ALZHEIMER’S DISEASE RESEARCH CENTERS

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PURPOSE OF THIS RFA

The National Institute on Aging (NIA) invites applications from qualified institutions for support of Alzheimer's Disease Research Centers (ADRCs). These are designed to support and conduct research on Alzheimer's disease (AD), and to serve as shared research resources that will facilitate research in AD and related disorders, distinguish them from the process of normal brain aging and mild cognitive impairment (MCI), and lead to better diagnostic and treatment strategies.

Both the Executive and Legislative Branches of the Federal Government have expressed concern about the enormity of the problem posed by this disease. Congressional concern about Alzheimer's disease has focused on funding for research on the causes, treatment, and prevention of the disease, and on the cost of care. In 1984, Congress directed the National Institutes of Health (NIH), and in particular the National Institute on Aging (NIA), to foster further research related to Alzheimer's disease. The NIA Alzheimer's Disease Centers (ADCs) program is authorized by the Public Health Service Act, Section 445, and includes seventeen Alzheimer's Disease Research Centers (ADRCs) and twelve Alzheimer's Disease Core Centers (ADCCs).

The Alzheimer's Centers provide a platform for training as well as the
stimulation of research related to clinical-pathological correlations in normal aging and neurodegenerative diseases, studies of many basic research questions on AD and related dementias and strategies for prevention and treatment.

RESEARCH OBJECTIVES

Alzheimer's disease is estimated to affect more than four million older people in the United States. Although it is occasionally identified in patients in their forties and fifties, it is most frequently associated with advancing age. It doubles in prevalence with every five years past the age of 65; thus, extending life by ten years quadruples the probability of the disease. Alzheimer's disease is the most frequent cause of institutionalization for long-term care. It destroys the active, productive life of its victims and devastates their families financially and emotionally. It has been estimated that the United States spends as much as 100 billion dollars/year for the direct and indirect costs of care for patients with Alzheimer's disease. With the rapidly increasing percentage of the population over the age of 65, the number of persons with AD will increase proportionately, as will the toll it takes.

The principal aim of the ADRCs should be to enhance the performance of innovative research on AD and related topics. Centers are now also requested to concentrate their attention to better defining normal aging, the transition from normal aging to mild cognitive impairment (MCI) to the earliest stages of dementia, whether AD itself or other dementias associated with aging. Clinical and pathological information about the earliest cognitive changes will make it possible to develop strategies to prevent the disease from developing or slow its progression. Attention should also be paid to mixed dementias and overlapping neurodegenerative syndromes that sometimes occur with AD.

In order to foster the range of science necessary to advance AD research, Centers are being given the opportunity to diversify their clinical populations for specific scientific purposes. Centers are expected to provide an environment and core resources which will enhance cutting-edge research by bringing together biomedical, behavioral, and clinical science investigators to study the etiology, pathogenesis, diagnosis, treatment, and prevention of AD, and to improve health care delivery. Centers should also foster the development of new lines of research and provide a rich training environment for fellows and junior faculty to acquire research skills and experience in interdisciplinary AD research. The Centers provide investigators and research groups with well-characterized patients and control subjects, family information, and brain tissue and biological specimens and should incorporate contemporary biochemical/molecular techniques and pursue research, when feasible, in genomics and proteomics. Centers are encouraged to develop in accordance with local talents, interests, and resources, but should also be responsive to national needs related to Alzheimer's disease.

Centers should work together with other Alzheimer research groups in collaborative research activities and cooperate with other Federal, State, and Local agency-supported Alzheimer's disease programs as well as the Alzheimer’s Association in furthering mutual goals. Centers should cooperate with other NIA Centers such as Pepper, Shock, and RCMAR Centers when possible, as well as with Udall Centers sponsored by National Institute of Neurological Diseases and Stroke (NINDS) as well as the National Alzheimer’s Coordinating Center (NACC). Because of increased emphasis on collaborative research across multiple Centers, and additional required data reporting, Centers are now mandated to have a Data Management Core. Potential applicants are encouraged to utilize the strengths of their particular institutions in preparing an application that will cover the spectrum of required activities. While
The main function of the ADRCs is to support cutting-edge research either directly or indirectly by providing well-characterized patients, patient and family information, and tissue and other biological samples from persons with AD and from age-matched control subjects for research projects. As research into the causes of AD has begun to address preclinical stages, Centers should now place more emphasis on the clinical and neuropathological changes that distinguish the initial stages of AD from normal aging and place less emphasis on late stage AD. In addition, since several other of the neurodegenerative diseases (such as vascular dementia, Parkinson’s disease, Lewy body disease and frontotemporal dementia) have features that overlap or coexist with AD, ADRCs should organize the clinical cores to collect diagnostic information that allows differentiation among the various diseases while documenting features in common. To this end, applicants must agree to collect an expanded standard clinical data set that will be common to all Centers and be transmitted to the National Alzheimer’s Coordinating Center (NACC). Core resources from the centers should be used for research projects and pilot projects funded by the Center itself as well as for projects funded by NIH and other Federal agency grant mechanisms and by non-federal and private organizations.

ADRCs are required to include administrative, data management, clinical, and education cores. Another required function is neuropathological diagnosis that can be accomplished either by establishing a core or by subcontracting this function to other Centers or local organizations that have the capacity to carry out this function. This RFA reinstates the need to have an Education Core within each ADRC to underscore the importance given by NIA to education, information transfer, and subject recruitment. Other cores can be proposed if they contribute to the overall mission of the Center, are scientifically justified, support projects funded by the Center or by other mechanisms, and fit within the budget guidelines for the cores. ADRC applications will include, in addition, three research projects with a duration of up to five years (equivalent to small R01 grants) at least one of which should depend on clinical or neuropathology core resources at the home Center or another Center. The number of research projects funded and their duration will depend upon scientific quality. Funding for smaller ($35,000/year) one year pilot grants should also be requested.

The ADRCs provide a mechanism for integrating, coordinating, fostering and developing the interdisciplinary cooperation of a group of established investigators conducting programs of research on Alzheimer’s disease and related dementing disorders of older people. They provide financial, intellectual, patient, and biological specimen resources to support cooperative interactions among scientists in the local Center, other Alzheimer’s Centers and the research community at large. A prime objective of the Center Grant is to provide an environment that will strengthen research on AD and related disorders at the institution, increase productivity, and generate new ideas through formal interdisciplinary collaborative efforts both locally and nationally. The central focus may be clinical - pathological research, basic research or a combination. Applicants are strongly encouraged to include efforts to address the needs of, and research on, ethnically diverse populations.

