

2008 RESEARCH GRANTS PROGRAM

REQUEST FOR APPLICATIONS

ISSUED MARCH 3, 2008

Established in 1987, the CFIDS Association of America is the world's leading organization working to conquer chronic fatigue syndrome (CFS). The Association works toward this mission by building recognition of CFS as a serious, widespread medical disorder; securing a meaningful response to CFS from the federal government; stimulating high quality CFS research; improving health care providers' abilities to detect, diagnose and manage CFS; and providing information to persons with CFS and enabling the CFS community to speak with a collective voice.

The first program funded by the Association was its research grant program. Since 1987 the Association has provided nearly \$5 million in direct support of CFS research studies, has hosted scientific symposia and has cosponsored meetings to identify promising areas of investigation. To meet the unequivocal need for a more robust scientific enterprise for CFS, in late 2007 the CFIDS Association's Board of Directors announced the Campaign to Accelerate CFS Research to fuel a more intensive search for biomarkers, better diagnostics and more effective treatments.

The current purpose of the CFIDS Association's research program is to accelerate progress toward accurate diagnosis and effective treatment of CFS by directly supporting research studies, facilitating collaboration among investigators and pursuing increased investment in CFS research by public, private and commercial institutions.

Executive Summary

This Request for Applications (RFA) solicits research proposals that will advance the discovery of biomarkers and methods for early detection, objective diagnosis and effective treatment of CFS.

- The CFIDS Association of America intends to commit approximately \$600,000 to this RFA for award of successful applications responsive to this announcement.
- Interested investigators are invited to submit a Letter of Intent (LOI) in English using the form provided at: <http://www.cfids.org/profresources/loi.doc>. The deadline for receipt of the fully completed LOI is 17:00 (U.S. Eastern time) on April 14, 2008. Investigators are expected to adhere to the LOI format, provide all requested information and are limited to five pages in length (including budget) plus two additional pages for supporting documentation and/or pilot study data. Other formats or attachments beyond the stated page limit will not be evaluated. Letters of Intent and allowable attachments should be submitted in a single electronic portable document format (PDF) file to research@cfids.org.
- Investigators who submit LOIs that describe projects determined to fall within the funding priorities and budgetary guidelines of this RFA and meet all other eligibility

guidelines will be invited to submit a comprehensive research grant application. Notification of the outcome of the review of LOIs will be made by April 21, 2008. Full applications will be due by 17:00 (U.S. Eastern time) on July 14, 2008.

- Awards issued under this RFA are contingent upon the availability of funds and the submission of a sufficient number of meritorious applications. Funding decisions will be communicated to applicants by September 30, 2008 and may be subject to conditions identified in the review process that will be required to be satisfied in order for funding approval to be conferred.
- It is anticipated that 6-8 awards will be issued under this RFA. The earliest date on which funding will begin is November 1, 2008.
- The maximum award is \$100,000 in total costs. Research grants are generally made to cover the direct costs of such items as salaries for professional and technical personnel, patient costs, equipment, supplies, travel to present findings at research meetings and other miscellaneous items. Institutional indirect costs cannot exceed 10%.
- The maximum term of awarded grants will be 18 months. A timeline for the proposed project is required as part of the LOI.
- There is no limit to the number of applications that an institution/organization may submit in response to this RFA.
- Applications may be submitted by nonprofit, public and commercial institutions with no restrictions as to geographic location.

Nature of the Research Opportunity

With more than 3,500 peer-reviewed biomedical publications since 1987 and \$187 million spent by the U.S. government on CFS research since 1990, there is a tremendous body of evidence on which to base current funding priorities for CFS. To identify funding gaps and high-priority research directions, the CFIDS Association of America conducted an examination of the peer-reviewed literature, reviewed documents produced by expert panels convened by U.S. government agencies and performed an informal inventory of research being supported worldwide. This examination led to the issue of this RFA soliciting proposals aimed at discovering biomarkers and advancing methods for early detection, objective diagnosis and effective treatment of CFS. Knowledge acquired from studies funded under this RFA will be used to augment the evidence base for clinical practice and health policy (i.e., insurance reimbursement, documentation of vocational disability, etc.). This RFA is the first in a series of requests to be issued under an expanded research program launched by the CFIDS Association of America in November 2007. The timing of and priorities for future RFAs will depend on evolving scientific opportunities and budgetary factors.

