

# NIH GUIDE

# for GRANTS and CONTRACTS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 9, No. 10, August 29, 1980

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*The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.*

*Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.*

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

**ANNOUNCEMENT**

NIH-NCI-DCCR-TRCCB-80-7

NATIONAL CANCER INSTITUTE

TITLE: *CANCER PATIENT COMPLIANCE WITH THERAPEUTIC REGIMENS*

*Application receipt date, January 15, 1981*

BACKGROUND INFORMATION

In the most general sense, compliance may be understood as the extent to which a person's behavior (for example, taking medications, following diets, or changing life style) coincides with medical or health advice. Lack of patient cooperation with diagnostic, treatment, or rehabilitation efforts across chronic disease states is a major and growing concern for health care providers. Although there is no reason to assume that the problem of non-compliance is less acute in cancer patient populations, to date only one careful investigation of cancer patient compliance has been carried out. That research, as well as widespread clinical evidence, suggests that across the whole gamut of cancer control activities, noncompliance is a major problem for this group, also.

There are two major reasons for measuring compliance behavior in cancer patients. First, in the development of new forms of treatment, the compliance distribution for subgroups of patients and types of treatment should be taken into account in order to interpret the effects on disease course and outcome. Interpretation of the results of clinical trials is not possible without taking into account the proportion of patients not complying with the protocol. Unfortunately, this distribution of compliance behavior for cancer treatment protocols has not been systematically assessed.

Second, in clinical application aimed at control of the disease (ranging from diagnostic procedures and follow-through to post-primary treatment rehabilitation), patient cooperative behavior needs to be monitored. Patient cooperation may be enhanced by application of such procedures as behavioral modification techniques, including stimulus control and reinforcement of appropriate behavior.

Whether compliance measurement is an essential part of therapeutic trials and the development of more effective treatments, or whether such measurement is utilized in monitoring cooperation with proven treatment and enhancing the latter--valid and reliable methods of measuring compliance are essential. Findings in the current compliance literature are inconsistent, and study results are non-comparable because "compliance" is not adequately defined, different measures of compliance response to the same regimen are utilized, and these same measures are not accurate indicators of the criterion behavior.

RESEARCH GOALS AND SCOPE

1. One aim of research supported in this area will be to develop valid direct and indirect measures of cancer patient compliance to diagnosis, treatment, and rehabilitation recommendations. Direct methods of measuring compliance to self-administered treatment regimens include, for example, the assessment of level of drug in the blood, or the measurement of urinary excretion of medication, metabolites, or drug markers. Assays for methotrexate, hexamethylmelamine, allopurinol, L-phenylalanine mustard, tamoxifen, and prednisone, for example, already exist, and behavioral investigators would need to collaborate with pharmacologists in the further development and utilization of such measures for these self-administered treatments. Studies of compliance using drugs for which assays are not available will be excluded from consideration. In addition to the development and/or utilization of reliable drug assays, investigators should consider individual pharmacokinetic variations (for example, differential bioavailability of medication, genetically determined variations in metabolism and effects of repeated dosage on metabolic rate) in order to assess patient compliance to treatment. This RFA will not support the development of assay techniques for assessing drug levels independent from a behavioral study focus which addresses the nature of compliant behavior in cancer patients. Investigators proposing to measure drug compliance with new forms of treatment currently being developed, and for which no reasonably valid assay technique exists, should emphasize the development of indirect measures of compliant behavior.

Indirect methods of measuring compliance to diagnostic, treatment, or rehabilitation recommendations include the assessment of therapeutic outcome, utilization of interview reports, and the use of other forms of patient and/or family self-report. While these latter, indirect methods have proven difficult to develop as accurate indices of patient behavior (for example, outcome is determined by other factors than patient cooperation), it is still possible to assess objective, but indirect signs of compliance (such as clinical evidence of self-care activities). As direct measurement of compliant behavior is less feasible with regimens that do not involve medication, it is imperative to develop broader tools with which to assess the extent of patient cooperation in a therapeutic endeavor.

Creative research is therefore needed to develop valid measures of cancer patient compliance. Such measurements will provide the methodologic tools for assessing compliance variance as it relates to the development of new treatment, as well as for monitoring compliance behavior in those patients at high risk for noncompliance with accepted forms of treatment.

