Guidelines
Centers
of
Research Translation

National Institute of Arthritis and Musculoskeletal and Skin Diseases

National Institutes of Health

Department of Health and Human Services

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GUIDELINES FOR THE CENTERS OF RESEARCH TRANSLATION (CORT)

I. THE NIAMS CENTERS OF RESEARCH TRANSLATION PROGRAM

I.A. Introduction

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) leads the federal effort for the conduct and support of research into the causes, treatment and prevention of arthritis and musculoskeletal and skin diseases, the training of basic and clinical scientists to carry out this research, and the dissemination of information on research progress in these diseases.

In fulfilling its mission to support research and research training, NIAMS employs a number of support mechanisms. These include various types of research projects, program projects, and career development programs; institutional training grants and individual training fellowships; and a number of center grant mechanisms. The center grants are interrelated to and interdependent upon all of the other support mechanisms.

The following guidelines provide information about the Centers of Research Translation program, suggestions for preparation of an applications and criteria for review.

I.B. Overview of the Centers of Research Translation (CORT) Program

Two major features of the CORT program include: 1) the overarching aim of disease-specific research translation, and 2) the inclusion of resources and an administrative structure to facilitate research translation. The expectation for a CORT is that the projects will be translational in nature, directed at elucidating the relevance of basic research to a human disease.

Translational research is applied and clinical scientific research that is directed towards testing the validity and limits of applicability of knowledge derived from basic science and engineering to the understanding of human diseases and health. It could be research involving living human subjects (i.e., clinical) but it might also be non-clinical involving the study of human genes, tissues, specimens, or cells. Thus, although it is directed towards generation of knowledge about humans, it could be non-clinical or clinical research. It could be knowledge useful to persons (individuals, families, populations) affected by or at risk for specific diseases.

Overall, the CORT should encompass a multidisciplinary approach to a disease-targeted theme with individual projects providing synergy for the theme. For purposes of the projects within a CORT, translation is NOT to be interpreted as requiring one project to depend on another. That

is, the outcomes of a clinical research project would not be dependent on the outcome of a basic research project. Rather, the projects should demonstrate a synergy in which the outcomes of each project inform the others.

- A CORT will be focused on one of the diseases in the NIAMS mission. The focus cannot be generic, e.g., autoimmune diseases, musculoskeletal disorders, or skin diseases. The diseases within the NIAMS mission may be found at: http://www.niams.nih.gov/rtac/funding/faq.htm.

- There must be an existing research base supporting the projects.

- The projects must represent a multidisciplinary approach to the theme. Principal investigators should be drawn from different research disciplines, and may be based in different departments, divisions and/or institutions.

- There must be a minimum of three highly meritorious projects with at least one basic and one clinical project. Overall the CORT concept is dual, embracing both the translation of new scientific information to clinical application and of clinical findings to new research.

    - Clinical research. NIH defines human clinical research as: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies. (2) Epidemiologic and behavioral studies. (3) Outcomes research and health services research. Note: Studies falling under Exemption 4 for human subjects research are not considered clinical research by this definition.

- Each CORT will have an advisory group that includes scientific members who can facilitate the translational process and lay members who can bring the patient perspective about the disease to the group. The advisory group will have a dual role. One role will be to provide scientific and lay oversight of the ongoing progress of the CORT projects. A second role will be to review and recommend pilot and feasibility project applications for submission to NIAMS.

I.C. Structure of a CORT

The minimal structure for a CORT will be:

- At least three highly meritorious translational research projects with at least one basic and one clinical project;
- An Administrative Core with an advisory group that includes scientific and lay members.

- The CORT Director should also be the principal investigator of one of the research projects.

One or more research cores may also be proposed if they are critical to at least two of the projects and will enhance the quality of the research.

Once a CORT is established, pilot and feasibility projects to develop new directions in the translational theme may be submitted to NIAMS as administrative supplements. Pilot and feasibility projects will be solicited once per year during the second and third year of CORT funding. Up to three projects may be submitted annually. The scientific review of these individual pilot and feasibility project applications will directed by the CORT advisory group. The role of NIAMS will be to determine funding based on funds available and the institute's portfolio. Pilot and feasibility projects are optional.

II. APPLICATION AND REVIEW PROCESS

II.A. Preapplication Process and Letter of Intent

Applications are solicited by Requests for Applications published in the NIH Guide to Grants and Contracts. See the NIAMS website for current RFAs:
http://www.niams.nih.gov/rtac/funding/grants/rfalist.htm

Individuals with a potential interest in applying for a CORT grant are strongly encouraged to talk with a NIAMS program director to review their concept for a CORT application. The NIAMS program directors and the scientific areas of their portfolios may be found at http://www.niams.nih.gov/rtac/index.htm

Consultation between NIAMS staff and potential applicants prior to submission of the formal application may be useful. Applicants should not construe advice given by the NIAMS staff as assurance of favorable review. The staff will not evaluate or discuss the merit of the scientific aspects of the proposal.