Research Goals and Objectives

The objective of this RFA is to solicit proposals for scientifically sound, original and innovative research that will advance the discovery of biomarkers and methods for early detection, objective diagnosis and effective treatment of CFS. Topics of specific interest include, but are not limited to, proposals for hypotheses that may lead to identification of:

- Surveillance and screening markers and/or strategies for detecting CFS before symptoms present, when symptoms first present (at acute onset, to distinguish CFS from other conditions) or at any other stage in the natural history of the illness.

- Known and novel infectious triggers for CFS, including in vitro and animal model systems and computer simulations of infection and/or immune response coupled with laboratory data that will yield markers for biological conditions that result in the individual's inability to recover from the illness arising from an acute infection.
- Laboratory, clinical, imaging or genomic (gene expression profiling, multigene test panels, etc.) markers that can be used to objectively diagnose CFS.
- Markers and/or strategies for objective identification of CFS subtypes that will advance diagnosis and therapy.
- Markers, surrogate endpoints or clinical endpoints that reproducibly and reliably quantify and predict the clinical effects of specific treatments.
- Effective therapeutic approaches to symptom management or underlying pathophysiology, including exploration of existing, orphan or novel drug families.
- Markers and/or strategies to predict CFS vulnerability and disease risk.

Proposals that leverage existing resources and infrastructures for sample collection and data management/analysis are particularly encouraged. Cooperative research mini-networks that link experienced CFS researchers and clinicians to investigators in other areas relevant to CFS are highly encouraged, as well. Applicants are encouraged to focus hypotheses on body systems known to be important in the biology of CFS including the hypothalamic-pituitary-adrenal (HPA) axis, immune system and autonomic nervous system. Explorations of novel subtypes of CFS are welcomed. For example, subtypes characterized by results of the FDA-approved pharmacogenomic test for drug metabolism (AmpliChip Cytochrome P450) have the potential to enhance treatment decision-making with respect to certain drugs frequently prescribed for CFS. Proposals that demonstrate strong potential to augment the evidence base for clinical practice and health policy (i.e., insurance reimbursement, documentation of vocational disability, etc.) will be given additional weight.

Instructions to Interested Investigators

Eligibility: Letters of Intent may be submitted by nonprofit, public and commercial institutions with no restrictions as to geographic location. If invited to submit a full research application, the applicant's institution will be required to demonstrate that it is a viable ongoing concern with which the Association can confidently enter into a granting relationship. All financial information will be kept strictly confidential in accordance with the confidentiality requirements stated herein.

Current members of the Association's Board of Directors and Scientific Advisory Committee are not eligible to receive Association research grants as principal investigators. However, they may serve as unpaid consultants or collaborators for Association-supported projects and may seek grants once their service on the Board or Scientific Advisory Committee has ended. Multidisciplinary and collaborative efforts are encouraged.

Postdoctoral fellows are eligible to submit Letters of Intent as principal investigators under this RFA. However, any postdoctoral fellow who applies is required to collaborate with an Administrative Principal Investigator (PI) who serves as the director of the laboratory or facility in which the research will be conducted. The Administrative PI will be responsible for assisting in providing all institutional documents required for the project and will be required

to sign any award. Responsibility for the planning, direction and execution of the proposed project will be solely that of the principal investigator. Training- or mentoring-only proposals are not appropriate for this RFA. For proposals involving postdoctoral fellowships as applicants, biographical information is required for both the postdoctoral fellow and the Administrative PI.

