

## Appendix C-1

### DoD BAA Solicitation

PART: U.S. GOVERNMENT PROCUREMENTS (MODIFICATION)

SUBPART: SERVICES

CLASSCOD: A--Research and Development

OFFADD: DIRECTOR, USAMRAA, 820 CHANDLER ST, FORT DETRICK MD 21702-5014

SUBJECT: A--A--PERSIAN GULF WAR ILLNESS RESEARCH

SOL CBD700-0000-0001

POC Contracting Officer Craig D. Lebo (301) 619-2036 (Site Code DAMD17)

DESC: The U.S. Army Medical Research and Acquisition Activity previously announced in the Commerce Business Daily the interest in obtaining proposals for the conduct of research in the area of Persian Gulf War Illnesses (see CBD Issue PSA #1738, dated December 10, 1996 and CBD Issue PSA #1761, dated January 14, 1997). These previous Department of Defense announcements, which solicited research proposals on four topics related to Persian Gulf War Illnesses are modified as indicated below with due dates as follows: (1) Determine the feasibility of epidemiological studies in human subjects, including those thought to be near Kamisayah, Iraq during the first two weeks of March, 1991 or (2) Conduct animal studies, designed to assess the possible long-term or delayed clinical effects of low level or subclinical exposures to chemical warfare agents. Additional details concerning these two topics are provided in the first announcement (CBD Issue PSA #1738, dated December 10, 1996). There is approximately \$2.0M available for this effort and proposals will be considered from federal and nonfederal agencies. Proposals must be received NLT 4:00 p.m. EST, 19 February 1997. (3) Investigation of causal relationships between illnesses and symptoms among Gulf War veterans and possible exposures to hazardous material; chemical warfare agents; stress; potentially hazardous combinations of inoculations (i.e., anthrax and botulinum

toxin) and investigational new drugs (i.e., pyridostigmine bromide) during military service in the Southwest Asia theater of operations during the Persian Gulf War. Approximately \$9.5M is available only to principal investigators and institutions independent of the Federal Government in accordance with the provisions of the Byrd Amendment. Proposals must be received NLT 4:00 p.m. EST, 11 March 1997. (4) Studies of historical war syndromes, including investigation of factors which create a confluence of cognitive, emotional and physical factors to produce chronic, non-specific symptoms and physiological outcomes (e.g., neurologic, immunologic and endocrine responses). There is approximately \$5M available for proposals from federal and nonfederal agencies. Proposals must be received NLT 4:00 p.m. EST, 30 April 1997. Large scale epidemiological studies must include provisions for scientific and public advisory committees as recommended by the Presidential Advisory Committee on Gulf War Veterans' Illnesses and Persian Gulf Veterans Coordinating Board. Research proposals are customarily in two to four year durations. Proposals should be submitted in accordance with Broad Agency Announcement 95-1 which is available on the internet. The web site is: <http://www.usamraa.army.mil>. Send proposals to: Commander, U.S. Army Medical Research and Materiel Command, ATTN: MCMR-AAA, Fort Detrick, MD 21702-5012.

CITE: (I-029 SN026078)

Appendix C-2

CDC Call for Proposals

[Federal Register: May 5, 1997 (Volume 62, Number 86)]

[Notices]

[Page 24449-24453]

From the Federal Register Online via GPO Access [wais.access.gpo.gov]

[DOCID:fr05my97-80]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

[Announcement 748]

Cooperative Agreements to Conduct Studies of Illnesses Among  
Persian Gulf War Veterans; Notice of Availability of Funds for Fiscal  
Year 1997

Introduction

The Centers for Disease Control and Prevention (CDC) announces the availability of fiscal year (FY) 1997 funds for a cooperative agreement to conduct studies of illnesses among Persian Gulf War (PGW) veterans. CDC is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a national activity to reduce morbidity and mortality and improve quality of life. This announcement is related to the priority area of Environmental Health. (For ordering a copy of "Healthy People 2000" see the section WHERE TO OBTAIN ADDITIONAL INFORMATION.)

Authority

This program is authorized under the Public Health Service Act, section 301 (42 USC 241).

Eligible Applicants

Eligible applicants include all nonprofit and for-profit organizations. Thus, State and local health departments, State and local governmental agencies, universities, colleges, research institutions, hospitals, other public and private non-profit organizations, including small, minority and/or woman-owned businesses are eligible to apply.

Note: An organization described in section 501(c)(4) of the Internal Revenue Code of 1986 which engages in lobbying activities shall not be eligible to receive Federal funds constituting an award, grant, contract, loan, or any other form.

Applications will be considered for funding to conduct studies in one or more programmatic interest areas. Applicants interested in conducting more than one study must submit a separate application for each. If a single study addresses more than one programmatic interest area, only one should be identified as the primary interest area. The programmatic interest area should be clearly indicated for each study.

