Resources for Long-Term Follow-Up of Participants in Gene Transfer Protocols:** See NOT-RR-04-005.

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 hospital 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 (i.e., 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 that differ from those recommended in the last peer review, must be reviewed and approved by NCRR prior to initiating the modifications. Detailed floor plans—including a list that indicates the use and square footage for each room, a narrative justification, and an estimate of cost for the revised GCRC sites—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 decide to 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 regardless 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 usually is essential for research and patient care procedures. Adequate storage space and utility rooms—in keeping with JCAHO guidelines—also must 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 either 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 usually is 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 and specifically designed 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 on or near the GCRC. This may include a metabolic kitchen, depending on the scope of bionutrition activities. An office for the Bionutrition Research Manager should be located on or near the GCRC.

F. Office and Conference Space:

Office space for the PD, the administrative staff, and the RSA should be provided on or near the GCRC. Offices for an Associate/Assistant PD, Core Laboratory Director, or other personnel are sometimes justified. A conference room often is 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 and upgrade information technologies that meet the evolving needs of the investigators.

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 (NOGA), 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 NCRR's DCRR and the OGM. 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 and, where significant, should be approved by the GAC. As described below, Category A activities may be commingled with other patient-oriented research activities (such as Categories B and D activities), provided appropriate program and resource utilization and cost accounting is maintained for each study. In addition, other patient-oriented research units may be colocated with a GCRC, provided appropriate fiscal accountability exists.

B. Personnel Costs:

Salaries and wages of personnel may be charged to the grant in proportion to the time devoted 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 that 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, provided that such equipment is not otherwise available to the GCRC from within the institution. Equipment not requested in initial or renewal 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, RSA, and the GCRC administrative office may be purchased with grant funds provided in the supply budget category. Routine hospital, drug, and raw food supplies ordinarily are 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 PDs, RSAs, Informatics Core Managers, Biostatisticians, Administrative Directors, Nurse Managers, and Research Bionutritionists, and travel of GCRC personnel for consultation with NCRR. These travel/meeting costs are specifically indicated on the NOGA. Funds for patient travel are allowable charges to a GCRC grant only under the conditions specified below under "Other."

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.

Payments from the GCRC grant to research participants (including for travel) may be made when all three of the following conditions are met:

1. Research participants are compensated in amounts that are not coercive, as approved

by the IRB;

2. The protocol, to be performed on the GCRC, is a GCRC-sponsored pilot project with no external funding; and

3. Payment from the GCRC grant and the amount of the payment is approved by the GAC.

In addition, if NCRR prior approval has been received, payment for patient travel may be made when only conditions one and three (above) apply.

G. Patient-Care Costs:

l. General: Research patient-care costs incurred under GCRC grants by the grantee institution/hospital must be computed using research patient-care rates or amounts established by the appropriate Regional Office of the Division of Cost Allocation of the Department of Health and Human Services (DCA, DHHS). Such rates must be used by the grantee institution/hospital in all requests and claims for reimbursement for research patient-care costs. The grantee institution/hospital must submit patient-care rate proposals annually to the DCA, DHHS Regional Office and reply promptly to inquiries from that Office. If a hospital incurring research patient-care costs under a GCRC grant is a consortium participant and not the grantee institution/hospital, then the grantee institution/hospital will be responsible for establishing with the consortium hospital an appropriate rate or amount that will be reimbursed for such costs. However, if the consortium hospital has an established research patient-care rate agreement with DHHS, then the DHHS rate must be used for calculation and reimbursement of research patient-care costs.

Inpatient utilization is based on midnight census. If a patient's participation in an approved protocol exceeds 24 hours but does not entail presence on the unit at midnight of the following day, the utilization may be recorded as a single inpatient day, plus a single outpatient visit of the appropriate category.

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. **Research Patients (Category A):** 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 institution through the GCRC grant or the investigator's research grant. Persons who are hospitalized for research purposes only, but whose care is partly supported by non-GCRC funds, (e.g., other grants, industry, the Centers for Medicare & Medicaid Services under its Clinical Trials Final National Coverage Decision) also may 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 or outpatient visit, 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 or outpatient visit. Examples would be persons with genetic or other abnormalities of interest to the investigator, and those persons who, although sick, would not have 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 below.) 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 that 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 by industry. 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 below.)

d. **Non-Research Patients (Category C):** Patients who are not participating in a research project may be admitted to the GCRC solely for the purpose 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 NCRR is required. The request is to be co-signed by the appropriate Business Official.

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 (e.g., 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). 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 count only 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 (APR) and listed as "research meal visits." If a research subject comes to the GCRC for more than eating or picking up a research meal (such as contact with a bionutritionist for a diet history, diet instruction, or a procedure—such as anthropometric measurements), then it may be counted in the census as an outpatient visit.

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 APR, and it must be included as a credit in the patient care computation pages of the APR.

   For each project, an appropriate credit, preferably based on an hourly rate, must be computed. When developing a rate, include all utilized components of the GCRC (i.e., program directorship, administration, RSA, 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 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.

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

	Discrete	**Per Diem**
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 calculated as the number of square feet applicable to these areas, multiplied 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, salaries for a Nurse Manager and specialized clinical research nurses may be paid from the GCRC grant. The number of nurses depends on the level of activity and the intensity of nursing care required.

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 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 that 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 that 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 PI or a collaborator. Research ancillary charges must be reduced to cost (discounted according to the Medicare or GCRC rate), 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 the

GCRC 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.

12. **Off-Site Research Visits (non-JCAHO):** As stated on the first page of these GCRC Guidelines, "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." Accordingly, any inpatient day or outpatient visit reported in the GCRC census must take place in such an accredited or certified facility.

    The GCRC Guidelines were modified (effective April 1, 2003) to allow low-risk research activity (e.g., administering a questionnaire, buccal swab) by GCRC grant-supported personnel (e.g., nurses) to take place in facilities that are neither JCAHO-accredited nor Medicare- or Medicaid-certified (e.g., school, church, home, museum). Such activity is to be reported in the GCRC census, not as inpatient days or outpatient visits, but rather as a new category called "off-site research visits" (ORVs). The following caveats apply to any GCRC research activity that takes place off site:

    a. Although all GCRC protocols continue to require approval of the IRB and GAC before they may be initiated, and a DSM plan, the GAC review of protocols involving ORVs must include (and document in the minutes) an assessment that the facility in which the ORV is to be conducted will not compromise research subject safety or data confidentiality, and that the medical coverage will be appropriate for the risk level of the proposed research activity.

    b. As with all GCRC protocols, the protocol should not be coercive, and investigators should exercise appropriate sensitivity regarding the populations to be studied.

    c. Only category A and B ORVs are allowed. GCRC personnel are not allowed to participate in category C or D activity in non-accredited facilities.

    d. Currently, ORVs are allowed only when they are part of a study receiving NIH or comparable peer-reviewed support other than the GCRC (M01) grant.