The Center Grant may incorporate ancillary activities such as longitudinal studies and prolonged patient care necessary to support the primary research effort. The spectrum of activities should comprise a multi-disciplinary approach to the problem of Alzheimer’s disease. An important role of Centers is to perform collaborative
studies on particular research topics and to serve as a regional or national resource for special purpose research. Currently many of the Centers are active participants in NIA multi-disciplinary/multi-Center studies such as the initiative on the genetics of late onset AD and are contributing subjects and blood samples for multiplex family projects. All Centers are required to be linked with the NACC and the network of Centers linked to NACC is being used to standardize clinical and pathological diagnostic procedures, to pool patient information more effectively and to study unique aspects and subtypes of this very complex and heterogeneous disease process.

MECHANISM OF SUPPORT

This RFA will use the NIH P50 award mechanism. As an applicant you will be solely responsible for planning, directing, and executing the proposed project. This RFA is a one-time solicitation. New proposals or competing-continuation applications for ADRCs will only be accepted by solicitation under future RFAs. The anticipated award date is April 1, 2005.

This RFA uses the non-modular budgeting format (see http://grants.nih.gov/grants/funding/modular/modular.htm). Follow the instructions for non-modular budget research grant applications. This program does not require cost sharing as defined in the current NIH Grants Policy Statement at http://grants.nih.gov/grants/policy/nihgps_2001/part_i_1.htm.

FUNDS AVAILABLE

The NIA intends to commit approximately $16 million in fiscal year 2005 to fund eight new and/or competing renewal ADRC grants in response to this RFA. An applicant should request a project period of five years. The total costs (direct + F&A) requested for new applications may not exceed $1.4 million for the first year. Competing renewal applications have no overall limit but the combined budgets (direct + F&A) for all cores (both required and optional), the other listed required functions, satellites, and pilot grants may not exceed the combined cost of all presently funded core activities including satellites and pilot grants awarded during the final year of the present funding period plus a 3% increase. In addition all applications should request three research projects. Although the financial plan of the NIA provides support for this program, awards pursuant to this RFA are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications. Limited funds are available for competing supplement applications. Competing supplement applications for projects or optional cores will be limited to a maximum of two during a 5-year funding cycle.

ELIGIBLE INSTITUTIONS

You may submit an application if your institution has any of the following characteristics:

- For-profit or non-profit organizations
- Public or private institutions, such as universities, colleges, hospitals, and laboratories
- Units of State and local governments
- Eligible agencies of the Federal government
- Domestic institutions/organizations
- Foreign institutions are not eligible to apply

Your institution should support an ongoing base of high-quality Alzheimer's research or research in other neurodegenerative diseases, or in aging of the nervous system. To be eligible your institution must support:
o at least five principal investigators with any PHS agency (or comparable peer-reviewed federal, state, or foundation) funded research grants related to neurodegenerative diseases or aging of the nervous system and each with at least two years of support remaining at the time of application.

or,

o one or more program project grants (P01s) related to neurodegenerative diseases or aging of the nervous system and with at least two years of support remaining at the time of application.

The work that you propose in the ADRC should be different from the ongoing supported research. NIA will review overlap of existing support through P01s or other mechanisms and adjust support of the center appropriately prior to any award. Your institution can have only one active Alzheimer’s Center receiving NIA support.

INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

The P.I. should be a scientific leader experienced in the field of Alzheimer’s and/or other neurodegenerative disease research and must be able to coordinate, integrate, and provide guidance in the establishment of programs in Alzheimer's disease research and allied areas. A significant time commitment (at least 10%) must be made by the P.I. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

SPECIAL REQUIREMENTS

An Alzheimer's Disease Research Center will be an identifiable organizational unit formed by a single institution or a consortium of cooperating institutions. Therefore, lines of authority must be clearly specified. Each applicant institution will name an ADRC Director (P.I.) who will be the key figure in the administration, management and coordination of the ADRC grant. The Director will be responsible for the organization and operation of the ADRC. The Director should be a scientific leader experienced in the field of Alzheimer's disease research and must be able to coordinate, integrate, and provide guidance in the establishment of programs in Alzheimer's disease research and allied areas. An Associate Director may be named who will be involved in the administrative and scientific efforts of the Center.

Applicants must commit to cooperate fully and to share specimens with other research scientists both within and outside the Centers network as well as data concerning patients and control subjects with the NIA - sponsored National Alzheimer’s Coordinating Center (NACC) where data from all AD Centers is centrally stored. Any genetic specimens collected by the Center should be made available to the National Cell Repository for Alzheimer’s Disease (NCRAD), if they meet the criteria for inclusion in the repository, in accordance with agreed upon protocols and policies. Centers may also be requested to contribute other biological samples such as serum and cerebrospinal fluid, using agreed upon protocols, for trans-center studies examining biomarkers that might relate to risk, diagnosis or progression of AD. The Steering Committee of the NACC in conjunction with the ADC Directors and the NIA sets policies that allow the individual Centers to conduct research on patients and control subjects collected by the individual Center while also sharing common data sets with NACC. Applicants should follow NIA policies on data and sample sharing.

In order to assure active collaboration with other Centers, the ADRC
Director and other staff should attend semi-annual meetings of the ADC Directors and other ad hoc meetings arranged by the ADCs or the NIA to share research findings during scientific discussions and poster sessions, participate in planning for cooperative research or help to refine and standardize operating procedures among the Centers. The ADRC application should include funds for travel of the Director and other key personnel 1) to the semiannual meetings of the Center Directors, 2) for at least 2 ad hoc meetings on special topics, 3) for visits of Center investigators to other ADCs for the exchange of scientific ideas, planning of multi Center research projects and to receive training in specialized techniques, 4) for the Administrator to attend the Administrators' meeting and 5) for core leaders to attend meetings with core leaders from other ADCs.

The required elements for an ADRC include cores, research projects, and pilot research projects. Additional cores may be proposed but only if they are needed to advance the local research effort and if they fit within the budget limits described elsewhere in this RFA. Applications must include a data management core that also includes a capacity to provide biostatistical consulting to the scientific staff associated with the ADRC. Applicants must have the capacity to provide neuropathological confirmation of the diagnosis for all subjects who die while enrolled in the clinical core of the center and to store selected brain specimens for research. This may be accomplished by either having a Neuropathology core or by using the services of another Alzheimer's Center Neuropathology Core or by a pathologist specializing in neurodegenerative diseases.

Specific instructions for preparing overall progress reports (for competing renewal applications), progress reports and plans for individual cores and research projects, and a list of review criteria are detailed later in this RFA.

Cores

A core is a shared central laboratory or clinical research facility, service, or resource whose function is essential to the scientific purpose of the ADRC. Each core is directed by an investigator with substantial expertise related to the core. Facilities may be proposed that will enhance productivity or in other ways benefit a group of investigators to accomplish stated goals. Several important and related considerations are (1) the degree to which currently funded investigators within or outside the Center will use and will benefit from core resources, (2) the degree to which the cores coordinate with each other to further the overall Center mission and (3) the degree to which the resources will promote new and/or expanded AD research efforts locally, regionally or nationally. Applicants should document and describe briefly the projects, both existing and planned, whether funded by the Center or not, that have, or will depend upon resources provided by the requested cores. At least one of the proposed ADRC projects must depend directly upon resources provided by the clinical core or the neuropathology component of the Center.