The letter of intent and any inquiries about the overall program, should be directed to:

Madeline Turkeltaub, CRNP, Ph.D., FAAN
Deputy Director, Extramural Program
NIAMS/NIH
6701 Democracy Blvd., Suite 800 – MSC 4872
Bethesda, MD 20892-4872
[Bethesda, MD 20817 (for express/courier service)]
Phone: (301) 594-2463
FAX: (301) 402-7478

For fiscal and administrative matters, contact:

Melinda Nelson
Grants Management Officer
NIAMS/NIH
6701 Democracy Blvd., Suite 800 – MSC 4872
Bethesda, MD 20892-4872
[Bethesda, MD 20817 (for express/courier service)]
Telephone: (301) 594-3535
FAX: (301) 480-5450

II.B. Application Procedure

The research Grant Application Form PHS 398 is to be used in applying for these centers. These forms are available at most institutional offices of sponsored research and from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910 Bethesda, MD 20892-7910, telephone (301) 435-0714, E-mail: grantsinfo@nih.gov or from the Internet Web site at: http://grants.nih.gov/grants/forms.htm

Each project and each core included in the CORT application should be written as an individual project using form PHS 398. Page limitations will apply to the individual projects. It is desirable for CORT applications to be arranged in a specified format. A detailed Table of Contents is strongly suggested (see Exhibit I). This not only makes it easier for reviewers to use, but it can also serve as a checklist for the applicant institution in preparing the application. The arrangement of materials should follow both the instructions in the form PHS 398 application kit and the more specific instructions detailed in Section IV of these guidelines.

Receipt dates for CORT applications are announced in the Request for Applications. *For applications submitted in response to RFAs, the application must ARRIVE AT NIH on or before the receipt date.*

The RFA label available in the application package must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review.

The original and three (3) signed, exact photocopies of the application should be sent to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040 - MSC 7710
Bethesda MD 20892-7710
[Bethesda, MD 20817 (for express/courier service)]

In addition to mailing the application to the Center for Scientific Review send two (2) copies of the application and ALL 5 copies of any appendix material to:

Madeline Turkeltaub, CRNP, Ph.D., FAAN
Deputy Director, Extramural Program
NIAMS/NIH
6701 Democracy Blvd., Suite 800 – MSC 4872
Bethesda, MD 20892-4872
[Bethesda, MD 20817 (for express/courier service)]
Phone: (301) 594-2463
FAX: (301) 480-4543

All appendix material must be clearly marked with the name of Center Director and the appropriate project or core. Separate copies of appendix material should be supplied for each core or project to which it is applicable (See Section IV.C.).

II.C. Review Process

Applications submitted for CORT grants will first be screened for completeness by the Center for Scientific Review and for responsiveness by NIAMS staff. Applications which are complete and responsive will be evaluated for scientific merit by a group of expert consultants convened by the Review Branch of the NIAMS. Each application should be complete upon submission. Site visits are not anticipated. A second level of review will be performed by the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council.

II.D. Center Evaluation Procedure

Since the NIAMS is interested in funding only the most highly meritorious research, individual components of lesser quality may not be funded, even if recommended, under the "umbrella" of the Center grant mechanism. Each project and core (including the administrative unit) will be individually reviewed for scientific merit and assigned a rating by committee consensus. Merit ratings will also be voted for the center elements: qualifications of the center leadership, the research base, the institutional environment and resources. To be funded, there must be at least three highly meritorious translational projects, including one basic and one clinical research project.

After the review of the individual components of the application, an application may be judged "non-competitive" and not scored, or may be discussed and assigned an overall priority score. This score will reflect not only the individual quality of the projects, cores, and administration, but also how the proposed CORT will bring together all these elements in a workable unit. The overall score may be higher or lower than the "average" of the descriptors based on the assessment of whether the "whole is greater than the sum of its parts." (See Section III.J.)

III. PRESENTATION OF THE PROPOSED CENTER

This section of the guidelines describes the required and optional components of the proposed CORT and the review criteria to be applied. The suggested content order for the overall application will be covered in Section IV. Note that these applications will be reviewed by a committee that will have three or more applications to review; therefore, it is very helpful for investigators to use cross-references in these center applications. A detailed Table of Contents is especially invaluable in providing a key for cross-references, e.g., *see Section I.A.2. for more details.* Exhibit I is an example of a detailed Table of Contents.

Note that NIH has policies for the inclusion of women, minorities and children which **must** be addressed in **each** project proposal and in **each** core, even if only to indicate why a full discussion is not applicable. The reviewers will be instructed to address the adequacy of inclusion plans for the work proposed as part of the scientific and technical merit evaluation. These policies may be accessed at the following sites:
Women & Minorities: http://grants.nih.gov/grants/funding/women_min/women_min.htm
Children: http://www.nih.gov/grants/funding/children/children.htm

The NIH expects investigators supported by NIH funding to make their research data available to the scientific community for subsequent analysis based on a data sharing plan approved as part of the award; see the NIH Data Sharing Policy website at http://grants.nih.gov/grants/policy/data_sharing/. This requirement on data sharing is an extension to NIH policy regarding sharing research resources, which expects that recipients of NIH support will provide prompt and effective access to research tools. The data sharing plan for the center should be described in the Administrative Core.

III.A. Overview

Each application should have an OVERVIEW - a narrative section that serves as a synopsis of the key elements of the proposed Center of Research Translation, the qualifications of the Center Director, Associate Director and CORT advisory group, the research theme, research base, and the resources and environment for the Center. *This section is intended to be read by all reviewers, even if they are not assigned to projects within this application, so that each reviewer can get a comprehensive view of the proposed Center.*

An additional purpose of the Overview is to provide reviewers with a sense of how the Center will leverage its resources. A Center operates on two levels. The first level is to assemble

outstanding proposals and carry out the proposed research. The second level is to provide leadership at an institutional or broader level to promote quality research through the intellectual and material resources of the Center.