13. **GCRC Modified Classification for Rare Disease Research:** Advances in the treatment of rare diseases are not sufficiently likely to be commercially viable to attract industry-supported development. This is acknowledged by the Orphan Drug Act that specifically permits the Secretary of the DHHS to make grants and/or contracts to assist in defraying the costs of qualified clinical testing of drugs, devices, or foods for rare diseases and conditions.

    The GCRC Program, following this lead, modified the GCRC research category

classification to facilitate testing of new agents for patients with rare diseases. Consequently, clinical trials of drugs and other candidate therapies or interventions for rare diseases may be classified by the local GAC as category A, instead of D, for industry-initiated protocols as described below. (All investigator-initiated trials, designed by a single investigator or a consortium of investigators, are already classified as category A.)

The protocol must be for a rare disease. Rare disease refers to "any disease or condition that either (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug or other therapeutic agent." A broad group of appropriate experts—including some from outside the institution—must review and find the protocol meritorious, prior to its presentation to the GAC. The protocol must conform to the format and policies required by the GAC.

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, or anesthesiology, has a contractual agreement with the grantee institution or participating hospital. Administrative approval by 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. Real or apparent conflicts of interest must be avoided. 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 may be paid by the grant. (See Physical Facilities Section.) 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 (i.e., *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 workers, 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.

M. Reporting Requirements:

A Non-Competing Grant Progress Report (NIH form 2590) is required annually as part of the non-competing continuation award process, as described in the NIH Grants Policy Statement, http://grants1.nih.gov/grants/policy/nihgps_2003/index.htm. Instructions for the NIH form 2590 can be found at: http://grants.nih.gov/grants/funding/2590/2590.htm. For NCRR-supported Center and Resource grants, the PHS form 2590 incorporates an Annual Progress Report (APR), which provides information in greater detail than the standard NIH form 2590. The NCRR uses the information contained in the APR to facilitate programmatic stewardship of the grant and to respond to inquiries from other governmental agencies and the public. Specific instructions for completing an APR and including it with the NIH form 2590 can be found at http://aprsis.ncrr.nih.gov.

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

Division for Clinical Research Resources

Guidelines for the General Clinical Research Centers Program (M01)

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

October 2005

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

Contact Information:

Division for Clinical Research Resources
National Center for Research Resources
National Institutes of Health

6701 Democracy Boulevard
Room 906
Bethesda, MD 20892-4874

Telephone: (301) 435-0790
Fax: (301) 480-3661
E-mail: CRADir@ncrr.nih.gov

Division for Clinical Research Resources Web page

INSTRUCTIONS FOR PREPARING A GCRC APPLICATION

(for applications submitted in 2006 or thereafter)

I. ELIGIBILITY FOR GRANT SUPPORT

Medical institutions and hospitals are eligible for GCRC Program support. The primary purpose of a GCRC is to provide the clinical research infrastructure to investigators who receive their primary research funding from the other components of 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 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 Federal agencies, private foundations, and other peer-reviewed sources. The resources of a GCRC may include inpatient and outpatient facilities, specialized personnel, Core Laboratories, and other Core facilities.

II. SUBMISSION AND REVIEW OF APPLICATIONS

As GCRC applications exceed $500,000 in direct costs per year, permission must be obtained from NCRR prior to submission of an application. Investigators interested in submitting a new, renewal, or amended application should consult with DCRR staff long before the proposed submission date. If approved for submission, one of the submission dates listed below will be designated for acceptance of the application. In addition, NCRR will specify the maximum number of years of support that may be requested in the application, and the maximum direct costs that may be requested in each of these years.

Each new or competing GCRC application submitted to NIH is evaluated by two groups—first, by the Initial Review Group (Clinical Research Review Committee or a Special Emphasis Panel of the NCRR); and then, by the NARRC, which makes its recommendations to the Director of NCRR. Evaluation of a new or competing renewal GCRC application includes assessment of the GCRC's role in enabling research that leads to publications, its value as an institutional and regional resource, its utilization by investigators in multiple disciplines, the type of peer-reviewed research projects supported, program relevance, and the use of the GCRC as a clinical research training facility.

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

Received By	CRR Committee Review	Council Review	Earliest Possible Funding Date
October 1	February	May	July 1
February 1	June	September	December 1
June 1	October	January	April 1

Form PHS 398 is available at: http://grants.nih.gov/grants/forms.htm.

SUGGESTED STEPS IN PLANNING A GCRC APPLICATION

A. Examine these 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. A sufficient number of investigators with peer-reviewed sources of support will utilize the GCRC for clinical research;

2. The use of GCRC resources will be multidisciplinary;

3. Number and category of research inpatient days and outpatient visits required by the research projects;

4. Plans for implementation of an RSA program;

5. Biostatistical, Informatics Core, Core Laboratory, bionutrition, and administrative support is justified for the proposed research;

6. Optimal location for the GCRC within the institution; and

7. Institutional support.

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. Determine whether the hospital is JCAHO-approved and has a currently effective 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 DCRR staff.

III. SPECIFIC APPLICATION INSTRUCTIONS

Form PHS 398 must be used for all new and competing GCRC applications. The specific instructions in these GCRC Guidelines are in addition to the instructions of 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 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: Deputy Director, Office of Review, National Center for Research Resources, 6701 Democracy Boulevard, Room 1001, Bethesda, MD 20892-4874; or for express/courier service use Bethesda, MD 20817. Hand-delivered applications will not be accepted.

When submitting an amended (-A1) application, summarize—in an "Introduction" section—the substantial additions, deletions, and changes that have been made in all sections, including all projects. 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.

The Revised NIH Policy on Submission of a Revised (Amended) Application states that NIH will not consider any -A3 or higher amendment.

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 Clinical Research Review Committee. The reviewers are under no obligations to consider late material.

Pay close attention to type size specifications and limitations in the Form PHS 398 instructions.

PHS 398 Form Page 1
FACE PAGE

ITEM 1. TITLE OF PROJECT: General Clinical Research Center

ITEM 2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION: No

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

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

ITEM 4. HUMAN SUBJECTS RESEARCH: Yes

ITEM 5. VERTEBRATE ANIMALS: See instructions for Form PHS 398.

ITEM 6. DATES OF PROPOSED PERIOD OF SUPPORT

The entire proposed project period may not exceed the number of years specified by NCRR. Applications cannot be funded until the NARRC has completed its review.

ITEM 7 through 15. See instructions for Form PHS 398.

PHS 398 Form Page 2
DESCRIPTION, PERFORMANCE SITES, KEY PERSONNEL,
OTHER SIGNIFICANT CONTRIBUTORS, AND HUMAN EMBRYONIC STEM CELLS

DESCRIPTION: Describe the major resources provided and areas of investigation to be undertaken on the GCRC in lay language.

PERFORMANCE SITE(S): See instructions for Form PHS 398.