Letters of Intent Submission Procedures: Interested applicants should submit a Letter of Intent (LOI) in English due by 17:00 U.S. Eastern time on April 14, 2008. Please adhere to the format of the LOI (<http://www.cfids.org/profresources/loi.doc>), provide all requested information and limit the LOI to five pages (including budget). Supporting documentation and/or pilot study data can be provided but must be limited to 2 additional pages. Other formats or attachments beyond the stated page limit will not be evaluated.

Letters of Intent and allowable attachments should be submitted in a single electronic portable document format (PDF) file to research@cfids.org. If submission by postal mail is preferred/required by the PI/institution, please mail to: Research Program, CFIDS Association of America, PO Box 220398, Charlotte, NC 28222-0398. Electronic submissions must have a time/date stamp before 17:00 U.S. Eastern time on April 14, 2008. Postal submissions must be mailed in time to be received by April 14, 2008. LOIs received after the stated deadline will not be reviewed.

Investigators who submit LOIs that describe projects determined to fall within the funding priorities and budgetary guidelines of this RFA and meet all other eligibility guidelines will be invited to submit a comprehensive research grant application. Notification of the outcome of the review of LOIs will be made by April 21, 2008. Full applications will be due by 17:00 (Eastern time) on July 14, 2008.

Review of Complete Applications: Only those investigators invited to submit complete Research Grant Applications will be eligible for review of their applications. A Scientific Advisory Committee (SAC) comprised of scientific peers will review grant applications based on scientific merit. An Ad-Hoc Research Committee (AHRC) of the Association's Board of Directors will review the SAC's summary of the proposals, scores and reviews, and will supplement those recommendations with an evaluation of strategic issues related to funding and other factors relevant to the overall research program. The recommendations of both the SAC and the AHRC will be presented to the Executive Committee of the Association's Board of Directors for the purpose of making fully informed funding decisions about the applications.

Award of Grants: Grant decisions rest with the Executive Committee of the Association's Board of Directors, acting upon the recommendations of the SAC and AHRC. Funding may be contingent on the submission of additional information or revisions to the approved proposal.

Duplication of Support: When requests for the support of a project are submitted to more than one granting agency, support from the Association cannot duplicate other support. However, Association support is permitted to supplement support from other institutions.

Funds Available: Funds of up to \$600,000 have been budgeted for this program in 2008-09; however, awards pursuant to this RFA are contingent upon the availability of funds and the

receipt of a sufficient number of applications of high scientific merit that meet the requirements of this RFA. Applicants may request a project period of up to 18 months and maximum total budget of \$100,000 including direct costs and indirect costs. Indirect expenses for funded grants are capped at 10% of the total grant award. In the event of collaboration between multiple institutions, indirect costs are only paid once – either to the PI's institution as a percentage of total direct costs or, in the case of multiple PIs and multi-site studies, one institution will be assigned as the administrative center and will receive and be responsible for distributing funds including indirect costs. In no case may the total of all indirect costs paid exceed 10% of the total award.

Confidentiality of Information: In processing and reviewing Letters of Intent or full applications, the Association will use its best efforts to not disclose confidential or proprietary information submitted. Members of the Association's Board of Directors, the Ad Hoc Research Committee (comprised of Board members and Association staff) and the external Scientific Advisory Committee are required to sign non-disclosure agreements. However, the Association has no other mechanisms to maintain or guarantee the confidentiality of information, and as a not-for-profit corporation, does not have the financial resources to: (a) sustain liability for disclosure of information, nor (b) institute mechanisms to maintain the confidentiality of information. Submission of a Letter of Intent is deemed to verify acceptance of these provisions.

The CFIDS Association of America treats all Letters of Intent, applications, financial information, research projects and associated research information (collectively, the "Confidential Information") in confidence using no less than reasonable care in protecting such Confidential Information from disclosure to third parties who do not participate in the grant review process. All Confidential Information will be used by the Association and its grant reviewers only internally for the purposes of reviews and assessments, and will be shared only in accordance with its sharing policy stated herein. Notwithstanding the Association's and its reviewers' obligations regarding such Confidential Information, such obligations cover any information retained in their unaided memories and may not be used without the permission of the disclosing party. Notwithstanding the foregoing, the obligations governing the disclosure and use of Confidential Information do not apply with respect to Confidential Information that it can be demonstrated:

- a) was generally known to the public prior to the effective date of this RFA; or
- b) becomes generally known to the public through no unlawful or unauthorized act of omission by any recipient of Confidential Information, or in violation of this RFA; or
- c) was independently developed by any recipient prior to the effective date of this RFA; or
- d) was disclosed to a recipient by a third party who has the right to make such disclosure.