2. A second aim for research supported by this RFA initiative is to foster research into the nature of cancer patient compliance which will lead to a greater understanding of the sources of individual and group variation in compliance behavior. The distribution of compliance behavior by treatment, patient subgroup, and treatment setting needs to be determined in conjunction with both randomized, treatment trials, as well as in the clinical application of standard treatment techniques. In addition,

sources of variance in compliance behavior related to diagnostic follow-through, adjunct health recommendations, after-care and rehabilitation regimens need to be systematically assessed. Such knowledge will allow for more valid interpretation of outcome in clinical trials, including the development of more accurate dose-response curves for different sub-populations of patients. Better understanding of the nature of noncompliance in cancer patients will also allow for the prediction of non-compliant behavior in order to intervene with those at high risk for noncompliance.

3. A third aim of this research area will be to develop techniques that effectively modify compliant behavior for sub-populations of patients. The most effective techniques can then be applied by care givers in the health delivery system to high risk noncompliers in order to optimize cooperation in these patient groups.

#### MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional NIH grant-in-aid and successful applicants will plan and execute their own study effort. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 409 (P.L. 78-410, as amended; 42 USC 286) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is described in the Catalog of Federal Domestic Assistance number 13.339, Cancer Control. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

It is expected that six to eight high quality applications will be supported in the area of cancer patient compliance, and approximately \$1,000,000 over a three-year period for direct costs, plus an amount for allowable indirect costs, has been set aside for this research effort. In order to assure research support for projects examining a broad spectrum of cancer control activities, 50% of the awards will be made to projects concerned with the indirect measurement of compliant behavior, and 50% of awards will support studies concerned with the direct measurement of medication compliance. These initial applications should not cover a period of longer than three years, and it should be noted that renewal applications will compete with all research grant applications received by NIH.

#### REVIEW PROCEDURES AND CRITERIA

Applications responding to this RFA will be reviewed by a standing or special Division of Research Grants (DRG) study section. The general criteria by which DRG study sections evaluate RFA-solicited research projects are the same as DRG's criteria for all other research applications. That is, the same standards of scientific excellence will be the criterion of peer review acceptability.

Criteria specific to this RFA include an operational definition of cancer patient compliance appropriate to the cancer patient sub-population and regimen being studied, the correspondent development and/or utilization of a valid and reliable measurement(s) of compliant behavior, and the utilization of an experimental or quasi-experimental research design in the study of cancer patient compliance. Pharmacological studies in which the investigator proposes to develop assay techniques independently from an investigation into the nature of cancer patient compliance and/or its enhancement will not be considered

responsive to this RFA. Applicants without a history of research with cancer patients must for this project demonstrate a collaborative research effort with investigators in relevant biomedical specialties.

Applicants whose submissions are judged as unresponsive to the RFA by DRG will be given an opportunity to have their applications considered along with all other unsolicited grant applications received by NIH for that particular review cycle.

Applications judged responsive and subsequently approved by review groups will be funded in priority order. Responsive applications that are approved but which cannot be funded with earmarked funds will not be placed in competition with unsolicited applications for regular program funds.

#### METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the business or grants and contracts office at most academic and research institutions or from the Division of Research Grants, NIH. The phrase "PREPARED IN RESPONSE TO RFA: CANCER PATIENT COMPLIANCE WITH THERAPEUTIC REGIMENS" should be typed across the top of the first page of the application. Additionally, a brief covering letter should accompany the application indicating that it is being submitted in response to this RFA announcement. The original and six copies of the application should be sent or delivered by January 15, 1981 to:

Application Receipt Office  
Division of Research Grants  
National Institutes of Health  
Room 240, Westwood Building  
Bethesda, Maryland 20205

In addition, one copy of the application should be sent to:

Dr. Sandra M. Levy  
Division of Cancer Control and Rehabilitation  
National Cancer Institute  
Room 621, Blair Building  
Silver Spring, Maryland 20205

For further information, investigators are encouraged to contact Dr. Levy at the above address or by telephone: (301) 427-8656.

RESEARCH GRANT APPLICATIONS SOUGHT BY

**ANNOUNCEMENT**

THE NATIONAL CARIES PROGRAM,

NATIONAL INSTITUTE OF DENTAL RESEARCH

The National Caries Program supports efforts to develop practical methods to reduce the incidence of coronal and root caries and ultimately eliminate these major health problems. The objective of this announcement is to encourage submission of high quality applications for research grants to study the etiology, pathogenesis, and prevention of dental caries. Since the disease results from demineralization of the susceptible tooth surface by acid produced by oral flora from dietary carbohydrates, the interests of the National Caries Program focus on four strategy areas:

- I. Combat the responsible microbial agents.
- II. Increase the resistance of the tooth and host.
- III. Decrease caries conducive properties of the diet.
- IV. Improve delivery and acceptance of caries preventive measures.