KEY PERSONNEL:

Include only the PI, PD(s), Principal RSA, 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.

PHS 398Form Page 3
RESEARCH GRANT TABLE OF CONTENTS

TABLE OF CONTENTS

Structure the table of contents and 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)
B. Budget for Entire Proposed Period of Support
C. Budgets Pertaining to Consortium/Contractual Arrangements and Budget Justification

PART II. BIOGRAPHICAL SKETCHES

PART III. ENVIRONMENT
A. Physical Facility
B. Institutional Commitment

PART IV. RESEARCH RESOURCES PLAN
A. Background and Introductory Statement
B. Past Progress/Organizational Structure/Future Plans
C. Scientific Highlights/Publications
D. Program Leadership
E. GCRC Advisory Committee
F. Administration and Financial Management
G. Nursing
H. Research Subject Advocate
I. Training and Career Development
    1. Clinical Research Feasibility Funds
    2. Medical Student Program
J. Cores
    1. Biostatistics
    2. Informatics
    3. Bionutrition
    4. Core Laboratory
    5. Specific Core
K. Protocols
L. Data and Safety Monitoring Plan
M. Data Sharing Plan

PART V. TABLES

A. Protocols Table
B. Publications Table
C. High Utilization Protocols of the Center
    1. High Inpatient Protocol Utilization
    2. High Outpatient Protocol Utilization
    3. High Ancillary Dollars Protocol Utilization
D. Aggregate Utilization of GCRC
    1. Aggregate Inpatient Utilization by Year
    2. Aggregate Outpatient Utilization by Year

PART VI. MATERIALS

A. Affiliated Clinical Research Resources
B. GAC Minutes
C. DSM Plans
D. APR Investigator Support Lists
E. Individual Protocol Information Sheets

PHS 398 Form Pages 4+5
BUDGET PAGES

PART I. BUDGET

A. Detailed Budget for the Initial Budget Period: For all new and competing continuation applications, the first budget period should be 12 months.

Itemize specific needs for the first budget period as follows:

1. Personnel: Instead of providing the budget justification for requested Personnel on Form Page 5, provide it later in the application under the appropriate category (e.g., Program Directorship, Nursing, or Cores).

2. Equipment: Separately list each requested item of fixed and movable equipment costing more than $5,000. Provide a separate narrative justification for each equipment item requested, and indicate the investigators' projects that require the equipment.

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.

In Schedules 1-8 (see page I-10), include each research project proposed for use of the GCRC that is expected to be active in the first year of the grant, if funded, including projects already underway at the time of the application. List them by project PI, in alphabetical order, including both those for which ancillary support is or is not requested. Exclude projects that will be completed by the first year of the grant. All projects should be included, even if they are awaiting approval by the GAC or the IRB at the time of submission of the application. As the last item in Schedules 1-8, a final item may be included with project title of "Additional Anticipated." This entry should be based on [the average actual recent new GCRC projects approved monthly] multiplied by [the number of months from this application submission to the new project period start date].

(Download Schedules 1 – 8 as Microsoft Excel Spreadsheets.)

The number of category A days requested in item 6 on the following Patient Care Computation should match the total number of category A days in Schedule 1. The total ancillary costs requested in Item 6 on the following Patient Care Computation should match the total ancillary costs requested (hospital plus outside) in Schedule 1. The number of category A visits and ancillary costs requested in item 10 on the Patient Care Computation should match the total number of category A visits and ancillary costs in Schedule 5. This also applies to the numbers for category B days and visits, etc.

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

INPATIENT

RATE USED

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

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

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

---

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) $_____

---

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 $_____

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 5)

__*__ 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 Outpatient 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	SPID	Project Title	Days Per Year	Hospital Ancillaries*	Outside Ancillaries*
TOTALS					

* Annual total costs for tests; charges adjusted to cost by category per patient care rate agreement.

Schedule 2
Category B Inpatient Projects

Investigator	SPID	Project Title	Days Per Year	Hospital Ancillaries*	Outside Ancillaries*
		TOTALS			

* Annual total costs for tests; charges adjusted to category per patient care rate agreement

Schedule 3
Category A Inpatient Scatter-bed Projects

Investigator	SPID	Project Title	Days Per Year	Hospital Ancillaries*	Outside Ancillaries*	Scatter-bed Research Nurse Hours**
TOTALS						

* Annual total costs for tests; charge adjusted to cost by category per patient care rate agreement.

** Only include hours of nurses paid by the GCRC grant, not nurses included in a per diem charge.

Schedule 4
Category B Inpatient Scatter-bed Projects

Investigator	SPID	Project Title	Days Per Year	Hospital Ancillaries*	Outside Ancillaries*	Scatter-bed Research Nurse Hours**
TOTALS						

* Annual total costs for tests; charges adjusted to cost by category per patient care rate agreement.

** Only include hours of nurses paid directly by the GCRC grant, not nurse hours in a per diem charge.

Schedule 5
Category A Outpatient Projects

Investigator	SPID	Project Title	Average Hours Per Visit	Visits Per Year	Hospital Ancillaries*	Outside Ancillaries*
			TOTALS			

* Annual total costs for tests; charges adjusted to cost by category per patient rate agreement.

Schedule 6
Category B Outpatient Projects

Investigator	SPID	Project Title	Average Hours Per Visit	Visits Per Year	Hospital Ancillaries*	Outside Ancillaries*
			TOTALS			

* Annual total costs for tests; charges adjusted to cost by category per patient care rate agreement.

Schedule 7
Category D Inpatient Projects

Investigator	SPID	Project Title	Days Per Year	Industrial Sponsor

TOTALS

Schedule 8
Category D Outpatient Projects

Investigator	SPID	Project Title	Industrial Sponsor	Average Visit Hours	Visits Per Year	Dollars Projected To Be Credited to the Grant

TOTALS			

Note that in the Schedules on the preceding pages, numbers of days and visits projected for the first year of the proposed budget period for each project are to be entered. Make sure that the numbers are consistent between these Schedules and other places in the application where such data for these protocols are given again.]

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

(EXPLANATION OF ITEMS REQUIRED IN TABLE OF CONTENTS)
Use appropriate Form PHS398 Additional Pages

PART II. BIOGRAPHICAL SKETCHES

Provide biographic sketches in PHS 398 format for the PI, the PD, Associate and Assistant PD, and all professionals for whom salary support is requested. Arrange the biographical sketches in alphabetical order, and provide an alphabetized list of names with their page numbers.

PART III. ENVIRONMENT

A. PHYSICAL FACILITY
Describe the GCRC facility in sufficient detail to identify each physical component. Include schematic line drawings, reduced to the size of the continuation pages (that remain readable), and identify the size and use of each room. Indicate the proposed 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 footage 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.

Attach (Part VI. Materials) a brief description of all available or projected facilities for clinical research at the institution and affiliated institutions (e.g., 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.