The Overview serves to introduce the proposed program, to identify the theme for the disease to be addressed in the proposed Center and to state the Center objectives. Describe the disciplines brought together for the proposed Center and explain the strategy for achieving the objectives of the overall program. It is important to emphasize the events that have led to the current application, and **especially to describe the anticipated unique opportunities for translational research within the proposed CORT**. Briefly describe each of the proposed projects, identifying whether it is basic or clinical, and how that project qualifies as translational research and addresses the translational theme of the Center. Briefly describe any research cores that are included in the application and how each core will assist each of the proposed projects.

III.B. Qualifications of the CORT Leadership

The emphasis in this section should be on the qualifications of the Center leaders. The administrative plans are presented in the Administrative Core (see Section III.G.)

The Director of the CORT, aided by an Associate Director and an advisory group, is expected to provide leadership to focus all research projects on translational aims relevant to the disease theme. Either the Center Director or Associate Director must be a clinical investigator who is responsible for the translation of basic research to clinical research to assure a mutually supportive interaction between scientists conducting basic research and those performing clinical investigation. The qualifications of the clinical investigator and the plan to promote patient based research should be described.

The advisory group should consist of 3 to 6 members and meet formally at least annually to review the scientific progress and to identify and review new opportunities for research translation. The members of the advisory group should include scientists, both from the parent and from other research institutions, and one or more lay members who can bring the patient perspective about the disease to the group. The advisory group will play a role in determining which applications for pilot and feasibility projects are submitted to NIAMS.

Describe the qualifications of the Center Director and Associate Director to lead the CORT. Describe the qualifications of each member of the advisory group and the rationale for including these individuals. Applicants are advised to include sufficient information to address the following review criteria:

Review Criteria for CORT leadership:

- Do the Director and Associate Director have the leadership and research qualifications to lead a Center? Does the leadership team (Director, Associate Director, and advisory group) have the collective expertise to assure focused development and implementation

of high quality and meaningful translational research projects?

- Is the management program proposed appropriate for soliciting, reviewing and prioritizing pilot and feasibility project applications for submission to NIAMS?

III.C. Research Base for the CORT

Describe the research base upon which the CORT builds, including descriptions of independently funded research projects so that reviewers can determine the extent and quality of research activities related to the proposed CORT. The descriptions should include: the principal investigator and other key research personnel, the project's objectives and progress toward them; the project's relevance to the NIAMS disease area, and up to 5 important publications that have resulted from this research in the past five years. In addition, it is helpful to include a table of the relevant research grants (see Exhibit II). Describe how members of this research base will interact with the proposed CORT. Applicants are advised to include sufficient information to address the following review criteria:

Review Criteria for Research Base:

- Is there a substantial productive and funded research base? Is the research base sufficiently broad to foster new multidisciplinary translational research?

III.D. Institutional Environment and Resources

Briefly describe the features of the institutional environment that are relevant to the effective implementation of the proposed program. As appropriate, describe available resources, such as clinical and laboratory facilities, participating and affiliated units, patient populations, geographic distribution of space and personnel, and consultative resources. Indicate if any of the proposed cores will utilize or expand cores already existing at the institution. What institutional commitments for space or other resources are there for the proposed CORT? Include any letters of support for the proposed Center by appropriate institutional officials.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. Details of the interactions of the CORT staff with the GCRC staff and research personnel may be provided in a statement describing the collaborative linkages being developed. A letter of agreement from the GCRC Program Director must be included with the application. Applicants are advised to include sufficient information to address the following review criteria:

Review Criteria for Institutional Environment and Resources:

- Is there evidence of a supportive institutional environment for the proposed CORT? Will the CORT add an important multidisciplinary element to the institutional environment? Does the proposed CORT utilize available resources well?

III.F. Program for Pilot and Feasibility Projects

It is envisioned that the synergy present in the research projects of the CORT will lead to new ideas and the need to test new hypotheses relevant to the translational theme of the CORT. The CORT advisory group will review such proposals and recommend which should be submitted to NIAMS for consideration. NIAMS will determine the priority for funding all submitted pilot and feasibility projects applications and make appropriate administrative supplemental awards to the CORTs.

The primary eligibility criteria for a CORT pilot and feasibility project are:

- The hypothesis to be tested arises from the CORT research and addresses the CORT theme;
- The hypothesis to be tested has the potential for developing ground-breaking technology or methodology that may lead to significant expansions of biomedical research horizons, precipitate a paradigm shift in research, or lead to substantial improvements in human health;
- The work proposed does not overlap with the aims of currently supported projects but should be integrated with the translational theme;
- The investigator should be clearly independent and have a faculty appointment; the investigator may be a new investigator or be well established;
- CORT pilot and feasibility projects may request up to $50,000 per year in direct costs for one or two years.

Pilot and feasibility projects will not be a part of the initial CORT application. Once each CORT is established, pilot and feasibility projects will be solicited once a year during the second and third year for funding in years three and four. Up to three projects may be submitted each time. Describe how the CORT, in consultation with the CORT advisory group, will solicit, review, and prioritize pilot and feasibility projects applications for submission to NIAMS.

The structure of a pilot and feasibility project application is described in Section VI.

Review Criterion for the Pilot and Feasibility Project Program:

- Is the management program proposed appropriate for soliciting, reviewing and prioritizing pilot and feasibility project applications for submission to NIAMS?

III.G. Administrative Core

The purpose of a CORT is to exploit translational opportunities for a disease targeted theme through a minimum of three research projects. The Administrative Core is responsible for the planning, development, coordination, and overall administration of the CORT. A key role of this unit is to foster productive interactions at the host institution through Center personnel and the CORT advisory group.