Examples of areas of needed research include:

- Development of reliable and feasible methods for early detection of caries prior to irreversible tooth damage. Methods are also needed to predict susceptibility to caries.
- Physico-chemical characterization of the caries process in enamel and cementum, and of the changes occurring during remineralization of the lesion. Identification of the factors responsible for differences in caries susceptibility of the different regions of tooth enamel.
- Determination of the cariostatic mechanisms of action of fluoride and the influence of other dietary trace elements both on the tooth and on the cariogenic oral flora.
- Evaluation of the impact of non-carbohydrates and of carbohydrates other than sucrose on the cariogenicity of the diet.
- Synthesis or isolation and taste, stability, and safety evaluation of new, potentially noncariogenic sweeteners; determination of the effects of such sweeteners on microbial metabolism, plaque formation, and caries development.
- Determination of the special characteristics of oral microorganisms associated with cariogenicity. Genetic studies of cariogenic organisms should aid identification of these virulence factors and assessment of their importance.

- Differences in the oral flora associated with smooth surface, pit and fissure and root surface caries is a subject that requires examination. The number and distribution at various tooth sites and elsewhere in the oral cavity of potentially cariogenic organisms such as Streptococcus mutans, S. sanguis, S. salivarius, S. mitior, Rothia sp., enterococci, lactobacilli, and actinomyces should be determined. Recent studies have emphasized S. mutans as a major etiological agent; the cariogenic potential of other organisms needs to be assessed.
- Examination of the salivary and microbiological determinants of plaque formation and ecology, including salivary pellicle, adherence factors, bacterial, and salivary components which influence the growth, composition, and metabolic activity of the plaque flora. For example, the possibility of bacterial antagonism to S. mutans in plaque and the antibacterial actions of the salivary non-specific immune factors, lysozyme, lactoferrin and lactoperoxidase, individually and in combination with specific antibodies, should be explored. Development of in vitro model systems, in which environmental factors can be controlled, will facilitate studies of plaque ecology.
- Development of a caries vaccine. This will require identification of immunogenic cell surface components of cariogenic organisms, methods of estimation of immune responses to such antigens, assessment of the contributions of systemic and secretory responses, elucidation of the mechanism of uptake and sequence of antigen processing in peripheral and central secretory immune sites, and evaluation of the importance of cell mediated immunity of mucosal surfaces in caries etiology and prevention.

Legislative authority for this program is found in Section 301 of the Public Health Service Act (P.L. 78-410 as amended; 42 USC 241), as administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. The Catalog of Federal Domestic Assistance number is 13.840, Caries Research. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Discussions of these and other important topics for investigation have been published in the proceedings of National Caries Program sponsored conferences referenced below.

#### Application and Review Procedures

Applications for research grants should be submitted on application form PHS 398 which can be obtained from the institution's application control office or the Division of Research Grants, NIH, Bethesda, Maryland 20205. Application receipt dates are November 1, March 1, and July 1.

Applications will be reviewed by the appropriate DRG Study Section and by the National Advisory Dental Research Council. The customary review criteria for research project grants will apply.

Inquiries concerning interests or draft proposals may be addressed to:

John D. Townsley, Ph.D.  
Chief, Caries Research Grants and  
Contracts Branch  
National Caries Program  
National Institute of Dental Research  
Room 522, Westwood Building  
5333 Westbard Avenue  
Bethesda, Maryland 20205