B. INSTITUTIONAL COMMITMENT
Describe the resources that the institution has provided for the GCRC in the entire last project period (since the last competitive renewal). Have these resources been sustained over the entire period? If there have been changes over that period, explain the changes

and the rationale for increase or decrease in resources provided.

Detail the resources that the institution will provide in the proposed project period. Include any resources which were previously provided that will continue (e.g., rent-free physical facilities, FTEs, equipment, etc.). Describe, in detail, any new resources that the institution will provide and the time line for their provision. Any institution-wide capital-improvement plans, renovations, or construction projects should be explained.

PART IV. RESEARCH RESOURCES PLAN

If this is an amended (revised) application, see page 16 of the PHS 398 instructions (Rev. 09/2004, as updated 6/13/2005) and include an introduction to the revised application here.

A. Background and Introductory Statement
This section describes the institutional atmosphere for research, both current and historical. Relevant information may include the following:
- Brief description of the origin of the institution and its past contributions to research, especially clinical research (limited to one page);
- 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;
- 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;
- 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;
- 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. Past Progress/Organizational Structure/Future Plans
In competing renewal applications, provide a description of the overall GCRC activities in the funding period since the last competitive application and their impact on basic and clinical research at the institution. Include activities targeted at recruitment of investigators who have not previously used the GCRC and retention of those already active on the GCRC. Address the diversity of protocols utilizing the GCRC and changes over the past grant period. Include activities focused on increasing enrollment in studies on the GCRC by the local and regional community. Describe the overall and interactive impact of the core activities on the GCRC. Include responses to previous weaknesses of the GCRC. Include information about collaborations with other institutions and their participation in GCRC activities.

Give an overview of proposed structure and function of the GCRC in the next grant period. Include overall rationale and integrated description of any proposed changes.

Details of changes should be included in the appropriate sections; however, this section should provide the expected overall impact of composite changes. When submitting a new application, provide an overview of the structure and function of the proposed GCRC. Highlight activities or changes related to identified areas of weakness (whether by previous external review or internal review). Provide rationale for and expected outcomes of the proposed plan. Include timelines and benchmarks for internal evaluation of the unit.

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—that supports the grant and states that the research area will be available on a continuing basis.

C. Scientific Highlights/Publications

Highlight major scientific publications resulting from protocols that have utilized the GCRC since the last competitive renewal. Include information on which resources the published study utilized on the GCRC. Include other significant contributions to basic or clinical research to which the GCRC has directly contributed. Scientific highlights and accomplishments should represent advances or achievements that had an impact on prevention, diagnosis, or treatment of disease, understanding of underlying normal or disease physiology, community or public health, or advances in medical practice. Provide information on the acknowledgement of the role of the GCRC with each highlight.

D. Program Leadership

Describe the administrative structure under which the GCRC will operate, including the responsibilities of the PD(s), Associate PDs, and the GAC. Provide a description of the leadership personnel, their qualifications, areas of responsibility, and past activities when submitting a renewal application. Include the proposed plan for leadership of the GCRC in the new grant period.

The Principal Investigator should be an individual whose authority transcends departmental boundaries, usually the Dean of the medical school. The PI appoints the Program Director and members of the GAC, including its chairperson. The PI derives no salary support from the GCRC grant but must contribute at least 1% effort to the grant.

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. Associate and Assistant PDs should be active investigators at the GCRC and recipients of peer-reviewed funding as PIs or co-investigators. PDs and Associate PDs must be licensed physicians. The PD ultimately is responsible for the day-to-day oversight of GCRC activities. Describe the professional background of the PD, Associate Director(s), and/or Assistant Director(s), including training, publications in peer-reviewed journals,

current research funding, history of demonstrated scientific and administrative leadership, and the extent to which they use GCRC resources. Describe the specific areas of responsibility (e.g., overseeing Training or Core Laboratory or Pediatric Unit) of the Associate and Assistant PDs and their activities and plans for management of these areas.

Support for the total program leadership of the GCRC should not exceed 1.0 FTE—except possibly for very large or complex GCRCs. Ordinarily, no more than 50 percent of the PD's time is supported for the administrative oversight of the GCRC; exceptions should be detailed and well justified. Associate and Assistant PDs also may be supported for administrative oversight, not usually in excess of 25% of time for each individual—unless unique GCRC needs require support up to 50 percent effort of an established funded investigator, such as an Associate Director. Justify all effort requested for Program Leadership, and clearly outline how many total FTEs are currently funded by the GCRC grant and how many FTEs are requested in this application. If there is a difference, explain and justify. If personnel have changed, explain.

E. GCRC Advisory Committee

Describe the responsibilities of the GCRC Advisory Committee (GAC) and any subcommittees. Provide a membership list, with academic titles, that clearly delineates voting and non-voting members. Assure that no personnel receiving salary support from the GCRC grant are voting members of the GAC. Describe the administrative relationship between the PI, PD, and GAC.

Indicate the procedures for coordination among PI, PD, GAC, and individual investigators regarding patient care responsibilities and review and approval of submitted research projects and their data and safety monitoring plans. Describe the process for classification of studies as Category A or B. Describe the GAC process for assuring implementation of the NIH policy on the inclusion of women, minorities, and children as study subjects. Describe the process by which the GAC reviews and designates industry-related studies as Category A or D. Describe the relationship between the GAC and IRB. Indicate if any GAC members attend IRB meetings.

Describe the role of the GAC in setting GCRC policies and overseeing the GCRC activities and budget. Describe the materials the GAC reviews and how often.

Attach (Part VI. Materials) copies of six (6) GAC minutes as follows: first, provide minutes for the most recent two meetings for which the minutes have been written; then, provide minutes for two successive GAC meetings one year previously; then, provide minutes for two successive GAC meetings one year previous to that.

F. Administration and Financial Management

Provide background information about the Administrative Director, including any special qualifications, and how long she/he has been in the position. Discuss her/his duties and that of any assistants. Provide information on the interaction and integration with the institution(s) on cost accounting, billing, and documentation of cost allocation.

Discuss financial management within the Institution and GCRC and the office or person responsible for: the preparation of the proposed patient care rates; the preparation of the financial status reports; authorization of grant expenditures and verification of the charges to the grant; patient bills; costs by project; involvement in budget preparation for this application; review of routine cost stepdown in patient care rates; census data records by category (A, B, C, or D) and by inpatient days, outpatient visits, or scatter-bed days; allocation and accounting for nursing services, and records for annual and expenditure report requirements. Provide information on the systems, their security, records back-up, and SOPs for financial and administrative management of the GCRC including those at the GCRC and those at the institution(s).

How many total FTEs are currently funded by the GCRC grant for Administration, and how many FTEs are requested in this application? If there is a difference, explain and justify.