Required Cores and Functions

ADMINISTRATIVE CORE: The administrative core should set the overall direction of the Center and ensure optimal utilization of Center resources. Effective development of Center programs requires interaction among the Director, the principal investigators of the cores, the principal investigators of research and pilot projects using the cores, other researchers at the applicant institution, appropriate institutional administrative personnel, the staff of the awarding agency, and the members of the community in which the Center is located. The ADRC should recognize that it is part of a large network of ADCs and be prepared to work cooperatively with the other Centers.
and the National Alzheimer’s Coordinating Center.

The success of the ADRC is dependent upon involving scientific and professional personnel from a variety of disciplines and subspecialties who interrelate in order to facilitate the acquisition of new knowledge. In addition to coordination of the ADRC, the Director, with the advice of his or her executive committee, will be responsible for allocating and monitoring ADRC funds and identifying and selecting key personnel. An executive committee (composed of core and project leaders and the administrator) will be established to assist the Director in making the scientific and administrative decisions relating to the Center. The executive committee should seek outside advice and consultation, both from within the institution and from other institutions, in its monitoring and development of the scientific content and direction of the program.

A committee to review pilot grant applications should be established and include scientists from outside the ADRC with expertise relevant to the types of pilot applications received by the Center. This committee will make funding recommendations to the Director. Alternatively, the external advisory committee could be responsible for pilot reviews.

An external advisory committee to the ADRC, consisting of scientists from outside of the institution or consortium, will also be established. Unless already appointed, external advisory committee members should not be recruited until the NIH review process is complete. This committee will be used to evaluate the programs of the ADRC, research progress, the effectiveness of communications within the ADRC, interactions with NACC, and any other activities for which outside expertise is required or desirable. The external advisory committee may serve as the review committee for pilot grant applications. The committee should meet annually and prepare a report including recommendations to assist the ADRC. A member of the NIA extramural program staff should be invited to attend each meeting as an observer. A copy of the advisory committee report should be routinely sent to the NIA with the annual progress report.

The administrative requirements of the ADRC will necessitate the assistance of an administrator with business management expertise. It is important that such an individual be identified and be directly involved with the fiscal and administrative aspects of the ADRC application and grant. The administrator should be a member of the executive committee. While budget formulation and planning will undoubtedly begin with the Director in collaboration with the scientific staff, the administrator must be involved in the process and provide consultation in matters of fiscal administration and be familiar with NIH grant-related compliance policies. The administrator should attend the annual ADC Administrators’ meeting.

It is expected that the ADRC administrative structure will facilitate the following:

1) coordination and integration of ADRC components and activities; (for example, the clinical and data management cores with the neuropathology and education components)

2) direction for future planning and optimal utilization of resources

3) support and advice for the ADRC Director in his/her oversight of the activities of the Center

4) interaction with the scientific and lay communities to develop relevant goals for the ADRC

5) assurance of compliance with human subjects, animal welfare,
scientific integrity, and financial policy requirements of NIH

6) interaction with other Centers, the Data Coordinating Center and other researchers to develop trans-ADC and outside research projects

7) interaction and involvement with other research programs of the University including the provision of core resources for development of related projects

8) timely and routine transmissions of appropriate ADRC data sets to the NACC

CLINICAL CORE: The Clinical core provides well-characterized patients and control subjects for cutting edge research projects involving e.g. clinicopathological correlations, comparison of disease states to normal aging, and drug/intervention studies. The Clinical core in close collaboration with the Education core of the Center is the primary contact point with the community. The Core provides resources to patients, aging control subjects, and caregivers while charting the course of the disease in patients and age-related changes in the research population being followed by the Center. Previously, clinical cores of ADCs have usually been based in university medical center neurology or psychiatry department memory disorders clinics and have concentrated mostly on middle to later stages of AD. With this RFA NIA is providing the opportunity to structure clinical cores to include special control or elderly populations that might be available to some applicants such as an ethnic or minority population, a religious community or a community population living in elderly housing where the likelihood of being able to study the full spectrum from normal aging to mild cognitive impairment to AD would be possible.

Recent improvements in evaluation for memory disorders in normal aging and MCI present new opportunities for research on early stages of disease and decrease the necessity to enroll middle and later stage patients. In addition, our increased understanding of the relationship of AD to, or coexistence with, other neurodegenerative diseases commonly seen in the elderly population provides the opportunity to broaden the mission of the ADRCs to include mixed dementias and diseases such as vascular dementia, Lewy body disease, frontotemporal dementia, and Parkinson’s dementia in order to better differentiate among them, to recognize commonalities and to study older demented individuals with mixed etiologies and medically co-morbid conditions. Therefore it is more appropriate that applicants concentrate on preclinical AD, normal aging, MCI and early AD as well as enhancing the recruitment of research subjects with other neurodegenerative diseases rather than concentrating only on full blown or pure AD. If applicants choose to diverge from the traditional structure (memory disorders clinic model) of the clinical core by including special populations, the responsibility is on the applicant to provide a complete description of the characteristics of the subject population and to justify the added value to research at the Center resulting from using a different subject population so peer reviewers can evaluate the comparative strengths and weaknesses of proposed clinical core subject populations.

The clinical core, in addition to patient and control subject recruitment, provides evaluation, and diagnosis, maintains a patient registry, conducts longitudinal follow up of patients and control subjects, and acquires clinical and laboratory data including agonal data pertaining to the last several weeks of life if post mortem material is to be used for molecular research. Procedures and facilities should be described related to collection, storage, and distribution of biological samples, including, but not limited to, cell lines, cerebrospinal fluid (CSF) and plasma. Applicants should follow agreed upon protocols for multi-center projects involving specimen
collection. Details for collecting specimens, recording information about clinical status of patients immediately preceding and at time of death, and procedures for storage and distribution of human biological samples to investigators both within and outside the Center should be provided. See the supplementary instructions section in this RFA for details regarding informed consent.

Data on preclinical stages of AD (MCI), possible and probable AD, other neurodegenerative disorders and normal aging should be collected and transmitted to the Data Management core. The data must be shared with the National Alzheimer's Coordinating Center according to standardized protocols developed by the ADC Directors, the Clinical Core leaders and the Steering Committee of NACC. A clinical task force is presently developing the criteria for collection of an expanded standard clinical data set from all Centers. Applicants must state in this section of the application that they agree to provide this expanded data set to NACC where it will be combined with data from other Centers and made available to scientists for collaborative studies.