Telephone: (301) 496-7884

### References

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J. Dent. Res. 53: 153-318, 1974.
- <sup>1</sup>Identification of Cariogenic Bacteria by Fluorescent Antibody  
and Other Techniques. Ed. A.S. Bleiweis, J. Dent. Res. 55:  
A1-A206, 1976.
- <sup>1</sup>Immunological Aspects of Dental Caries. Ed. R.J. Genco,  
J. Dent. Res. 55: C1-C230, 1976.
- <sup>1,2</sup>Immunological Aspects of Dental Caries; Selection of Immunogens  
for a Caries Vaccine. Ed. W.H. Bowen, R.J. Genco, T.C. O'Brien,  
Special Suppl. Immunology Abstracts, Information Retrieval, Inc.,  
Arlington, Va. 1976.
- <sup>1</sup>Cariostatic Mechanisms of Fluorides. Ed. W.E. Brown, Caries  
Research 11: Suppl., 1976.
- <sup>2</sup>Microbial Aspects of Dental Caries. Ed. H.M. Stiles, W.J. Leosche,  
T.C. O'Brien, Special Suppl. Microbiology Abstracts B, Information  
Retrieval, Inc., Arlington, Va. 1976
- <sup>1,2</sup>Prediction of Dental Caries. Ed. B.G. Bibby, R.J. Shern, Special  
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Arlington, Va.. 1978.
- <sup>1,2</sup>Sweeteners and Dental Caries. Ed. J.H. Shaw, G.G. Roussos, Special  
Suppl. Feeding, Weight and Obesity Abstracts, Information Retrieval,  
Inc., Arlington, Va. 1978
- <sup>2</sup>Secretory Immunity and Infection, Proceedings of the International  
Symposium on the Secretory Immune System and Caries Immunity.  
Ed. J.R. McGhee, J. Mestecky, and J.L. Babb, Plenum Press, London  
and New York, 1978.

- 1,2 Saliva and Dental Caries. Ed. I. Kleinberg, S.A. Ellison, and I.D. Mandel. Special Suppl. Microbiology Abstracts B, Information Retrieval, Inc., Arlington, Va. 1979.

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1 - A limited number of copies are available gratis from the National Caries Program.

2 - Copies may be purchased from the publisher.

DRR INVITES APPLICATIONS FOR PROPHET

**ANNOUNCEMENT**

COMPUTER RESOURCE

DIVISION OF RESEARCH RESOURCES

The Division of Research Resources invites applications from qualified groups of biomedical research scientists who need access to the data management and interactive analytical capabilities of its PROPHET computer network. The PROPHET System is a national time-shared computer network which was initiated--and continues to be developed and managed--by the Biotechnology Resources Program, Division of Research Resources, National Institutes of Health.

The PROPHET computer network offers a unique, sophisticated, comprehensive set of tools for table-making, statistical analysis, graphing, curve fitting, mathematical modeling, and molecular modeling. Scientists construct tables into which they enter their data in much the same manner as they would in the familiar laboratory notebook. Tabular data can be corrected, expanded, updated, re-arranged, merged into other tables, reconstructed into new tables, or deleted. Once data has been stored within a table, the data from one or more columns can be sorted, displayed as a graph, fit with an appropriate line or polynomial function (which also can be displayed if desired) and analyzed by a number of statistical programs. The molecular modeling tools enable the user to construct a molecule (by introducing its coordinates on a graphics tablet), compute a model (using an energy minimization program), and project the model in a 3-D like representation. The mathematical modeling and molecular modeling capabilities of the PROPHET System are useful to a wide range of biomedical research scientists including investigators exploring structure-activity relationships and conducting studies to determine mechanisms of drug action.

The PROPHET computer system does not require the biomedical researcher to be proficient in computer science. Users address the system using easily remembered English language commands in sentence syntax. In many cases, a particular command will initiate an interactive quiz which elicits all of the information necessary to perform a particular job. This reduces the number of commands which the user must remember.

User assistance is provided by a variety of mechanisms: an easily comprehended primer, additional more detailed manuals, regular visits by the technical assistance staff, a 24-hour telephone hot line to the technical assistance

This program is described in the Catalog of Federal Domestic Assistance number 13.371, Biotechnology Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (P.L. 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

staff, and an annual user colloquium. The communication established via these mechanisms serves as the driving force for continuous system development and growth. A powerful programming language, PL-PROPHET, exists for the more advanced users, enabling them to create their own program de novo, by linking together existing programs, or by a combination of these two approaches.

Successful applicant sites are provided with a graphics display terminal, graphics tablet, and hard copy unit. Access to the central PROPHET time-shared computer is accomplished via a telephone communications network. Users at different PROPHET sites, distributed throughout the United States, are able to collaborate with one another via the shared central computer and its data files.