Leadership. The Center Director is responsible for the organization and operation of the Center. An Associate Director should be named who will be involved in the administrative and scientific aspects of the Center, and will serve as Acting Center Director in the absence of the Director. Either the Center Director or Associate Director must be a clinical investigator who is responsible for the translation of basic research to clinical research to assure a mutually supportive interaction between scientists conducting basic research and those performing clinical investigation. The qualifications of the clinical investigator and the plan to promote patient based research should be described.

Lines of authority. Describe in detail, and by diagram if appropriate, the chain of responsibility for decision-making and administration. Include to whom the Center Director reports and the administrative structure as it relates to the investigators responsible for the research projects and core units.

CORT Advisory Group. A CORT advisory group representing scientific expertise and lay persons relevant to the disease theme should be identified. Their collective expertise should reflect key issues addressed in the disease theme. (Their qualifications are to be presented elsewhere in the application in a section on Qualifications of the Center Leadership - see Section III.B.) Describe the structure for using the advisory group to provide scientific oversight for all active CORT research studies. Describe how lay input from the advisory group will be incorporated.

Enrichment Program. The Administrative Core may include limited funds for program enrichment (i.e., seminars, visiting scientists, etc). Plans for an enrichment program should be included in the application and in the budget of the Administrative Core.

Data Sharing Plan. The NIH expects investigators supported by NIH funding to make their research data available to the scientific community for subsequent analysis based on a data sharing plan approved as part of the award; see the NIH Data Sharing Policy website at http://grants.nih.gov/grants/policy/data_sharing/. A data sharing plan for the research data from the CORT should be included in the Administrative Core.

Time Commitment. The CORT director is expected to make a commitment of at least 15 percent effort to the overall administration of the program plus 20 percent effort as a principal investigator of a CORT project. The CORT Associate Director is expected to commit at least 10% effort to administration. Administrative support personnel may be budgeted in at no more

than one full time equivalent (FTE) which may be divided among one or more positions. This FTE must be fully justified.

CORT Travel. Applications should include $2,500 yearly travel expenses in the Administrative Core to pay for two individuals to attend one 2 day meeting related to the CORT program.

Review Criteria for the Administrative Core:

- Is there scientific and administrative leadership, commitment and ability, and adequate time commitment of the CORT Director and Associate Director for the effective management of the CORT? Is either the Center Director or Associate Director a clinical investigator who will be responsible for the translation of basic research to clinical research?

- Is the management proposed appropriate for scientific administration as well as fiscal administration, procurement, property and personnel management, planning, budgeting, etc.?

- Is there a plan for the establishment and maintenance of internal communication and cooperation among the CORT investigators? Are there plans for effective use of the CORT advisory group?

- Is the management program proposed appropriate for soliciting, reviewing and prioritizing pilot and feasibility project applications for submission to NIAMS?

III.H. Projects

Using Form PHS 398, name and number each project sequentially so that it can be readily distinguished from other projects in the program. Each research project should be clearly identified by the same title as that provided in the Table of Contents. The project should begin with the abstract and budget pages and should follow the instructions for Form PHS 398. Describe each section in the same detail and format as required for a regular research grant application so that the scientific merit can be judged on the basis of the written proposal. Adhere to the page restrictions indicated in the instructions for Form PHS 398.

For each project begin Section B, Background and Significance, with a paragraph that clearly states how that project contributes to the theme of the CORT as a whole, and the translational nature of each project. If it is a clinical research project, describe the rationale of including it as a clinical research project within the theme of the CORT.

The budget for each research project should reflect the instructions for Form PHS 398. A detailed budget is required for the first year; budget estimates are required for all subsequent years of support. Explicit and detailed budget justifications must be included for all years.

Budget pages must be labeled so that they can be readily associated with the particular projects to which they apply.

The project principal investigator should devote at least 20 percent effort to the research.

Each project using human subjects must include a detailed plan for protection of human subjects and inclusion of women, minorities, and children as described in the PHS 398 instructions.

If the proposed project is a clinical trial, a data safety and monitoring plan must be included in the project proposal. The following activities should be included in a monitoring plan:

- Overview of the research protocol with emphasis on data integrity and patient safety issues.
- Monitoring of adverse effects and determining stopping rules for the trial.
- Protecting the confidentiality of the trial data and the results of monitoring.
- Twice yearly review of recruitment and adverse events by a Safety Officer or a Data Safety and Monitoring Board (DSMB).

Note that the NIAMS will determine at the time of award whether a Safety Officer or a DSMB will be appointed for each clinical trial. NIAMS will appoint the Safety Officer or DSMB members in consultation with the principal investigator. The Safety Officer or DSMB members must not be affiliated with the host institution. NIAMS will provide logistical support when a DSMB is required and will provide any travel funds or consultant fees for DSMB members.

If the proposed project will use vertebrate animals, a complete description of their use and care must be included as found in the instructions for the PHS 398 application.

Review Criteria for projects:

- Significance
  Does this study address an important problem? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field? Does this study clearly address the theme of the CORT? Will the outcomes inform the other projects in the CORT? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive the field? Does the project advance the theme of the CORT and inform the other projects?

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

- Innovation
  Is the project original and innovative? For example: Does the project challenge existing paradigms or clinical practice, and address an innovative hypothesis or critical barrier to

progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

- Investigators
  Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?

- Environment
  Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies take advantage of unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

III.I. Research Core(s)

Each core must be written using Grant Application Form PHS 398. Name and assign a letter designation to each unit. An abstract must be written for each core.