The clinical core may perform a limited amount of developmental work, but should not directly support research per se. The developmental work allowable in a clinical core must be directly related to the function of the core. It may be directed toward improving and expanding the core functions, e.g., improving existing diagnostic strategies, or developing additional methodologies, techniques or services. Proposed developmental work should be described as completely as possible in the application. Planning for patient and age-matched control subject recruitment should include sensitivity to research design and biostatistical analysis. Procedures for communicating recruitment needs to the Education Core and for evaluating success should be outlined. The application should include a description of the types (with specific examples) of research projects and clinical trials that use or will use the core and what benefits will obtain to other research activities from the existence of the clinical core. While conducting clinical drug trials is one function of a clinical core, it should not be the major effort of the core.

Efforts to recruit diverse population subgroups including minorities and rural populations must be outlined. One option is to set up Satellite Diagnostic and Treatment Clinics (SDTCs) designed to increase the heterogeneity of the research patient pool and to enhance the research capabilities of the ADC by extending the activities of the clinical core. Existing Centers should retain any satellites already in existence unless there are compelling reasons to restructure these components. New satellite clinics may be proposed as part of the clinical core. The satellite clinics are not required to conduct research but should serve as vehicles for the recruitment, diagnosis and management of AD patients control subjects from rural and minority communities, who are then offered the opportunity to participate in research protocols, clinical drug trials and autopsy. Effective satellites usually include multicultural staff members who have links to the community being involved. In addition, the satellite should have clearly delineated interactions with the educational outreach activities of the Center. Applicants should detail appropriate strategies for outreach to recruit and retain ethnically diverse subjects and describe the culturally sensitive materials that will be used. The inclusion of patients with different characteristics will assist investigators in providing answers to questions about AD diagnosis, treatment, and management strategies that are likely to be applicable to the broad U.S. population. Additionally, a more diverse patient pool will facilitate investigations of the neuropathology and genetics of AD in minority groups as well as studies of care giving and family burden in rural and minority group cohorts.

DATA MANAGEMENT and STATISTICS CORE: This core should provide data
management and statistical consulting to the research projects and the cores of the ADRC. Data cores are important to facilitate local analyses and collaborations between and among Centers and with NACC. The data core must be adequately funded and staffed to allow required tasks to be carried out. (New applicants may contact NACC to learn more about NACC procedures and the regular updates to the datasets required from all Centers; http://www.alz.washington.edu/ ) A model for the data core might consist of two arms: 1) computing and data base management and 2) statistical consultation and liaison with other cores and projects. The core director must be keenly aware of and experienced with database management practices and computing but is not necessarily the architect and day to day manager of the database. The core director must have the time and the authority to work administratively with other cores/projects. The core should include a systems manager for computing and database management who will be the architect of the database structure and responsible for its maintenance. This person will be an experienced database programmer and systems analyst with sufficient background to select and implement database management software, represent data structures, specify and organize data flow, construct detailed “error-check” programs, develop/implement data checking and cleaning procedures, and provide for data entry and access, as well as information distribution, through electronic means (e.g., the internet or intranet). Communication and cooperation with all cores and projects where data are (or will be) generated, with NACC, and a close working relationship with the statistics arm of this core should be primary goals for this core. The systems manager should be given the authority:

1. to establish data flow schemes,
2. to construct data forms (electronic or hard copy; following core/project specified content),
3. to implement a Center-wide system of subject ID numbers that meets privacy standards
4. to require adequate filing systems for raw data within the cores/projects and within the data core itself,
5. to establish a mechanism to track data edits,
6. to provide for longitudinal follow-up data storage/retrieval consistent with the protocols of the center.

The staff of the data core must work with clinical and research personnel to interpret their data into computer usable form, and simultaneously work with statisticians to insure that the data are represented in a fashion that will allow the desired analysis files to be produced and analyses to be accomplished. Data core staff should have a working relationship with core/project data collectors and must have their cooperation to reconcile errors and missing or incomplete data elements as discovered through error check programs or through ‘hands-on’ inspection procedures. In addition the core staff is required to work cooperatively with the NACC staff and respond appropriately to data calls issued by NACC.

A biostatistician(s) should be involved in the design and analysis of studies within the Cores and projects and will work closely with the data manager to insure analysis files are produced consistent with the needs of the question at hand. It is expected that the Clinical and other cores and projects in the ADC, where data are collected, will fully cooperate and participate with the data core by providing data in the form specified and in a timely way. Cooperation, concurrence and collaboration should continue from the initial specification of data content through data collection to database management and analysis.

NEUROPATHOLOGY: Neuropathology operations are expected to provide state of the art diagnostic services and collection of well-prepared brain material appropriate for the research requirements of local research efforts as well as cooperative research across Centers and with other
researchers outside of Centers. Centers must be able to provide postmortem diagnosis on cases and normal control subjects enrolled in the clinical core and on other well documented AD cases and controls. A significant value of having the Center infrastructure is the support of research studies that permit clinical-pathological correlations across Centers. Therefore, Centers should agree to follow standardized procedures so that cross-Center correlations are possible. (New applicants may contact NACC to get the most recent pathology requirements). Centers can choose to establish a neuropathology core or can obtain services from outside the Center (usually another Alzheimer's Center).

Procedures and facilities should be described related to criteria for diagnosis, and the collection, storage, and distribution of brain tissue and other biological samples, including, but not limited to, cell lines, cerebrospinal fluid (CSF) and plasma. While Centers are encouraged to have brain banks, less emphasis should be placed on the routine collection and storage of late stage Alzheimer’s brains (unless specific research questions call for these) and more emphasis placed on collection of brain material in a fashion that will support the specific research efforts of investigators affiliated with the local Center and other scientists. If collection of special material is proposed (e.g. tissues from Parkinson’s disease, oldest old controls, frontotemporal dementia, prion diseases, mixed dementias, or stereologically prepared specimens) justification should be included. Data gathering and storage activities should be coordinated with those of the Clinical Core and the Data Management Core.

To facilitate data sharing and cross-Center comparisons of diagnosis, all Centers should use the neuropathological criteria for Alzheimer’s disease developed by the NIA-Reagan Institute Working Group (Neurobiology of Aging, vol. 18, suppl 4, pp S1-S2, 1997). If tissue from other diseases is collected, list the clinical diagnostic criteria used. More detailed criteria for research purposes should also be described. Pathology data should be included in the data set transmitted to NACC as recently redefined by Center neuropathologists and approved by the Center Directors group. (New applicants may get information from NACC about the pathology data set). If the applicant chooses to include a neuropathology core in the application, the core may propose a limited amount of developmental work, but should not emphasize research per se. The developmental work allowable must be directly related to the function of the core. It may be directed toward improving and expanding the core functions, e.g., improving existing, or developing additional methodologies, techniques or services. Proposed developmental work should be described in the application. Neuropathologists from the ADCs meet yearly to share ideas and discuss technical aspects of tissue sampling, development of standardized tissue processing for diverse research protocols, cataloging and data management, and banking and distribution of tissues and biological samples. All Centers are expected to send a representative to this meeting.

The procedure for prioritizing the use of tissues and other biological samples stored at the Center should be discussed along with a brief description of potential research projects that will use the samples. Provisions for obtaining informed consent and protecting the privacy of research subjects must be detailed. Procedures to provide coded samples to investigators that protect the identity of the patients should be described.