Smoke-Free Workplace

CDC strongly encourages all grant recipients to provide a smoke-free workplace and promote the non-use of all tobacco products and Pub. L. 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities that receive Federal funds in which education, library, day care, health care, and early childhood development services are provided to children.

## Availability of Funds

Approximately \$1.2 million will be available in FY 1997 to fund up to two cooperative agreements. It is expected that the average award will be up to \$600,000 (direct and indirect costs). It is expected the award will begin on or about September 1, 1997, and will be made for a 12-month budget period within a project period of up to three years. The funding estimate is subject to change based on the availability of funds. Applications which request more than the \$600,000 per year cap will be returned to the applicant as non-responsive. Continuation awards within the project period will be made on the basis of satisfactory progress and the availability of funds. Applicants may enter into contracts, including consortia agreements (as set forth in the PHS Grants Policy Statement) as necessary to meet the requirements of the program and strengthen the overall application.

## Use of Funds

### Restrictions on Lobbying

Applicants should be aware of restrictions on the use of HHS funds for lobbying of Federal or State legislative

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bodies. Under the provisions of 31 USC Section 1352 (which has been in effect since December 23, 1989), recipients (and their subtier contractors) are prohibited from using appropriated Federal funds (other than profits from a Federal contract) for lobbying Congress or any Federal agency in connection with the award of a particular contract, grant, cooperative agreement, or loan. This includes grants/cooperative agreements that, in whole or in part, involve conferences for which Federal funds cannot be used directly or indirectly to encourage participants to lobby or to instruct participants on how to lobby.

In addition, the FY 1997 HHS Appropriations Act, which became effective October 1, 1996, expressly prohibits the use of 1997 appropriated funds for indirect or "grass roots" lobbying efforts that are designed to support or defeat legislation pending before State legislatures. This new law, Section 503 of Pub. L. No. 104-208, provides as follows:

Sec. 503(a) No part of any appropriation contained in this Act shall be used, other than for normal and recognized executive-legislative relationships, for publicity or propaganda purposes, for the preparation, distribution, or use of any kit, pamphlet, booklet, publication, radio, television, or video presentation designed to support or defeat legislation pending before the Congress, \* \* \* except in presentation to the Congress or any State legislative body itself.

(b) No part of any appropriation contained in this Act shall be used to pay the salary or expenses of any grant or contract recipient, or agent acting for such recipient, related to any activity designed to influence legislation or appropriations pending before the Congress or any State legislature.

Department of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 1997, as enacted by the Omnibus Consolidated Appropriations Act, 1997, Division A, Title I, Section 101(e), Pub. L. No. 104-208 (September 30, 1996).

## Background and Definitions

### Background

Between August 1990 and July 1991, approximately 697,000 U.S. military personnel were deployed to the Persian Gulf as part of Operations Desert Shield and Desert Storm. Shortly after returning to the U.S., many Persian Gulf War (PGW) veterans began to report a variety of symptoms which they suspect may be related to their military service in the Persian Gulf. The symptoms most commonly reported among PGW veterans have been fatigue, musculoskeletal complaints, and cognitive dysfunction. A variety of possible etiologies for PGW veterans' illnesses have been postulated. The possible etiologies have included infectious agents (e.g., leishmaniasis), environmental and ambient pollutants (e.g., sand, petroleum products, pesticides, Chemical Agent Resistant Coating (CARC) paint,

and smoke from oil-well fires), medical prophylaxes (e.g., anthrax and botulinum toxin vaccines, and pyridostigmine bromide), depleted uranium munitions, and biologic and chemical warfare agents.

Much of the current knowledge on the prevalence of illnesses among Gulf War veterans comes from self-referred registries established by the Department of Defense (DOD) and the Department of Veterans Affairs (VA). The DOD and VA Persian Gulf registries have added useful information on the spectrum of health concerns among Persian Gulf War veterans. The most recent analysis of DOD's Comprehensive Clinical Evaluation Program (CCEP) data on 18,598 Gulf War veterans found no evidence for a unique illness affecting Gulf War veterans. Instead CCEP participants reported a wide variety of symptoms affecting multiple organ systems. The most common primary diagnoses were psychological conditions (ICD-9-CM Codes 290-319--18.4%); symptoms, signs, and ill-defined conditions (ICD-9-CM Codes 780-700--17.9%); and musculoskeletal system diseases (ICD-9-CM Codes 710-739--18.3%). However, these registries are of limited value as a database for determining the actual incidence and prevalence of illnesses because they are not representative of the population of Persian Gulf War veterans.