G. Nursing

Provide background information about the Nurse Manager, including how long she/he has been in the position, and about the stability of the nursing staff in general. Describe research training opportunities and requirements for GCRC nurses on a continuing basis. Discuss how duties are divided among nursing personnel (e.g., inpatient, outpatient or scatter-bed, adult or pediatric) and how changing needs of protocols are accommodated. Indicate costs benefits of these plans. Provide information, including flexibility in determination, about: staffing patterns; extent of weekend research activity on the GCRC; source of staff coverage for leave and holidays; and any involvement with nursing students. Justify the number of nursing personnel in terms of total number of inpatient days, outpatient visits, off-site activities and scatter-nurse hours and acuity of studies. How does the nursing staff handle specialized protocols—assign individual nurses or teams to those protocols, provide group training for all protocols, or other? Discuss advantages for your GCRC.

How many total FTEs are currently funded by the GCRC grant for Nursing, and how many FTEs are requested in this application? If there is a difference, explain and justify.

H. Research Subject Advocate (RSA)

Provide details of the activities and responsibilities of the RSA(s) at your GCRC. In particular, describe activities/responsibilities related to: consultation with and education of the GAC, PD, investigators, nurses, laboratory and other core personnel related to human subjects protection issues on the GCRC; counseling research participants; DSM plans; safety monitoring, including adverse events/serious adverse events; policies and procedures to enhance protection of human subjects on the GCRC; and liaison with institution human subjects protection offices, including IRBs. Responsibility assigned to the RSA may be divided among two or more qualified individuals. Provide the name, degree (e.g., M.D., R.N., Ph.D.), and effort funded by the GCRC grant (e.g., 0.5 FTE) for these individuals. Describe the training and experience of each that qualify him/her for

this role. If more than one individual is fulfilling the RSA role, discuss the division of responsibilities among them. Discuss the reporting arrangements and experience to date, regarding the reporting by the RSA to the PI of the GCRC grant (or to the PI's designee).

If reporting is to the PI's designee, indicate whether this individual meets the requirements of the Guidelines (a high-ranking official in the institution who has an understanding of clinical research and is free from conflicts with the independent role of the RSA.) How many total FTEs are currently funded by the GCRC grant for Research Subject Advocate, and how many FTEs are requested in this application? If there is a difference, explain and justify.

I. Training and Career Development

Describe the role of the GCRC as an institutional resource in the clinical research training and career development of physicians, dentists, nurses, biostatisticians, and others. If organized institutional programs, such as K30, K12, or other training programs, utilize the GCRC, explain the relationship between the programs and the GCRC. Is mentoring available for trainees utilizing the GCRC, whether they are in an organized program or not? If the GCRC has supported trainee research in the past funding period, whether through institutional programs or others, provide information on numbers of trainees and if publications resulted from their studies. Describe training programs and their impact on the institution for other professionals, including dentists, nurses, coordinators, laboratory or core professionals, and others.

Medical Student Programs:

If the application is requesting funds 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; and evaluation plan. If in the previous grant period, funds were used to support medical student programs, describe the results since the last competitive renewal—including number of students funded each of these years, what was accomplished, and their current activities.

Clinical Research Feasibility Funds Program (CReFF):

If funds are requested for a CReFF program, provide information on guidelines for eligibility, selection criteria, and an evaluation plan. If a CReFF program was supported in the last grant period, provide for each recipient: the faculty rank of individual; title of project; dates of funding; funds received; accomplishments and publications.

J. Core Resources and Laboratories (now includes Biostatistics, Informatics, Bionutrition)

Discuss each Core Resource or Laboratory separately, as distinct units, under separate

subheadings (e.g., Biostatistics, Informatics, Bionutrition, Sample Processing, Chemistry or Assay, Exercise or Physiology, Body Composition, Genetics, Imaging, Sleep, Mass Spectrometry, and any others).

The primary functions of Core Resources and Laboratories are to provide sophisticated support to a large number of ongoing GCRC protocols and to develop or validate new methods for this purpose. In addition, the resources or laboratories may provide clinical research training for investigators, fellows, students, and technicians. Core Resource and Laboratory availability and activities vary widely across GCRCs. Some GCRC institutions may already provide such resources or laboratories on a fee-for-service model; at other GCRCs, the investigator demand is not high. Cost sharing of Core Resource and Laboratory functions should be sought from funded investigators.

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 GCRC Core Laboratories; rather, they are supported through ancillary funds. However, such tests may be offered in a GCRC Core Laboratory when this is critical for timeliness, when an extreme degree of accuracy is needed, or if patient safety is at stake.

The GAC is responsible for reviewing the Core Resources and Laboratories to ensure that their activities are serving the research needs of a wide array of investigators, that tests or measurements performed are not routine, and that priorities are set for the support and use of the Core activities. In all cases, NIH-supported investigations are to be given the highest priority.

The application should justify continuation and proposed new Core Resources and Laboratories in terms of the resource needs of institution investigators. For proposed continuing or new Core Resource or Laboratory, the following information must be provided.

1. The name of proposed Core Resource or Laboratory and type of service to be performed;

2. The proposed space and location;

3. For all resources, describe the specific services, tests, or analyses to be offered. Include information on current and expected use per investigator and the current and expected number of investigators who will utilize the Core. Is use required by all investigators? Is there dominance of usage by only one or two investigators or groups? If so, explain and justify. How will the Core be able to be able to respond to increasing or decreasing needs of investigators?

4. Description of the criteria the GAC will apply when deciding usage of the Core by investigators or studies;

5. Relationship to the resources or laboratories of the PD and the Associate/Assistant PDs. Is there any intermingling of personnel, space, or equipment of the Core Laboratory with other laboratories, such as the PD's research laboratory or the hospital's clinical chemistry laboratory? If so, how are appropriate charges made;

6. Describe the qualifications of Core Resource or Laboratory Director and staff with justification for level of support requested; describe standard operating procedures and quality control procedures, including participation in external national or international quality control and accreditation activities; indicate ability to provide data in electronic format to investigators; describe how the program will protect privacy and confidentiality of data (if appropriate), and adhere to other relevant regulations (e.g., HIPAA regulations on informatics systems);

7. Will training be available? If so, describe.

8. Is support provided by the institution and other grants, and process for determining "cost-sharing;" and

9. How many total FTEs are currently funded by the GCRC grant for Core Laboratories, and how many FTEs are requested in this application? If there is a difference, explain and justify.

K. Protocols

Delineate responsibilities for research and concurrent medical care delivery, as well as emergency care by investigators. Describe where clinical care activities and research activities are performed, where information from these activities is recorded, and who has access to these data. Describe role of interns, residents, and fellows in research activities, in concurrent medical care delivery, and in emergency coverage. Delineate the role of the PD and RSA in oversight of clinical activities on the GCRC.

In addition to provision of the required tables, provide an overview narrative describing the breadth of protocol activity; diversity of investigators; scientific areas of research; balance of trainee and investigator usage; level and proportion of NIH supported research; justification for proportion of industry studies; explanations for any category C utilization; number of studies started, completed, and abandoned. When submitting a renewal application, provide information related to activities since the last competitive renewal and for the proposed new grant period.