A core may be a unit designed just for the CORT projects or may be an institutional core unit. However, funds may only be requested for CORT use, and the core must serve a minimum of two projects within the CORT, with no project dominating use of the core.

The core principal investigator should devote at least 15 percent effort to the core.

Describe the core unit and the various services it would provide. The justification for the core must include the value added by having services provided through the core rather than within the individual projects.

Describe the personnel, facilities, management and any special arrangements such as cooperation with other established cores. The techniques to be used and the quality control procedures should be documented and justified. Indicate which core services each project would utilize.

It is helpful in presenting the scope of the core to prepare a table indicating the research projects each core unit will serve and the estimated proportion of the cost (in dollars) of the core unit associated with each research project.

Each core using human subjects must include a detailed plan for protection of human subjects and inclusion of women, minorities, and children.

If the core proposes to use vertebrate animals, a detailed description of animal care and use must be included (see the PHS 398 instructions).

Review Criteria for research cores:

- Will the core have utility to at least two of the CORT projects?
- Is the quality of services high? Are there procedures for quality control? Is the core cost effective?
- Do the services offered best fit within a core structure? If this is an add on to a preexisting core, what is the benefit to the CORT over direct purchase of services from the existing core?
- Are the personnel appropriate?
- Are the facilities and equipment adequate? Is there institutional commitment to the core?

III.J. Review Criteria for the Overall Application

After the review of the individual components of the application, an overall priority score will be assigned to the application. This score will reflect not only the individual quality of the projects, cores, and administration, but also how the proposed CORT will bring together all these elements in a workable unit. The overall score may be higher or lower than the "average" of the descriptors based on the assessment of whether the "whole is greater than the sum of its parts:"

- The scientific excellence of the Center's research base as well as the relevance and interrelation of these separately-funded research projects to the goals of the Center and the likelihood for meaningful collaboration among Center investigators. The application must convey how the proposed Center will enhance significantly the established research base of the host institution.
- The overall environment for a Center. This includes the institutional commitment to the program, including lines of accountability regarding management of the Center, and the institution's partnership with the Center, and the institutional commitment to individuals responsible for conducting essential Center functions. This also includes the academic environment and resources in which the activities will be conducted, including the availability of space, equipment, facilities, and the potential for interaction with scientists from other departments and schools to enhance a multidisciplinary approach.
- The overall priority score assigned to the application will also reflect how well the policies regarding (a) the inclusion of women, minorities and children in study populations, and (b) the protection of human subjects from research risks.

IV. SUGGESTED CONTENT ORDER FOR APPLICATION

IV.A. General Information

It is desirable for CORT applications to be arranged in a specified format. This not only makes it easier for NIAMS staff and reviewers to find all the center components to be reviewed, but it can also serve as a checklist for the applicant institution in preparing the application.

Form PHS 398 is required for all applications. (See II.B. for how to obtain this form). Each budget unit (project or core) should be written in the style and within the page limitation described in the PHS 398 instruction kit. To aid in the review of these applications, the applicant should assemble the component units following the format described below. Applicants may also consult with NIAMS staff concerning the technical aspects of preparing the application.

IV.B. Content Order for the CORT Application

IV.B.1. Face Page of Form PHS 398.

Complete all items on the face page as directed. In the title block, item 1, put "NIAMS: CORT." Mark item 2 "yes" and write in the RFA code as listed in the NIH Guide to Grants and Contracts and "NIAMS: CORT" for the title.

IV.B.2 Page 2, Description

Describe the goals and objectives of the CORT overall and of the component projects and cores. Do not exceed the space allowed. Key personnel are those doctoral level investigators with a percent effort on the grant: Director and Associate Director, investigators on the projects and cores, and consultants.

IV.B.3. Table of Contents

Discard this page from Form PHS 398 and write a Table of Contents appropriate for the CORT grant application. See Exhibit I for a suggested format. The Table of Contents is paginated to follow the list of Key Personnel. **Do not use letters (e.g., 4a, 4b, 4c, etc.)** The Table of Contents should list all components. Each project and core should be listed by the title and Principal Investigator. Specifically list the locations of the checklist and the various requested supporting documents, e.g., animal and human subject assurances.

IV.B.4. Budgets

For budget pages, see Exhibits III, IV, and V. Use form pages 4 and 5 in PHS Form 398 for all budgets. Justify and document all costs for current and future years throughout.

To provide budget information in a format that is clear to reviewers and therefore provides the most positive review possible, presentation of a consolidated budget for the first 12 months in a tabular form such as the sample shown as Exhibit III is suggested. The overall Center budget, "Summary Center Budget," is presented first using form PHS 398 page 4 entitled "Detailed

Budget for First 12-Month Period" (see Exhibit IV). Note that no details need be given for the individual categories. Page 5 of form PHS 398, "Budget Estimates for All Years of Support Requested Direct Costs Only," should then follow a composite like that in Exhibit IV, summarizing all individual budgets (see suggested format in Exhibit V). For the purpose of establishing future year budget requests, the applicant should use cost escalations as specified in the RFA or less. However, **the direct cost budget cannot exceed $1,000,000 in any year**. For purposes of establishing the $1,000,000 direct cost limit, the F&A (indirect) costs of subcontracts will not be counted. (See NOT OD-04-040: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-040.html)

Both first 12 month and 5 year individual budgets should be included *in the sections for each project and core.* Details and justifications for all budget items must be part of the individual budgets.