If any recipient of Confidential Information is requested to produce any of the Confidential Information pursuant to a legal or governmental proceeding, such recipient shall give the applicant or other owner of such Confidential Information (the "Discloser") as much prior notice of such requirement as is reasonably practicable under the circumstances and shall use its reasonable efforts to assist the Discloser of such Confidential Information in objecting to such request. If a recipient is compelled to disclose any of the Confidential Information pursuant to such legal or governmental proceeding, such recipient shall use its reasonable efforts to assist Discloser in obtaining confidential treatment for such Confidential Information, will disclose only that portion of the Confidential Information which is responsive to the order,

and will provide the Discloser with any copies of Confidential Information so disclosed; provided that such Confidential Information shall remain confidential until it falls into one of the categories specified above.

Conflicts of interest: Principal investigators and their paid collaborators submitting applications to this RFA will be excluded from serving as reviewers on their proposal. However, non-applicants who are invited to serve as reviewers may still have a conflict of interest that arises during the grant review process. A reviewer is judged to have a conflict of interest if (1) he or she is a collaborator, subcontractor and/or consultant with an investigator on the grant application; (2) the application is from the reviewer's own institution, regardless of whether or not the reviewer has had any involvement in preparing the application; (3) the reviewer, his/her immediate family or close professional associate(s) has a financial or vested interest in the outcome of the proposed research (even if no significant involvement is apparent in the proposal being considered); or (4) the reviewer has been involved in discussions regarding the application, is a provider of services, cell lines, reagents or other materials, or is the author of a letter of reference for the applicant.

When a conflict of interest is deemed to be present, the reviewer will be ineligible to review the proposal. Reviewers are also urged to avoid any actions that might give the appearance that a conflict of interest exists, even though he or she believes there may not be an actual conflict of interest.

Requirements for Funded Grants: Those investigators whose projects described in the Letter of Intent are deemed to be responsive to the research objectives of the RFA will receive a full grant application and a set of the Association's Policies Governing the Award of Research Grants. It is important for those submitting Letters of Intent to understand at the outset of the application process that support for approved applications will require the Principal Investigator and his/her institution to agree to:

- submit detailed progress reports at predetermined intervals once funding begins;
- participate in assessment conferences at predetermined intervals once funding begins;
- submit detailed financial reports on expenditures related to the grant at predetermined intervals once funding begins; and
- publish the results of funded research as rapidly as possible in the open scientific literature indexed for MEDLINE, consistent with high standards of scientific excellence and rigor, and to include acknowledgement of the funding provided by the CFIDS Association of America in all manuscripts and publications resulting from its support.

Non-compliance with any of these requirements may result in suspension of funding, revocation of the award and/or ineligibility for future support. Letters of Intent submitted by former Association grantees will be screened on the basis of how well the PIs met reporting and publication guidelines in force at the time of their earlier award(s).

Important Dates:

April 14, 2008	Deadline for Letters of Intent
April 21, 2008	Invitations issued to submit full applications
July 14, 2008	Deadline for full applications
September 30, 2008	Applicants informed of funding decisions (anticipated)

November 1, 2008

Earliest date on which funding may begin

Please direct inquiries regarding this Request for Applications to:

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Scientific Director
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PO Box 220398
Charlotte, NC 28222-0398
E-mail: research@cfids.org
Web: www.cfids.org

RFA: <http://www.cfids.org/profresources/2008rfa.asp>
LOI Form: <http://www.cfids.org/profresources/loi.doc>