L. Data and Safety Monitoring Plan

Provide a description of the GCRC's overall DSM Plan, including any GCRC-wide policies and procedures for establishing, monitoring, and evaluating protocol DSM plans. The overall GCRC DSM Plan must state that each GCRC protocol will have an individual GAC-approved DSM plan. The overall DSM Plan must state that for all protocols that place participants at significant risk, a DSMB will be included in the

protocol DSM plan. Describe how the GAC determines which protocols place participants at significant risk. The charter (or list of the responsibilities, meeting frequency, etc.) and membership of any DSMB, as detailed in the NIH Guidances on Data and Safety Monitoring, must be included in the DSM plan of any protocol that utilizes a DSMB. Describe in this section of the application the process for initial review, implementation, oversight, and continuing review of protocol DSM plans. Provide details concerning the GCRC's policies and procedures for monitoring and handling of adverse events and serious adverse events that occur on GCRC protocols.

Attach (Part VI. Materials) copies of GAC-approved DSM plans for at least five GCRC protocols, including at least one low-risk study and one study requiring a DSMB.

M. Data Sharing Plan

The Final NIH Statement on Sharing Research Data (February 26, 2003) states that "Starting with the October 1, 2003 receipt date, investigators submitting an NIH application seeking $500,000 or more direct costs in any single year are expected to include a plan for data sharing or state why data sharing is not possible." All new and competitive renewal GCRC applications are, therefore, required to include a section in the application to be entitled, "Data Sharing Plan." Please see the NIH Data Sharing Policy. (The Data Sharing Plan will not be evaluated in the scientific merit review of the application.)

PART V. TABLES

TABLE A. PROTOCOLS TABLE

Include all protocols that utilized the GCRC since the last competitive renewal (or were reported on annual progress reports that included data on protocols active since the last competitive renewal). Days of utilization should be totals of all days used in all years. Please include inclusive dates that the report covers. Order the table with currently open protocols first, pending protocols second, and closed protocols last.

TABLE B. PUBLICATIONS TABLE

Include in this table, the publications by SPID number since the last competitive renewal (or those included in the annual progress reports that cover data from the years since the last competitive renewal). If a SPID produced several publications, include a row for each publication, and if a publication was attributed to multiple SPIDs, it will be listed on a line with each SPID number.

TABLE C. HIGH UTILIZATION PROTOCOLS (TOP 20) OF THE CENTER

Table C1. High Inpatient Protocol Utilization

Include the top 20 protocols ranked by utilization of inpatient days since the last competitive renewal (or inpatient days reported in annual progress reports that cover *data from the years since the last competitive renewal*). If 20 protocols did not use inpatient days, list all inpatient protocols.

Table C2. High Outpatient protocol utilization since last competitive renewal

Include the top 20 protocols ranked by utilization of outpatient visits since the last competitive renewal (or visits reported in annual progress reports that cover *data from the years since the last competitive renewal*). If 20 protocols did not use outpatient visits, list all outpatient protocols.

Table C3. High Ancillary Dollars protocol utilization in last year
Include the top 20 protocols in ancillary dollars *used in the last year*.

TABLE D. AGGREGATE PAST AND PROPOSED UTILIZATION OF GCRC

Table D1. Aggregate inpatient utilization by year

Table D2. Aggregate outpatient utilization by year

(See page I-28 for Tables A – D.)

(Download Tables A – D as Microsoft Excel Spreadsheets.)

TABLE A
PROTOCOLS

SPID	Investigator	Title	Science Area	Trainee*	Status**	Support ***	Grant # (NIH) Source (non-NIH) Source (Other)	Inpatient Days		Outpatient Visits	Type¦	Other GCRC§
								Regular	Scatter			

* Trainee check if investigator is a trainee
** Status O=Open P=Pending C=Closed
*** Support N=NIH P=non-NIH peer O=other
¦ Type A B D
§ Other GCRC A=Ancillaries C=Core CI=Informatics CB=Biostatistics

Table B
Publications since last competitive renewal

SPID	Reference	Pub MED ID*

* For those in last year and if available from past years

Table C1
Top 20 Protocols - Inpatient Utilization
Include utilization since the last competitive renewal

Rank	SPID	Investigator	Title	Science Area	Inpatient Days	Type*	Date Opened	Date Closed	Publication**	Trainee***
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										

* Type - category A, B, or D
** Publication - check if a publication has resulted
*** Trainee - check if investigator is a trainee

Table C2
Tope 20 Protocols - Outpatient Utilization
Include utilization since the last competitive renewal

Rank	SPID	Investigator	Title	Science Area	Outpatient Visits	Type* A, B, D	Date Opened	Date Closed	Publication**	Trainee***
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										

* Type - category A, B, or D
** Publication - check if a publication has resulted
*** Trainee - check if investigator is a trainee

Table C3
Top 20 Protocols - Ancillary Dollars
Include for previous 12 months

Rank	SPID	Investigator	Title	Science Area	Ancillary Costs $	Type*	Date Opened	Date Closed	Publication**	Trainee***
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										

* Type - category A, B, or D or AO for ancillaries only
** Publication - check if a publication has resulted
*** Trainee - check if investigator is a trainee

Table D-1
Aggregate GCRC Utilization - Inpatient Days

	A	B	D	C	Sc-A	Sc-B
200?-200?						
used:						
awarded:						
200?-200?						
used:						
awarded:						
200?-200?						
used:						
awarded:						
PROPOSED						

Awarded = data from NGA
Used = actual
Proposed = proposed in first year of new project period

Table D-2
Aggregate GCRC Utilization - Outpatient Visits

	A	B	D
200?-200?			
< 1 hour			
1-3 hours			
3-6 hours			
6-10 hours			
> 10 hours			
TOTAL USED			
AWARDED			

200?-200?			
< 1 hour			
1-3 hours			
3-6 hours			
6-10 hours			
> 10 hours			
TOTAL USED			
AWARDED			

200?-200?			
< 1 hour			
1-3 hours			
3-6 hours			
6-10 hours			
> 10 hours			
TOTAL USED			
AWARDED			

PROPOSED			

Awarded = data from NGA
Used = actual
Proposed = proposed in first year of new project period

PART VI. MATERIALS

A. Affiliated Clinical Research Resources

Attach a brief description of all available or projected facilities for clinical research at the institution and affiliated institutions (e.g., 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.

B. GAC Minutes

Provide copies of six (6) GAC minutes as follows: first, provide minutes for the most recent two meetings for which the minutes have been written; then, provide minutes for two successive GAC meetings one year previously; then, provide minutes for two successive GAC meetings one year previous to that.

C. DSM Plans

Provide copies of GAC-approved DSM plans for at least five GCRC protocols, including at least one low-risk study and one study requiring a DSMB.