User groups gain access to the PROPHET System by making application to the Division of Research Resources. The application is reviewed by a DRR peer review group which evaluates each application with respect to (1) the merit of the ongoing biomedical research conducted by the group of applicants, (2) the need for computerized tools, in general, and the specialized tools available on the PROPHET System, in particular; and (3) the ability of the group to contribute to the evaluation of current PROPHET System tools and help initiate development of new tools. Successful applicants receive a graphics display terminal with accessories, and access to the PROPHET Computer System via a telephone line. After a 6-month familiarization period users are required to partially share the cost of system operation: the minimum cost per site is \$1,875 for each 3-month period. This fee includes access to the system, and provision of local graphics and communications hardware as well as user assistance. Individual users at each site who have government grants can obtain funds for use of the PROPHET network by including requests for appropriate funds in their individual research applications to each of their granting agencies. If you desire additional information, please write to:

Dr. Jack Hahn  
Biotechnology Resources Program  
Division of Research Resources  
National Institutes of Health  
Room 5B43, Building 31  
9000 Rockville Pike  
Bethesda, Maryland 20205

INTERSTATE SHIPMENT OF CERTAIN ETIOLOGIC AGENTS



The Center for Disease Control, Public Health Service, HHS has published a final rule as 42 CFR Part 72 which modifies the requirements for the interstate shipment of certain etiological agents, diagnostic specimens and biological products. (See Federal Register, Vol. 45 No. 141, pages 48626-48629 dated July 21, 1980). The requirements set forth in these regulations are intended to prevent the exposure and possible infection of transportation personnel and others to infectious materials in interstate transit. The regulations cover requirements for packaging, labeling, shipping and mailing, reporting of damaged shipments and failure of delivery. All NIH grantees and contractors who are engaged in the distribution or receipt of such material are urged to familiarize themselves with the cited regulations. It should be noted that the effective date of these regulations is August 20, 1980.

COMPREHENSIVE SICKLE CELL CENTERS

DIVISION OF BLOOD DISEASES AND RESOURCES

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

*Application receipt date, April 1, 1981*

The Sickle Cell Disease Branch, Division of Blood Diseases and Resources, National Heart, Lung, and Blood Institute, announces its intent to support on a competitive basis a limited number of Comprehensive Sickle Cell Centers, each capable of a wide range of activities encompassing basic and clinical research as well as programs designed to bring improved services to the community. The number of Centers to be supported in FY 1983 will be determined by merit of applications received and the availability of funds. The purpose of Comprehensive Sickle Cell Centers is to focus resources, facilities and manpower in a coordinated effort to solve problems of high priority related to sickle cell disease. In the setting of a Center it should be possible to coordinate efforts in fundamental and clinical research, clinical applications, education and demonstration programs and to bring the results from each component promptly to bear on the others.

A Center should be an identifiable unit within the sponsoring institution, which will usually be a university or research oriented hospital. It should be organized around a group engaged in ongoing research and community service in sickle cell disease. While a Center must devote its major effort to one or more specific problems, it must also encompass meaningful programs in: 1) basic, applied or developmental research; 2) clinical applications and/or trials of various modes of therapy; 3) hemoglobin diagnosis, utilizing standardized techniques; and 4) education and counseling related to sickle cell disease. Each center must be affiliated with an established medical institution with facilities available for clinical investigations in sickle cell disease.

I. MECHANISM OF SUPPORT

Although the support mechanism will be the grant-in-aid, it will differ from the traditional research project grant in the goal orientation of the center and in the degree of direct participation by the Institute's program staff. The grant may provide funds to support core resources, fundamental and/or applied research, clinical applications, demonstration

This program is described in the Catalog of Federal Domestic Assistance number 13.839, Blood Diseases and Resources Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (P.L. 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

projects to improve community services and certain activities in education, testing and counseling. Obviously, the proportional balance between research and demonstration will vary from center to center and will depend on local circumstances.

## II. COMMITMENT OF THE GRANTEE ORGANIZATION AND CENTER STAFF

It is expected that each center will have the flexibility to plan, direct and execute its own program reflecting local interests and resources. However, each Center must also be responsive to the identified objectives of the Sickle Cell Disease Program as to both program content and direction. The Center will be reviewed continuously by the staff of the Center and periodically by the staff of the Sickle Cell Disease Branch. This will involve assessment and evaluation of progress and plans of project activities.

Facilities and resources must be available for all of the primary needs of the center. Funds for new construction cannot be provided. Therefore, the facilities must be usable for the purposes of the Center with either no, or only very minor alteration and renovation. The applicant organization must be willing to make a long-term commitment of these physical resources to the Center. Both the physical facilities and the human resources of a Center should serve to foster effective interaction among individuals representing many different disciplines.