- This grant mechanism is not intended for the acquisition of equipment. Costly items of equipment should be funded through other sources.
- A separate, detailed budget for each project subcontracted to a consortium institution is required as well as a form PHS 398 face page signed by the principal investigator and appropriate officials in the consortium institution.
- It is not the purpose of a CORT grant to provide funding for alterations or renovations.
- Support for research training positions is not to be included.
- The production of audiovisual material with CORT grant funding is not appropriate.

IV.B.5. Biographical Sketches

Biographical sketches are required for all doctoral level personnel who are listed with a percent effort (including consultants) in the CORT application. The forms found in Form PHS 398 should be used. Begin with the CORT Director and place the remaining individual sketches in alphabetical order after the budget pages. These pages should not be duplicated in the individual component projects and cores.

IV.B.6. Assurance Documentation

See sample suggested table, Exhibit VI. In addition to the assurance pages, a master table listing the status of vertebrate animals and human subject approval dates and the human subjects education requirement certification will aid in the timely processing of your application.

IV.B.7. Narrative Sections

See Section III for content information. Present in the following order using continuation pages:

- **Overview**
- **Qualifications of the Center Leadership**
- **Research Base for the CORT**
- **Institutional Environment and Resources**
- **Pilot and Feasibility Project Program**

IV.B.8. Budgeted Components

See Section III. for content information. Present each individual project and core in the following order using the PHS 398 forms.

- **Administrative Core**
- **Translational Projects (minimum of 3)**
- **Research Cores (optional)**

Each component should be written as a separate unit following these guidelines and the instructions accompanying form PHS 398. It is important that each component include a section on vertebrate animals and on human subjects, gender and minority inclusion, and inclusion of children as participants in research involving human subjects, even if to indicate that a full discussion is not applicable. An individual target enrollment table must be included with each project using human subjects. Cores may cross reference detailed presentations to projects and vice versa as appropriate to avoid lengthy repetitions of complex arrangements.

- A cover page for an individual component is needed only when that component will be administered through a subcontract to another institution. Facilities and administrative (indirect) costs from these subcontracts do not count against the $1,000,000 cap for direct costs for a CORT.

- An abstract and key personnel page must be included for each component.

- A detailed budget for the initial budget period and budget for the entire proposed period of support [pages 4 and 5 of form PHS 398] must be included with each component. The budget justification should be thorough. Do not assume that any item or percent effort is obvious. Note that the following percent efforts are expected: CORT Director: 15% for the Administrative Core, 20% as project principal investigator; Associate Director: 10% for the Administrative Core; 20% as project principal investigator: Other Core Directors: 15%.

- The biographical sketches are put centrally in one location (see IV. B.) and should not be duplicated in the individual component.

- A resources page should be included for each component.

- The checklist page needs to be included with each institutional face page.

IV.C. Appendices

See the instructions in the PHS 398 booklet for appropriate appendix materials.

Following these suggestions will insure that correct appendix material can be sent to the appropriate reviewers:

- Each piece should be marked with (1) the name of the CORT Director - not the name of the component PI and (2) a **single** component of the application to which it pertains - CORT Leadership, Research Base, Resources and Environment, Administrative Core, or individual cores and projects.

- The marked materials should be grouped by the identified components. Thus, all five copies of appendices pertaining to a given project or component should be grouped together.

- The five sets of all appendix material, and a CD including all appendices, should be sent directly to the NIAMS and **NOT** to the Center for Scientific Review:

Madeline Turkeltaub, CRNP, Ph.D., FAAN
Deputy Director, Extramural Program
NIAMS/NIH
6701 Democracy Blvd., Suite 800 – MSC 4872
Bethesda, MD 20892-4872
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Phone: (301) 594-2463
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V. NONCOMPETING APPLICATIONS: ANNUAL REPORTING REQUIREMENTS

Annual progress reports, submitted as part of the noncompeting continuation application, are due two months before the anniversary date of the award. These reports are used by the National Institute of Arthritis and Musculoskeletal and Skin Diseases to review the Center and its progress. They serve to verify in detail the achievement of the objectives outlined in the initial application and award and are an important source of material for program staff in preparing reports, planning programs, and communicating scientific accomplishments.

The application for continuation of a PHS Grant, PHS Form 2590, is used to file the annual report. In addition, an overall progress report containing the following information should be included:

- A summary (equivalent to no more than four single space typewritten pages) of the goals and significant activities of the CORT. This summary should be prepared for a general audience. Honors and/or promotions of professional personnel should be mentioned.

- A discussion of the effectiveness of the CORT grant in furthering the goals of the CORT program. This should include a summary of the specific accomplishments that can be attributed to the CORT grant, e.g., new research funding, changes in curricula, or organizational improvements within the institution and in the community.

- An itemization of collaborative efforts the CORT established.

- A list of publications relevant to CORT funding should be provided.

- A discussion of problems that impede accomplishment of the stated goals in the administration of the CORT grant and plans to overcome them.

- The administrative component report should include a list of administrative meetings held, evaluations from advisory groups, speakers or symposia sponsored. These may be included as appendix material.

- A table listing the assurance dates for IACUC, IRB and certifications education for the protection of human research participants for key personnel for all CORT funded projects is optional, but will assist the timely processing of the award. (See Exhibit VI). The notice describing the requirement for education for the protection of human subject participants may be found at http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

- A detailed summary of each CORT funded component (including the Administrative Core) and project, including the title, principal investigator and key personnel, their percent effort, proposed budgets, description, progress, and evaluation. This progress report should include all CORT supported projects. It is especially important that the significance and ultimate utility of each project be discussed in the summary description and that this discussion be in terms understandable to an informed nonscientist.