EDUCATION and INFORMATION CORE: The three major activities of the Education Core are to 1) help recruit and retain subjects for particular research protocols and clinical trials, with a special emphasis on minorities and other underserved populations; 2) spearhead effective outreach programs that will publicize the ADRC and educate
families and caregivers; 3) support innovative development of professional staff on clinical and research skills related to Alzheimer’s disease and other dementias. These efforts afford an important liaison and outreach from the ADRC to patients, their caregivers and the professional community. Collaboration with the Alzheimer’s Association local chapters and other groups is expected for dissemination and transfer of information to the lay community and other educational activities and assistance with subject recruitment. The methods and techniques to be employed to disseminate information and the audience targeted to receive information should be defined including 1) approaches to training of professionals including possible reciprocal exchange programs between Centers to provide access to different research environments and technologies; 2) descriptions of seminar or lecture series, workshops and continuing education programs; 3) outreach to specific communities to publicize research; 4) collaboration with other organizations such as state and local agencies and the Alzheimer’s Association and 5) descriptions of materials (e.g. videos and printed matter) developed by the Center.

Attention should be directed to issues of cultural sensitivity and, where appropriate, the information should be structured so that it can effectively reach minority populations, including non-English-speaking people. Procedures by which the education and outreach activities are closely coordinated with the clinical core and satellite(s) (if appropriate) should be described, especially in recruitment of minorities and ethnically diverse populations. The education and outreach activities should also be prepared to support activities of the Centers group as a whole as well as recruitment for special NIA initiatives, such as subjects for genetic studies. Clearly stated objectives and a systematic plan as to how these objectives will be met are required. Specific assessment methodology is also required to evaluate the effectiveness of outreach programs. Collaboration with other ADCs and the NIA Alzheimer’s Disease Education and Referral Center (ADEAR) in subject recruitment, education and coordinated dissemination of educational materials is expected.

Optional Cores

The NIA, through the ADRC, will support additional cores that provide opportunities for scientific research beyond those attainable solely through support of the mandatory cores and other functions. However, any optional cores must support one or more Center research projects and fit within the budget restrictions outlined in the budget guidelines for the application. Support should not be requested for cores that only replace or centralize resources supported on individual project grants. In a Center grant application, it is not sufficient for the principal investigator merely to identify such centralized resources. Rather, it must be demonstrated exactly how each core would augment or enhance the present capabilities of investigators using center resources to make possible new activities at the home Center as well as other Centers. There should be a detailed discussion of the project(s) that will use resources of additional cores. Some examples of research support that core components could provide are: (1) imaging; (2) tissue and/or cell culture facilities; (3) complex instrumentation, e.g., electron microscopy, mass spectrometry, electrophysiology; (4) sequencing or microarray facilities (5) transgenic animal or cell preparation; (6) genetics; and (7) caregiving.

Research Projects

Applications should request funding for three research projects (similar to small R01s). The research projects should request up to five years of funding and propose studies that will advance our understanding of the basic and clinical underpinnings of Alzheimer’s
disease and related disorders in areas such as preclinical etiology, genetics, pathogenesis, epidemiology, diagnosis, therapeutic interventions including small scale clinical trials, patient management, and care giver issues. The projects should be similar in quality to small RO1 grants and subprojects of program project grants. It is required that at least one of the projects predominantly utilize patients or patient samples from the clinical core or neuropathology resources. The ADRC should not be the primary source of research funding for the project leaders funded by the Center.

Pilot Studies

A plan to support pilot studies for basic or clinical biomedical, epidemiological, caregiving, educational or behavioral research should be included and budgeted in the application. The description of a plan to solicit, review and administer pilot grants should be included in the Administrative Core and a separate budget including the total request for pilots should be submitted. Criteria for review of pilot studies should be developed and included in the application. This funding mechanism is intended to provide modest support that will allow an investigator the opportunity to develop preliminary data sufficient to provide the basis for an application for independent research support through other granting mechanisms. Pilot studies are typically limited to a nonrenewable single year of support. If described and well justified, two years of support may be requested. Any one investigator is eligible only once for pilot support, unless the additional proposed pilot study constitutes a real departure from his or her ongoing research. Some examples are:

1) A study proposed by an established investigator who has experience in areas other than Alzheimer’s disease research, and who wants to work in the Alzheimer research field; or a study by an established investigator who wants to try a new hypothesis, method, or approach that is not an extension of ongoing research.

2) A study proposed by a new investigator, with an interest in research in Alzheimer's disease, before the study has developed to the point of being suitable to apply for individual grant support.

3) A study to determine the availability of sufficient subjects with specific characteristics, such as ethnic or minority status, before undertaking a larger study.

4) A study based on data in the NACC data set to determine the feasibility of conducting larger new studies.

Each pilot project is limited to no more than $35,000 direct costs each year. If the pilot project is requested and justified for two years, the direct costs are limited to $35,000 per year.

No pilot applications should be submitted with the Center application but, instead, the number requested for each year (2 minimum, 3 maximum) and the plans for soliciting pilot proposals should be described. A plan must also be presented within the administrative core for peer review of the pilot studies including the structure and composition of the review panel. The panel should include scientists from outside the Center. One option is for the External Advisory committee to serve as the review panel for the pilot applications. Following review, those pilots chosen for funding should be submitted to the NIA for approval in the annual non-competing renewal application. Successful Center applicants should conduct a competition and submit the successful applications to NIA for the first year of pilot funding after receiving notice of grant award; in subsequent years competition for pilot awards should be timed so successful applications can be submitted with the non-competing renewal application for NIA review.
Progress Reports (for competing renewal applications)

Overall Progress Report: Address the major scientific achievements in research on AD and related topics carried out by Center personnel and by projects utilizing Center resources in the last funding period. Identify significant findings in research on aging, AD and other neurodegenerative diseases that were facilitated or supported directly through Center resources. Include summaries of progress in achieving the major aims of the Center and its projects and highlight major publications. Include details of how the presence of the ADRC has brought new investigators into the field and has stimulated non-ADRC funded research in the last funding period. Explain the Center’s role in generating new funding from grants as well as leveraging funds from donors and other private sources. Describe how the presence of the Center has facilitated and improved Alzheimer research at the Institution and beyond. When a project or optional core has terminated, include a final report with a summary of results and publications. If an optional core is continuing, include a progress report in that component write-up. Applicants should include tables detailing 1) Publications and grants (source, amount and title) resulting from each component funded by the ADRC, 2) Publications and grants (source amount and title) resulting from pilot projects, 3) Involvement in collaborative projects with other Centers including those funded by NACC, and 4) minority enrollment into research projects or clinical trials and specifically, into any research projects addressing minority issues.