Staff participating in the Center must also be willing to make a long-term commitment. In the administration of the Center, the Director should be able to provide leadership for all aspects of the program. He will be responsible for the organization and operation of the Center, for communication with the National Institutes of Health on substantive and operational matters, and for effective exchange of information with other Centers.

## III. GOALS AND SCOPE

The following broad goals of the National Sickle Cell Disease Program are directly applicable to the Center concept:

1. To foster research and development at both the fundamental and clinical levels. Investigations may be pursued in a wide variety of areas. However, studies of the clinical course ("natural history") of sickle cell disease are currently being conducted in the five-year multi-institutional Collaborative Cooperative Study of Sickle Cell Disease and therefore, are not appropriate to this Comprehensive Sickle Cell Center competition.
2. To initiate and expand community education programs. Community education should be provided in various settings which comprise the total community environment and personnel appropriate to those settings should be utilized. There should be educational programs for individual patients with sickle cell disease.
3. To educate medical and allied health professionals as well as community leaders about the problems of sickle cell disease and increase the

supply of health manpower trained to deal with these problems. The specific goals of educational programs, the methodologies to be employed and the ways in which the educational programs will be evaluated should be included in all program plans.

4. To provide genetic counseling based on accurate diagnosis of hemoglobin genotypes. All counseling should be non-directive. Adequate information should be provided counselees to enable them to make informed decisions about health-related issues affecting their lives. Criteria and qualifications for selecting counseling personnel must be described. Training approaches and evaluative methodology for developing and maintaining competent personnel in this area should be specified.
5. To develop improved clinical care of patients with sickle cell disease.

Comprehensive Sickle Cell Centers should be in a unique position to make major contributions toward achievement of these aims because of their potential for multidisciplinary programs, including research at both the fundamental and clinical levels. While each Center should be responsive in some measure to all the above goals, the major emphasis of the Center will depend upon the interests and areas of expertise of its investigators as well as on the physical and population resources available.

Personnel needs to meet the demands of various segments of the program must be justified. Procedures for evaluation of projects in each program component must be fully explained in the application. Development of training protocols for genetic counselors and educational assistants, social workers, outreach and community aides must be clearly stated as indeed must the methodology for documentation and analysis of the effectiveness of such programs.

#### IV. REVIEW PROCEDURES AND CRITERIA

The applications for Comprehensive Centers solicited in this announcement will be evaluated in national competition with each other. The technical review, conducted by the Division of Extramural Affairs, National Heart, Lung, and Blood Institute, with a panel of expert consultants, may involve a site visit. Final review will be by the National Heart, Lung, and Blood Advisory Council. Criteria for evaluation of the proposal will include:

- a. the importance of the Center's goals to the specialized problems of sickle cell disease
- b. the significance of the components of the program in achieving the overall goals of the Center
- c. the competence of the senior personnel in their respective fields
- d. the merit of all projects proposed
- e. the environment in which the program will be conducted

- f. the arrangements for internal quality control of ongoing work, continuity of the program, and day-by-day administrative management
- g. arrangements for providing fiscal management and allocation of the awarded funds
- h. the requested budget in relation to the proposed Center program
- i. integration of the various projects in the broad multi-disciplinary effort, particularly integration of the research and development effort with the community service activities
- j. the commitment of the grantee organization to the Center goals and the goals of the Sickle Cell Disease Program
- k. willingness to work cooperatively with other Centers and the NHLBI Sickle Cell Disease Program.

V. METHOD OF APPLYING

Proposals for Comprehensive Centers should be submitted on form PHS 398. These forms are available at most institutional business offices or from the Division of Research Grants, NIH. If questions arise that do not seem to be adequately answered in this announcement, or if a complete program announcement and instructions for application preparation are desired, inquiries may be directed to:

George B. Riley, Ph.D.  
Sickle Cell Disease Branch  
Division of Blood Diseases and Resources  
National Heart, Lung, and Blood Institute  
Room 504, Federal Building  
National Institutes of Health  
Bethesda, Maryland 20205

Telephone: (301) 496-6931

VI. TIMETABLE

- 1. Receipt of Letter of Intent.....January 1, 1981
- 2. Receipt of Application.....April 1, 1981
- 3. Notice of Review Action.....March 1, 1982
- 4. Award of Grants to Successful Applicants.....April 1, 1983