D. APR Investigator Support Lists

Provide copies of the "Source of Investigators' Support" section as they were submitted within the APR for each of the four most-recently submitted APRs.

E. Individual Protocol Information Sheets

For each individual research project listed in Schedules 1 – 8, provide the following information on an individual sheet for each protocol. Arrange the sheets in alphabetical order by project PI.

1. PI Name, Degree (e.g, M.D., Ph.D.), and Department (e.g., Medicine, Pediatrics).

2. SPID Number.

3. Project Title (Long Title).

4. Is this project supported by an NIH grant? If so, asterisk the project, and list the grant number, grant PI, and grant project period.

5. Is this project supported by a non-NIH peer-reviewed grant? If so, list the source of funding (e.g., American Cancer Society), grant number, grant PI, and grant project period.

6. Is this project supported by any funds other than given above? If so, identify the source of funding (e.g., Pfizer).

7. Utilization - Fill in the following table for projected GCRC utilization in the first year of this GCRC renewal.

Inpatient Days			**Scatter-Bed Days**		**Outpatient Visits**			**Scatter RN Hours**		
A	**B**	**D**	**A**	**B**	**A**	**B**	**D**	**A**	**B**	**D**

8. In addition to days, visits, scatter-nurse hours enumerated above, what other GCRC resources (e.g., Core Laboratory, Bionutrition, Biostatistician) are projected to support this project in the first year of this GCRC renewal?

9. Was this project (SPID) reported in the most-recently submitted Annual Progress Report (APR)?

10. If 9 is yes, fill in table below as was reported in the APR for this SPID.

Inpatient Days			**Scatter-Bed Days**		**Outpatient Visits**			**Scatter RN Hours**		
A	**B**	**D**	**A**	**B**	**A**	**B**	**D**	**A**	**B**	**D**

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

Division for Clinical Research Resources

Guidelines for the General Clinical Research Centers Program (M01)

Supplement II: Review Criteria for Evaluation of GCRC (M01) Applications

October 2005

An Administrative Document Issued by the
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Contact Information:

Division for Clinical Research Resources
National Center for Research Resources
National Institutes of Health

6701 Democracy Boulevard
Room 906
Bethesda, MD 20892-4874

Telephone: (301) 435-0790
Fax: (301) 480-3661
E-mail: CRADir@ncrr.nih.gov

Division for Clinical Research Resources Web page

REVIEW CRITERIA FOR EVALUATION OF GCRC APPLICATIONS
(for applications submitted after January 1, 2006)

I. REVIEW PROCESS

Review of applications for new or renewal applications for GCRCs submitted after January 1, 2006 will not include a site visit. All applications will be reviewed by the Clinical Research Review Committee or—at the option of the Office of Review—by a Special Emphasis Panel. Supplement I of this document includes the instructions to the applicants for preparing the application. This Supplement contains the review criteria that the reviewers will utilize in their evaluation of the applications.

II. FACTORS IN EVALUATION OF APPLICATIONS

Factors considered by the reviewers include: past activity, impact, management, and productivity of the GCRC since the last competitive renewal application (for renewal applications); the number and diversity of scientific areas of research supported on the GCRC; the collective impact of the GCRC on clinical research at the institution and nearby institutions; utilization of the GCRC to support clinical research training—at the institution—of medical students, physicians, dentists, nurses, psychologists, and others; and proportion of research and investigators utilizing the GCRC that have NIH and other peer-reviewed support. For new applications, criteria dependent on activities in the past funding period shall not apply; however, it is expected that new applicants will provide information, if available, on the impact of any similar programs at the institution that will be incorporated into the proposed GCRC.

III. REVIEW CRITERIA

ENVIRONMENT:

PHYSICAL FACILITY

- Is the physical facility, as described, consistent with the proposed level of activity, nature of the disease, and age of possible research participants (e.g., infants, pediatric, adolescents, adult, elderly, frail, obese), and research complexity of the protocols? Is the described safety equipment sufficient for the breadth of research described? Are the plans for regular maintenance appropriate?
- Are the nursing areas, RSA offices, and PD office in close proximity to the patient care area to facilitate interaction with GCRC staff and research participants?
- If the GCRC facilities span more than one area, is the described plan for interaction well thought out?
- Is the space for other activities, including cores—such as specimen collection, informatics, bionutrition, laboratory, and others—appropriately located relative to the special needs of these activities?

- Are any proposed alterations and renovations clearly described and justified?

INSTITUTIONAL COMMITMENT

- What resources has the institution provided since the last competitive renewal?
- Have they been sustained over the past granting period?
- Are the resources committed by the institution for the next granting period clearly outlined and consistent with the proposed support of clinical research at the institution?

RESEARCH RESOURCES PLAN:

PAST PROGRESS/ORGANIZATIONAL STRUCTURE/FUTURE PLANS

- Evaluate the direction, effectiveness, and progress of the GCRC over the last granting period in providing an infrastructure and resources that advance clinical research and research training.
- What GCRC activities have had a wide positive effect on clinical research at the institution and other institutions? What changes in structure or function of the GCRC are proposed in the GCRC application? How will these changes contribute to the advancement of clinical research for investigators at the institution?
- How has the GCRC leadership addressed the diversity of research and investigators utilizing GCRC? How effective have these activities been, and what—if any—changes will be made in the next funding period to increase diversity?
- Evaluate the response of the GCRC to unexpected problems and previous weaknesses.
- Is the proposed number and complexity of protocols reasonable, based on past protocols, utilization, and expected changes at the institution?
- Evaluate the likely overall impact of any proposed changes in infrastructure, allocation of resources, and management for the next grant period.
- Are proposed staff changes appropriate, and are they expected to enhance the GCRC?
- Overall, is the balance of proposed resources appropriate (nursing, specific cores, number of inpatient and outpatient visits, training, staff, etc.)?

SCIENTIFIC HIGHLIGHTS AND PUBLICATIONS

- Assess the breadth and quality of the GCRC publications and scientific highlights in advancing clinical research.
- Did the GCRC make a significant contribution to the scientific highlights and publications?
- Were other cited scientific accomplishments significant and dependent on the GCRC?

PROGRAM LEADERSHIP/DIRECTION

- Evaluate the effectiveness of the Program leadership in monitoring and

responding to changing needs in following areas:
    - the effectiveness and utilization of each of the GCRC resources, cores, and programs;
    - the diversity of the investigators and scientific areas of research utilizing the GCRC;
    - the activity and productivity of protocols;
    - effectiveness of training and educational activities of the GCRC;
    - impact of the GCRC on clinical research at the institution.
- Are any changes in Program leadership's management activities proposed in the next funding period to address any gaps or weaknesses? Evaluate the proposed plans.
- Is the GCRC leadership staff effective?
    - Are the PD, Associate PDs, and Assistant PDs productive, and are their responsibilities clearly defined?
    - Are the personnel, including PI, PD, and Associate or Assistant PDs, appropriately qualified for their proposed positions (including meeting requirements of the GCRC guidelines related to funding and GCRC activity), and is the percent effort appropriate?
- Is the organizational plan for the management of the GCRC for the next project period reasonable? Are the number and type of personnel appropriate?