In addition to text summaries, applicants should also include summary tables detailing:

1) ADRC and Non-ADRC funded grants and projects that use or have used major resources supplied by the ADRC, including principal investigator, source and period of funding, types and amount of resources and any resulting publications.

2) Collaborations with other AD researchers, other Centers, cooperative studies, and with biotechnology and pharmaceutical companies.

3) Clinical trial participation by patients enrolled in the Center including trial name, sponsor, number of patients, and dates. Detail separately NIH and pharmaceutical industry sponsored trials.

4) Institutional, state and other private and public resources committed to the Center and its investigators.

Clinical Core Progress Report: Describe the most important clinical core contributions to research on AD, related dementias and aging. Detail key findings and list publications resulting from use of core patients. Any developmental work carried out by the core should be presented and resulting publications listed. The Clinical Core Progress report should include Clinical Core objectives and progress in meeting them, including information about satellites (if applicable). Basic functions of the core should be summarized (using tables where appropriate) including numbers, race, gender, age of patients and controls recruited, diagnosis, percentage follow up and drop out rate, use of autopsy data in support of clinical correlations in research projects, and diagnostic confirmation by autopsy. Functions of Clinical Core in providing services (a) for ADC-funded and (b) non-ADC funded investigators should be clearly summarized. These would include numbers and kinds of subjects recruited and participation in clinical trials and other ongoing clinical research projects, both local and national. Applicants are required to ensure that patients’ privacy is protected as discussed elsewhere in this RFA.
Neuropathology Core Progress Report: Describe the most important neuropathology core contributions to research on AD, related dementias and aging. Competing renewal applications should outline previously stated core objectives and progress in meeting them. Any developmental work carried out by the core should be presented and resulting publications listed. The most important consideration in reporting progress should be reports of tissue use in research projects and the new insights obtained from these studies. Basic functions of the core such as number of AD and control autopsies, post mortem intervals (where this is important for specific research purposes), tissue dissection and storage, diagnoses, and type and quantity of tissue provided to investigators both funded by the Center and by other means should be clearly summarized (using tables where appropriate).

Education and Information Transfer Core Progress Report: Applications should include information about training activities that effectively impart knowledge to professionals and the lay public with the possibility of leading to improved health care for patients. Include efforts to assist the clinical core and NIA special initiatives, such as the genetics initiative, in subject recruitment, especially any efforts directed to recruitment of minority and ethnically diverse subjects. Using tables when appropriate, report the nature of training activities and the types of professionals trained - physicians (including medical students, residents, fellows), nurses, social workers etc. Detail the history of cooperative ventures of the Center with state and local agencies such as the Alzheimer's Association and community groups in coordinating training and education programs. List educational materials developed by the core and any that may have been provided to ADEAR for national distribution.

Data Management and Statistics: Summarize progress and activities related to data collection, data management and statistical consulting activities at the appropriate place in the application detailing where in the core(s) these activities were located. Include progress and interactions with NACC. Present evidence for meeting timetables for data transfer in the proper format to NACC. List projects and publications in which data management and statistical consulting played a role.

Budget Considerations

All ADRC proposals should request and provide justification for five years of support.

The total costs (direct + F&A) requested for new applications may not exceed $1.4 million for the first year. Competing renewal applications have no overall limit but the combined budgets (direct + F&A) for all cores (both required and optional), the other listed required activities, satellites, and pilot grants may not exceed the combined cost of all presently funded core activities (required and optional) including satellites and pilot grants awarded in the final year of the present funding period plus a 3% increase. Applicants should request three research projects each limited to $125,000 direct costs/year for up to five years. Direct cost requests for subsequent years may increase above the prior year direct cost award by no more than 3%.

The direct costs are to be distributed approximately as follows: (This proposed distribution is intended only as a general guideline and proportions may vary depending on whether this is a new application or a competing renewal, on the overall budget of existing Centers, and local needs. If additional cores are proposed, the distribution should be adjusted accordingly.)

- Administrative Core: 5%
- Pilot Studies: 5%
Clinical Core 35%
Data Management Core 10%
Neuropathology 10%
Education and Information Transfer Core 5%
Research Projects 25-35%

If large items of equipment are requested, the application must document what is already available and provide clear justification in terms of use by core staff and how it relates to research projects dependent on the core. General-purpose equipment needs should be included and justified only after surveying the availability of such items within the institution.

Research patient care costs (both inpatient and outpatient expenses) will be considered in the context of other existing institutional clinical resources. Attempts should be made by the applicant institution to utilize existing clinical facilities, such as General Clinical Research Centers and individually supported beds. Costs relating to the clinical efforts of the ADRC may be funded through the ADRC, provided there is no overlap of funding. Only those research patient costs directly related to ADRC activities may be charged to the ADRC.

Domestic and foreign travel of project personnel directly related to the core and scientific activities of the ADRC is allowable. Budgeting should include travel and lodging for 1) the semi-annual meetings of the Center Directors, 2) annual meetings of administrators, clinical core leaders, education core leaders, data managers, and neuropathology core leaders and, 3) representatives of the Center to attend ad hoc meetings called by the ADCs or the NIA to discuss research findings and plan cooperative projects, to promulgate data sharing, and to discuss standardization of procedures among the ADCs.

Requests and commitments for pilots in competing applications (new and renewal) will be budgeted as a separate line in the "composite" budget at $35,000 per pilot per year (without escalation). They should not be included in the Administrative Core budget or elsewhere in the application. A brief description of the first year pilot research and detailed pilot budgets for the first year of Center funding will be due shortly before the award of successful applications and future year pilots should be submitted with the annual non-competing renewal applications. Facilities & Administrative costs will be provided in accordance with these budgets.

Pilot grants are allowed for consortium arrangements but direct cost should not exceed $35,000 with total consortium cost budgeted not to exceed $40,000 for each pilot including the facilities and administrative costs of the consortium institution. No F&A costs will be provided to the grantee for pilot projects conducted by consortia. If consortium arrangements are contemplated, the following information should be provided in the application:

1) A list of all proposed performance sites both at the applicant institution and at the collaborating institutions

2) A separate, detailed budget for the initial and future years for each institution and, where appropriate, for each unit of activity at each institution.

3) A composite budget for all units of activity at each institution for each year, as well as a composite budget for the total proposed budget for each year.