- A budget page for the coming year for each component and project funded by the CORT.
- The timely review of the application will be facilitated by the inclusion of a composite budget for the entire CORT as illustrated in Exhibit IV.
- Other information that, from year to year, may be requested by the NIAMS staff.

The expanded progress report is in addition to, and does not replace, other management reports required by PHS policy.

VI. Guidelines for Pilot and Feasibility Projects

See Section III.F. for a discussion of the Pilot and Feasibility Project Program. Pilot and feasibility projects are NOT to be included in the CORT grant application.

Present each study separately using Form PHS 398. Follow the instructions and include:

(1) Face page, signed by the business office, and the description page, page 2;

(2) Budget with justifications (An individual application may request up to $50,000 direct costs and for no more than two years.);

(3) **Justification of eligibility: How does this project relate to the CORT theme? Where can the project lead?** This information should be included as part of the Background and Significance Section.

(4) Scientific proposal using form PHS 398 (including justification for core use if applicable); Note that items a - d of the Research Plan **(Specific Aims, Background and Significance, and Research Design and Methods) may not exceed a total of 15 pages.** This page limitation does not apply to subsections e – i; and

(5) Sections on Human Subjects, including the Inclusion of Women Minorities, and Children; Vertebrate Animals; Consultants/Collaborators; Consortium/Contractual Arrangements; and Literature Cited. If not applicable, mark them N/A.

Applicants are advised to include sufficient information to address the following review criteria:

Review Criteria for a Pilot and Feasibility Project:

Significance: Will the proposed work likely yield meaningful preliminary data leading to a research proposal?

Approach: Are the experimental approaches adequate?

Innovation: Is the research topic one that advances the translational theme and promotes innovative new research related to the CORT?

Investigator: Is the investigator qualified to carry out the work proposed?

Environment: Is the project appropriate to the CORT and its resources?

VII. GUIDELINES FOR SUPPLEMENTAL APPLICATIONS

Applications submitted for supplemental projects to an NIAMS CORT program must have prior approval of the NIAMS CORT Program Scientific/Research Contact. Applications submitted without prior approval will be withdrawn and returned to the applicant. Approval will be based upon the following:

- A component research project was recommended for less time than was the rest of the CORT in order to permit an early assessment of progress;

- A persuasive case can be made that an alternative, additional or expanded project is important for the CORT program AND the new total direct cost budget for the CORT will not exceed the budget cap.

Supplemental applications will undergo a competitive review by an Initial Review Group (IRG) convened by the NIAMS Review Branch. In general, applications should be submitted so that at least two years remain on the parent grant at the time of award of the supplement. Major factors to be considered in the evaluation of a supplemental application will include:

1. The relevance of the proposed research to the CORT concept outlined in these guidelines;

2. If a request for continuation, what findings have been developed that justify additional years;

3. Scientific merit of the proposed project, including significance, approach and innovation;

4. Competence of the investigators to accomplish the proposed research goals, their commitment, and the time they will devote to the research program;

5. How the CORT environment enhances the project;

6. Appropriateness of the budget for the proposed program; and

7. Appropriateness of plans to include children, women, and minorities in the study populations.

A supplemental project will be assigned a priority score based on its merit as an individual research project. The review will also comment on how the proposed project fits with the CORT program. Funding will be based on merit, program relevance and availability of funds.

EXHIBIT I SAMPLE TABLE OF CONTENTS

ABC University
Application for a Center of Research Translation
SAMPLE -- Table of Contents

Page #

2. **Table of Contents** .....
3. **Detailed Budget for Initial Budget Period** .....
4. **Budget for Entire Proposed Period of Support**
5. **Budgets** Pertaining to Consortium/Contractual arrangements .....
6. **Resources**
7. **Research Plan** .....
    a) **Specific Aims** .....
    b) **Background and Significance** .....
    c) **Preliminary Studies** .....
    d) **Research Design and Methods** .....
    e) **Human Subjects** .....
        (1) **Protection of Human Subjects** .....
        (2) **Inclusion of Women** .....
        (3) **Inclusion of Minorities** .....
        (4) **Inclusion of Children** .....
        (5) **Data Safety and Monitoring Plan** .....
        (6) **Target Enrollment Table** .....
    f) **Vertebrate Animals** .....
    g) **Literature Cited** .....
    h) **Consortium/Contractual Arrangements** .....
    i) **Letters of Support**

C. **Project 2: see above example**

D. **Project 3: see above example**

E. **Title Page: Research Core: Title; Principal Investigator, degree(s).**
1. **Abstract/Performance Site/Key Personnel** .....
2. **Table of Contents** .....
3. **Detailed Budget for Initial Budget Period** .....
4. **Budget for Proposed Period of Support** .....
5. **Budgets** Pertaining to Consortium/Contractual Arrangements. .....
6. **Resources** .....
7. **Research Plan** .....
    a) **Specific Aims** .....
    b) **Background and Significance** .....
    c) **Preliminary Studies** .....
    d) **Research Design and Methods** .....
    e) **Human Subjects** .....
        (1) **Protection of Human Subjects** .....
        (2) **Inclusion of Women** .....
        (3) **Inclusion of Minorities** .....
        (4) **Inclusion of Children** .....
        (5) **Data Safety and Monitoring Plan** .....
        (6) **Target Enrollment Table** .....
    f) **Vertebrate Animals** .....
    g) **Literature Cited** .....
    h) **Consortium/Contractual Arrangements** .....
    i) **Letters of Support** .....