GCRC ADVISORY COMMITTEE (GAC)

- Are the processes and procedures for protocols review, assessment, and prioritization appropriate and widely publicized at the institution?
- Is the organizational structure and composition of the GAC appropriate?
- Does the membership of the GAC include the necessary expertise for review of protocols, or are there clear procedures for obtaining additional expertise? Do GCRC grant-supported staff vote (by guidelines they should not)?
- How many protocols does the GAC typically review at a meeting? Is the meeting frequency sufficient to address protocol submissions in a timely fashion?
- Are the provided minutes clear, timely, and complete? Do they reflect appropriate input by GCRC staff and reviewers? Was there a quorum at the meetings? If not, how was this handled?
- Does the GAC include the appropriate mix of professionals needed to provide advice and oversight on the overall management of the GCRC?
- Does the GAC provide guidance on prioritization of GCRC resources, including core resources? Does the GAC address confidentiality procedures? Is the role of GAC and process for input clear?
- How frequently does the GAC review the function and management of the GCRC? Has this resulted in any changes in GCRC function or budgetary management?

ADMINISTRATION AND FINANCIAL MANAGEMENT

- Is the staffing and organizational structure of the administrative management

personnel appropriate? Is the administrative management of the GCRC effective?

- Are reliable systems, including the appropriate level of security, available and used for tracking GCRC usage, dollars, and data? Are the relationships of GCRC staff with university and hospital administrative and financial staff appropriate and effective?
- Are procedures in place to ensure the system is up to date, and are they audited? How are discrepancies identified and resolved?
- Are the systems used to track nursing, space, and patient care time and compensation integrated with the university and/or hospital to ensure appropriate allocation of usage and dollars?
- Is the process for reporting financial and utilization data to the GAC clearly defined in standard operating procedures?

NURSING

- Is the nursing administrative structure appropriate? Have the level of nursing support, coverage, and the mix of nursing personnel been appropriate for the number and mix of protocols active on the GCRC over the past granting period?
- Is the proposed level of support and mix of nursing personnel appropriate for the proposed level of protocol activity?
- Is research nursing training optimal?
- Is the management plan for nursing support practical and effective?
- Is this plan sufficiently flexible to adjust to changing research needs? Is the management cost effective?

RESEARCH SUBJECT ADVOCATE

- Has the RSA program been active and effective in the last granting period? Did the activities facilitate implementation of safe and ethical research and contribute to the safety of participants? Does the RSA work effectively with all members of the research team and institutional colleagues in ensuring safety of GCRC research?
- Are the GCRC procedures for serious adverse event reporting, clear, efficient, and effective?
- Have the activities emphasized in the program changed to meet emerging needs of the GCRC over the past grant cycle?
- Are the proposed activities for the next period appropriate and justified?
- Are the responsibilities, reporting structure, and percent effort of the current and proposed personnel clearly outlined, appropriate, and allocated for maximal impact?
- Does each of the personnel have specific training and expertise in ethics and human subjects protection? If not, how is this being addressed?
- Is the reporting structure of the RSA consistent with the guidelines? Are the roles of the PD and the RSA clearly outlined and appropriate?

TRAINING AND CAREER DEVELOPMENT

- Is the GCRC used as a research training environment by institutional programs for medical students, fellows, physicians, dentists, technicians, nurses, coordinators, social workers, bionutritionists, and others? Is there evidence of contribution of the GCRC to success of these programs? Do these programs provide benefit to the GCRC?
- Does the GCRC provide training and mentoring opportunities for junior investigators (physician, dentist, nurse, etc.)? What proportion of these investigators has been successful over the past granting period in obtaining independent support for their research?
- Does the GCRC offer specific medical student training programs, and what is their impact?
- Evaluate any data provided on the success of the GCRC training program, and the current and proposed mechanism for evaluation of the training programs.

CORES

Provide a separate evaluation of each core or core activity of the GCRC active during the past grant period and/or proposed in next grant period. Core activities include biostatistics, informatics, bionutrition, assay laboratory, and any specialized cores. Specialized cores could include, but are not limited to: sleep laboratory, exercise and physiology laboratory, genetics core, sample preparation core, imaging core, and mass spectrometry core.

Assess the following for each Core:

- Is the Core resource appropriately managed? Is the availability of the resources widely known? Does availability of specific activities change? Does the Core offer routine tests, or are its facilities available outside of the GCRC for research?
- Is the Core available to investigators while developing a protocol?
- How is quality controlled in the Core? Does the Core utilize national standards and participate in local and national quality-control activities or accreditation?
- Did the resource support a variety of investigators and protocols in diverse areas of research? Was disproportionate use by investigators or projects justified appropriately?
- Did resources contribute to research leading to cited publications?
- What processes are in place to monitor and evaluate—in an ongoing manner—the specialized activities of Core and their utilization? Evaluate the effectiveness of this process during the last granting period. How are resources reallocated if demand increases or decreases?
- Has the Core been cost effective?
- Is the Core Director well qualified for the position? Are other personnel trained, experienced, and qualified?
- Are any proposed changes meritorious, and will they provide resources to a wide variety of investigators and areas of science?

PROTOCOLS

- Evaluate the breadth and activity of the GCRC protocols over the past granting period.
- Evaluate the "turnover" of protocols on the GCRC; protocols closed and new ones opened.
- Is the applicant's proposed plan for monitoring and optimizing utilization and activity of the GCRC appropriate?
- Is category C utilization as low as possible, consistent with mission of the GCRC?
- Is the balance of industry and investigator-initiated studies appropriate?

Address the following topics for the top 20 protocols in 3 areas of utilization: 1) inpatient days, 2) outpatient visits, and 3) ancillary dollars:

- Is there diversity among investigators and type of research?
- Is there a wide range of activity, or does a small number of protocols, dominate usage?

DATA AND SAFETY MONITORING PLAN

- Is the Data and Safety Monitoring Plan for the GCRC consistent with the GCRC Guidelines and Federal requirements? (See Data and Safety Monitoring Plan and Reporting Serious Adverse Events (SAEs) on page 14.)
- Is the Data and Safety Monitoring plan feasible and implementation acceptable?

OVERALL EVALUATION

After evaluation of all the components of the GCRC as outlined above, the reviewers should assign an overall score for the application. The overall score should take into consideration the strengths and weaknesses of each component; the synergy or lack of synergy between the components; the administrative coherence of the application; proposed mechanisms to evaluate ongoing programs and address changing needs; and the overall strengths and weaknesses of the application. The emphasis on each criterion and each component may vary from one application to another, depending on the nature of the application and its relative strengths.