4) An explanation of the programmatic, fiscal, and administrative arrangements made between the grantee institution and the collaborating
WHERE TO SEND INQUIRIES

We encourage inquiries concerning this RFA and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues:

- Direct your questions about scientific/research issues to:
  Creighton H. Phelps, Ph.D.
  Program Director, Alzheimer’s Disease Centers
  Neuroscience and Neuropsychology of Aging Program
  National Institute on Aging
  7201 Wisconsin Avenue
  Suite 350
  Bethesda, MD  20892-9205
  Telephone:  (301) 496-9350
  FAX:  (301) 496-1494
  Email:  phelpsc@nia.nih.gov

- Direct your questions about peer review issues to:
  Mary Nekola, Ph.D., Chief
  Scientific Review Office
  National Institute on Aging
  7201 Wisconsin Avenue
  Suite 2C212
  Bethesda, MD  20892-9205
  Telephone:  (301) 496-9666
  FAX: (301)402-0066
  Email:  nekolam@nia.nih.gov

- Direct your questions about financial or grants management matters to:
  Deborah Stauffer
  Grants and Contracts Management Office
  National Institute on Aging
  7201 Wisconsin Avenue
  Suite 2N212
  Bethesda, MD  20892-9205
  Telephone:  (301) 496-1472
  FAX: (301) 402-3672
  Email:  stauffed@nia.nih.gov

LETTER OF INTENT

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Number and title of this RFA

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed at the beginning of this document. The letter of intent should be sent to:
Creighton H. Phelps, Ph.D.
Program Director, Alzheimer’s Disease Centers
Neuroscience and Neuropsychology of Aging Program
National Institute on Aging
7201 Wisconsin Avenue
Suite 350
Bethesda, MD 20892-9205
Telephone: (301) 496-9350
FAX: (301) 496-1494
Email: phelpsc@nia.nih.gov

SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). Applications must have a DUN and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the Universal Identifier when applying for Federal grants or cooperative agreements. The DUNS number can be obtained by calling (866) 705-5711 or through the web site at http://www.dunandbradstreet.com/. The DUNS number should be entered on line 11 of the face page of the PHS 398 form. The PHS 398 document is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

SUPPLEMENTARY INSTRUCTIONS:

The page limit of 25 pages for Items a-d of the Research Plan, as stated in the PHS Form 398 instructions, applies to each research project and core. Appendix materials should follow the instructions in the 398 form with the following exception: The complete Appendix materials should be submitted on a Compact Disc (CD) that is identified with the name of the principal investigator and the name of this RFA. All appendix materials for the complete application should be on a single CD. Appendix materials should be submitted to the Chief, Scientific Review Office, NIA (see address below).

Information that is not included with the original application may not be submitted after the receipt date except with prior approval from the responsible Scientific Review Administrator. This will usually only include major corrections or changes in personnel.

Table of Contents

Do not use Form Page 3, “TABLE OF CONTENTS” of Form 398 since it applies to applications for single projects. In its place, use the sample format provided in the following link http://www.nia.nih.gov/NR/rdonlyres/BE40D316-62CE-4075-B2DC-DC577E283A65/3114/P01GuideAttach.pdf. Number all pages consecutively. Since the first page of the application is the “Title Page,” begin the next page with the numeral “2”. Do not use lettered numbers (e.g., 2A, 2B, etc.).

Budgets. Insert a table describing the CONSOLIDATED DIRECT COSTS FOR FIRST YEAR OF REQUESTED SUPPORT, as shown in Attachment 3 in the above link for the three required cores, any optional cores and the three projects. Next, insert budgets for the first twelve months and for the entire proposed period for the overall program. Do not include detailed budgets for individual research projects and cores here; instead, place them with the corresponding project or core. Justify all items carefully according to the PHS 398 form instructions. A complete budget for a consortium project is to be developed and identified as such. The period of support may not exceed five years of support. Any questions about budget development may be directed to the Grants and Contracts Management Office at the address above.

Biographical Sketches. Follow the PHS 398 instructions. Include
sketches for all key personnel and place them in alphabetical order; however, place the principal investigator’s/program director’s biographical sketch first.


Sharing of Data and Biological Resources

Restricted availability of unique research resources, upon which further studies are dependent, can impede the advancement of research. The NIH is interested in ensuring that particular research resources developed through grants become readily available to the broader research community in a timely manner for further research, development, and application, in the expectation that this will lead to products and knowledge of benefit to the public health. Resources to be shared will include appropriate data, brain tissue and other biological samples collected. Data sharing will be accomplished through NACC.

To address this interest in assuring research resources are accessible, NIH requires applicants who respond to this RFA to submit a plan for exercising intellectual property rights, should any be generated through this grant, while making such research resources available to the broader scientific community.


NIA program staff will consider the adequacy of the plan and its consistency with NIH and NIA policies on data sharing and intellectual property when determining whether to recommend an application for award. The approved plan will become a condition of the grant award and Progress Reports must contain information on activities for the sharing of research resources and intellectual property.

At least one of the three projects should use patients or research samples from the clinical core or from neuropathology resources.

Each component core and project should be presented according to the Table of Contents. The cores should appear first, identifying required cores by letters as follows, (Core A = Administrative Core, Core B = Clinical Core, Core C = Data Management core); if the application includes a Neuropathology Core, it should be Core D; the Education Core should be Core E even if there is no Neuropathology Core. Optional cores should be identified with subsequent consecutive letters. Individual research projects should appear in the application after the cores and identified with consecutive Arabic numbers (Project 1,
Project 2, Project 3). Titles may not exceed 56 spaces.

Prepare each core or project as a separate section that begins on a new page of the application. Begin each with a title page (use the format of sample Attachment 2 in the link mentioned above; Do not use the face page of form 398) and include a detailed first year and summary budget for all years with each core and project. Continue to number the pages consecutively.

Informed Consent

Describe the procedures for 1) obtaining informed consent for research on cognitively impaired human subjects who may not have the capacity to consent, 2) obtaining consent for future participation in research studies if the patient becomes unable to consent (advanced directive for research) 3) obtaining consent to place data in the National Alzheimer's Coordinating Center's minimum data set and to share data and specimens with other qualified scientists, and 4) obtaining proxy or surrogate consent in the context of local and state law. Attach samples of information given to patients and families and copies of all consent forms. Attention should be paid to obtaining advanced directives for research, and obtaining autopsy permission from patients and families and informed consent for current and future use of biological samples by qualified investigators. Permission should be obtained for sharing of cells, DNA and phenotypic information and for storage in repositories.

USING THE RFA LABEL: The RFA label available in the PHS 398 (rev. 5/2001) application form must be affixed to the bottom of the face page of the application. Type the RFA number on the label. 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. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked. The RFA label is also available at: http://grants.nih.gov/grants/funding/phs398/label-bk.pdf.

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the Checklist, and three signed, photocopies, in one package 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)

Do not submit any appendix material to the Center for Scientific Review.

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

Mary Nekola, PH.D., Chief Scientific Review Office National Institute on Aging 7201 Wisconsin Avenue, Suite 2C212, Bethesda, MD 20892-9205

APPLICATION PROCESSING: Applications must be received by the application receipt date listed in the heading of this RFA. If an application is received after that date, it will be returned to the applicant without review.
Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and institute assignment within 8 weeks.

The Center for Scientific Review (CSR) will not accept any application in response to this RFA that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an Introduction addressing the previous critique.

PEER REVIEW PROCESS

Upon receipt, applications will be reviewed for completeness by the CSR and responsiveness by the NIA. Incomplete and/or non-responsive applications will be returned to the applicant without further consideration.