EXHIBIT II GRANTS SUPPORTING THE RESEARCH BASE

SAMPLE OF SUGGESTED FORMAT

Supporting Organization & Grant Number	Key Personnel	Title	Project Period	Current Annual Amount
NIH 5 R01 ARnnnnn	Chen, Ching-mei (PI) Doe, John	New Therapeutic Agents for Autoimmune Disease	3/1/2004 – 2/28/2009	$467,000
			TOTAL:	

EXHIBIT III CONSOLIDATED BUDGET FOR 1ST YEAR OF REQUESTED SUPPORT

SAMPLE OF SUGGESTED FORMAT

BUDGET CATEGORY	Project 1	Project 2	Project 3	Admin Unit Core A	Core B	Core C	TOTAL
Personnel							
Consultant Costs							
Equipment							
Supplies							
Domestic Travel							
Foreign Travel							
Patient Care Costs							
Alteration and Renovation							
Contractual Costs							
Other Expenses							
Total Direct Costs							

EXHIBIT IV INITIAL BUDGET PERIOD

Principal Investigator/Program Director (Last, First, Middle):

DETAILED BUDGET FOR INITIAL BUDGET PERIOD DIRECT COSTS ONLY		FROM 7/1/2006	THROUGH 6/30/2007

PERSONNEL *(Applicant organization only)*		TYPE APPT. *(months)*	% EFFORT ON PROJ.	INST. BASE SALARY	DOLLAR AMOUNT REQUESTED *(omit cents)*		
NAME	ROLE ON PROJECT				SALARY REQUESTED	FRINGE BENEFITS	TOTAL
	Principal Investigator						
SUBTOTALS →					443,180	137,525	580,705

CONSULTANT COSTS		15,000
SUPPLIES		212,485
TRAVEL		6,500
PATIENT CARE COSTS	INPATIENT	
	OUTPATIENT	
ALTERATIONS AND RENOVATIONS *(Itemize by category)*		
OTHER EXPENSES *(Itemize by category)*		28,595
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		$ 843,285
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	156,715
	FACILITIES AND ADMINISTRATIVE COSTS	139,487
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)* →		$ 1,139,487

EXHIBIT V BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD

Principal Investigator/Program Director (Last, First, Middle):

BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS		INITIAL BUDGET PERIOD (from Form Page 4)	ADDITIONAL YEARS OF SUPPORT REQUESTED			
			2nd	3rd	4th	5th
PERSONNEL: *Salary and fringe benefits. Applicant organization only.*		580,705	580,705	580,705	580,705	580,705
CONSULTANT COSTS		15,000	15,000	15,000	15,000	15,000
EQUIPMENT						
SUPPLIES		212,485	212,485	212,485	212,485	212,485
TRAVEL		6,500	6,500	6,500	6,500	6,500
PATIENT CARE COSTS	INPATIENT					
	OUTPATIENT					
ALTERATIONS AND RENOVATIONS						
OTHER EXPENSES		28,595	28,595	28,595	28,595	28,595
SUBTOTAL DIRECT COSTS		843,285	843,285	843,285	843,285	843,285
CONSORTIUM/ CONTRACTUAL COSTS	DIRECT	156,715	156,715	156,715	156,715	156,715
	F&A	139,487	139,487	139,487	139,487	139,487
TOTAL DIRECT COSTS		1,139,487	1,139,487	1,139,487	1,139,487	1,139,487

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD *(Item 8a, Face Page)*	$ 5,697,435
SBIR/STTR Only Fee Requested	
SBIR/STTR Only: Total Fee Requested for Entire Proposed Project Period (Add Total Fee amount to "Total direct costs for entire proposed project period" above and Total F&A/indirect costs from Checklist Form Page, and enter these as "Costs Requested for Proposed Period of Support on Face Page, Item 8b.)	$

EXHIBIT VI APPROVAL DATES

SAMPLE OF SUGGESTED FORMAT
HUMAN SUBJECTS APPROVAL DATES
HUMAN SUBJECTS EDUCATION REQUIREMENT
ANIMAL SUBJECTS APPROVAL DATES

GENERAL:

1. Initial application: IRB approval and certification is not required with the submission or prior to review and may be listed as pending prior to the review. The certification of IACUC approval must be submitted with the application or within 60 days after the application receipt date.

2. Initial funding: Additional information may be required prior to funding. The NIH no longer requires IRB approval and certification prior to NIH review. This information will be required when a decision is made to fund the application. Certifications for the Human Subjects Education Requirement may be submitted at the time of application but are not required until a funding decision is made. If the Human Subjects Education Requirement certification is not included in the application, please mark "pending".

3. Yearly progress reports: This table should be updated and included with each yearly progress report. Human Subjects Education Requirement Certifications are needed only for investigators new to the grant. Mark "previously submitted" for continuing investigators.

SPECIFIC:

Please make a table for each Performance Site. If there is only one performance site, then only one table is needed. A certification letter must be attached for each project using Human Subjects. Each letter should include the registered IRB number from the Office of Human Research Protections.

Performance Site: University A

Principal Investigator	Project	IACUC Approval Date*	IRB Approval Date*	Human Subjects Education Requirement *
Dr. A	1			
Dr. B	2			
Dr. C	3			
Dr. E	5			
Dr. B	Core A			
Dr. D	Core B			

Performance Site: University B
Human Subjects assurance number:
Animal welfare assurance number.

Principal Investigator	Project	IACUC Approval Date*	IRB Approval Date*	Human Subjects Education Requirement*
Dr. X	1 (subproject)			
Dr. D	4			
Dr. Y	Core B (subproject)			

* Attach certification letter or mark NA if not applicable