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by the NIA in accordance with the review criteria stated below. As part of the initial merit review, all applications will:

- Undergo a process in which only those applications deemed to have the highest scientific merit, generally the top half of the applications under review, will be discussed and assigned a priority score
- Receive a written critique
- Receive a second level review by the National Advisory Council on Aging

REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of your application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. The scientific review group will address and consider each of the following criteria in assigning the application’s overall score, weighting them as appropriate for each application.

- Significance
- Approach
- Innovation
- Investigator
- Environment

Your application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, you may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

(1) SIGNIFICANCE: Does your study address an important problem? If the aims of your application are achieved, how do they advance scientific knowledge? What will be the effect of these studies on the concepts or methods that drive this field?

(2) APPROACH: Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Do you acknowledge potential problem areas and consider alternative tactics?
(3) INNOVATION: Does your project employ novel concepts, approaches or methods? Are the aims original and innovative? Does your project challenge existing paradigms or develop new methodologies or technologies?

(4) INVESTIGATOR: Are you appropriately trained and well suited to carry out this work? Is the work proposed appropriate to your experience level as the principal investigator and to that of other researchers (if any)?

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

ADDITIONAL REVIEW CRITERIA: In addition to the above criteria, the following items will be considered in the determination of scientific merit and the priority score:

PROTECTION OF HUMAN SUBJECTS FROM RESEARCH RISK: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed. (See criteria included in the section on Federal Citations, below).

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH: The adequacy of plans to include subjects from both genders and all racial and ethnic groups (and subgroups) as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated. (See Inclusion Criteria in the sections on Federal Citations, below).

CARE AND USE OF VERTEBRATE ANIMALS IN RESEARCH: If vertebrate animals are to be used in the project, the five items described under Section f of the PHS 398 research grant application instructions (rev. 5/2001) will be assessed.

Sharing Research Data:

Applicants requesting more than $500,000 in direct costs in any year of the proposed research must include a data sharing plan in their application. The reasonableness of the data sharing plan or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or priority score. (See sharing policy in the sections on Federal Citations, below).

BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

Other Review Criteria:

In addition to the above criteria, applications will specifically be reviewed with respect to the following:

Progress in Achieving Stated goals (competing renewal applications)

- Adequacy of progress in stated goals from last application, most importantly, productivity as demonstrated by quality of scientific findings and their impact on AD research; include publications, honors and awards, grant funding, pilot grant success and research projects supported by core resources including collaborative research.

Scientific Potential of the Center (competing renewal and new
applications)

- Potential to develop critical new knowledge and unique and innovative contributions to AD research locally and nationally
- Scientific/technical merit and innovation in the proposed Center goals
- Expertise and productivity of Center investigators
- Ability of Center to participate in coordinated national efforts for collaborative research and data sharing with other scientists and research Centers

Organization of the Center (competing renewal and new applications)

- Adequacy of organizational plan and management structure to meet Center goals and the requirements spelled out in this RFA
- Merit and appropriateness of institutional resources including other funding and dedicated resources
- Appropriateness of functions described for External Advisory Committee
- Appropriateness of plans for review and award of pilot projects

Core Facilities (competing renewal and new applications)

- Appropriateness of proposed core resources to facilitate research goals of the Center and a plan for prioritizing their use
- Adequacy of utilization of core support in research (competitive renewals)
- Adequacy of plans to facilitate subject recruitment and follow-up to meet the stated research goals of the Center
- Appropriateness of community and professional education programs to facilitate goals of the Center
- Merit of data management and statistical consulting plans to meet the needs of the Center investigators and the required reporting standards
- Appropriateness of plans for diagnostic pathology and biological specimen collection, storage and distribution
- Appropriateness of core resources to support research projects locally as well as nationally for individual and collaborative projects

Research Projects (competing renewal and new applications)

- Potential for contribution to the field and expansion of knowledge concerning mechanisms of normal aging, MCI, AD and other neurodegenerative disease of the aging as well as the translation of research findings to diagnosis and care
- Appropriateness and quality of research proposed in each project along with the experience, competence, and commitment of the investigators.
- Availability of Center resources to support the stated aims of the project

These criteria will be applied to competing renewal applications by evaluating progress and future plans, and to new applications, by evaluating preliminary organizational work, experience with Alzheimer's and other neurodegenerative disease research, potential for developing new and exciting research, and specific plans for implementation of the new program.

RECEIPT AND REVIEW SCHEDULE

Letter of Intent Receipt Date: April 15, 2004
Application Receipt Date: May 18, 2004
Peer Review Date: Fall 2004
Council Review: January, 2005
Earliest Anticipated Start Date: April, 2005
AWARD CRITERIA

Award criteria that will be used to make award decisions include:

- Scientific merit (as determined by peer review)
- Availability of funds
- Programmatic priorities.

REQUIRED FEDERAL CITATIONS

HUMAN SUBJECTS PROTECTION: Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

SHARING RESEARCH DATA: Starting with the October 1, 2003 receipt date, investigators submitting an NIH application seeking $500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why this is not possible.

http://grants.nih.gov/grants/policy/data_sharing Investigators should seek guidance from their institutions, on issues related to institutional policies, local IRB rules, as well as local, state and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH: It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines are available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

REQUIRED EDUCATION ON THE PROTECTION OF HUMAN SUBJECT PARTICIPANTS: NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for research involving human subjects. You will find this policy announcement in the NIH Guide for Grants and Contracts Announcement, dated June 5, 2000, at
HUMAN EMBRYONIC STEM CELLS (hESC): Criteria for federal funding of research on hESCs can be found at http://stemcells.nih.gov/index.asp and at http://grants.nih.gov/grants-guide/notice-files/NOT-OD-02-005.html. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (see http://stemcells.nih.gov/registry/). It is the responsibility of the applicant to provide, in the project description and elsewhere as appropriate, the official NIH identifier(s) for the hESC line(s) to be used in the proposed research. Applications that do not provide this information will be returned without review.

PUBLIC ACCESS TO RESEARCH DATA THROUGH THE FREEDOM OF INFORMATION ACT: The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm.

Applicants are required to place data collected under this RFA in the National Alzheimer’s Disease Coordinating Center, which can provide protections for the data and manage the distribution for an indefinite period of time. The application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

STANDARDS FOR PRIVACY OF INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION: The Department of Health and Human Services (DHHS) issued final modification to the “Standards for Privacy of Individually Identifiable Health Information”, the “Privacy Rule,” on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR). Those who must comply with the Privacy Rule (classified under the Rule as “covered entities”) must do so by April 14, 2003 (with the exception of small health plans which have an extra year to comply).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on “Am I a covered entity?” Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants-guide/notice-files/NOT-OD-03-025.html.

URLs IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.
HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This RFA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople/.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance at http://www.cfda.gov/ and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284 and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and to discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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NIH Funding Opportunities and Notices

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