In December 1994, the National Center for Environmental Health (NCEH) initiated, through the cooperative agreement mechanism, a population-based epidemiological study to evaluate the health consequences of a sample of PGW veterans. The purpose of this study was to compare the prevalence of self-reported symptoms and illnesses among PGW veterans from Iowa with military personnel from Iowa who were not deployed to the Persian Gulf. The study found that PGW veterans from Iowa were more likely than those who did not serve in the Gulf War to report symptoms suggestive of cognitive dysfunction, depression, chronic fatigue, post-traumatic stress disorder, respiratory illness (specifically asthma and bronchitis), fibromyalgia, alcohol abuse, generalized anxiety disorder, and sexual discomfort. The conditions identified in this study appear to have had a measurable impact on the functional activity and daily lives of these Persian Gulf War veterans.

Among PGW veterans, minimal differences were observed between the National Guard or Reserve troops and the regular military personnel, indicating that all military personnel, regardless of type of military service, were affected by deployment to the Persian Gulf.

Findings from this study established the need to investigate further the causes, clinical nature, and public health implications of the higher rates of self-reported health problems of PGW veterans. More objective clinical measurement of the specific conditions identified in this study should be addressed to determine the underlying illnesses, medical conditions, or other concerns that might be related to these self-reported conditions.

The approach used in the Iowa study of PGW veterans was to assess the prevalence of known clinical entities. Other studies have used a data driven approach for assessing health differences between PGW veterans and other military populations. For example, in an investigation of PGW veterans from a Pennsylvania Air National Guard unit, investigators used factor analysis to develop a case definition of illness among PGW veterans. Additional research is needed to validate the case definition developed in the Pennsylvania study and to determine if data driven definitions or the use of known clinical diagnoses better characterizes illnesses among PGW veterans.

## Definitions

**PGW veteran:** A PGW veteran is defined as any regular duty or National Guard or reserve member who deployed to the Persian Gulf for some period from August 1, 1990, through July 31, 1991.

**PGW illnesses:** PGW illnesses are defined as any adverse health outcome that is more prevalent among military personnel who deployed to the Persian Gulf than among non-deployed military personnel.

**PGW illnesses research projects:** PGW illnesses research projects are defined as research designed to evaluate the health impact of military service in the Persian Gulf War.

**Veterans Service Organization:** A congressionally chartered group of men and women who have served their country in uniform during either peace or war. Examples of veterans service organizations include but are not limited to, Paralyzed Veterans of America, Disabled American

Veterans,

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American Legion, Veterans of Foreign Wars, and American Veterans.

## Purpose

The purpose of this program is to:

- A. Build the scientific base for determining the nature and etiology of illnesses among PGW veterans.
- B. Evaluate the role of stress-related disorders on the current health status of PGW veterans.
- C. Determine if PGW veterans are experiencing a unique illness or are experiencing a higher prevalence of a variety of known clinical entities.
- D. Determine the health impact of military deployment to the Persian Gulf.
- E. Assess the best approach for developing a case-definition for illness among PGW veterans.

## Program Requirements

In conducting activities to achieve the purpose of these cooperative agreements, the recipient will need to meet the requirements and is responsible for the activities under A. (Recipient Activities). CDC will be responsible for the activities under B. (CDC Activities).

### A. Recipient Activities

1. Collaborate with CDC and the appropriate State or local Health Department during the development and conduct of the study, and dissemination of the results.
2. Obtain approval of study procedures by an appropriate institutional review committee.
3. Develop and pilot test the study protocol and data collection instruments.
4. Provide timelines for completing all components of the study.
5. Assure and maintain the confidentiality of all study participants.
6. Conduct the analysis, interpretation, presentation, and reporting of the study findings in collaboration with CDC.
7. Upon completion of the study, provide CDC an electronic version of the final data set stripped of personal identifiers.
8. Act as the focal point for the development and dissemination of media releases, reports and publications.
9. Establish an independent Public Advisory Committee comprised of representatives from the State or local Health Department, local Veterans' Service Organizations, PGW veterans, other affected parties, and CDC.

### B. CDC Activities

1. Serve as collaborators in the development, analysis, and conduct of the study, as well as reporting and publishing of study findings.
2. Provide expert review, and comment on all study protocols, data collection instruments, analysis plans, media releases, draft and final reports, and publications generated by the recipient.
3. Serve as the principal point of contact with the Department of Defense, Department of Veterans Affairs, and other Federal agencies to secure names and locating information for the study participants.
4. Coordinate the related activities of the involved Federal legislative bodies, agencies, and national veterans service organizations.
5. Serve as a member on the Public Advisory Committee.

## Programmatic Priorities

Applicants must propose research that enhances the understanding of conditions and symptoms reported to be more prevalent among PGW veterans, or adds to the scientific knowledge needed to develop a case definition of illness among PGW veterans.

Enhance the understanding of conditions and symptoms reported to be more prevalent among PGW veterans. Conduct research on conditions known to be more prevalent among PGW veterans. These conditions include cognitive dysfunction, depression, anxiety disorders, chronic fatigue, post-traumatic stress disorder, other stress-related disorders, respiratory illness (specifically asthma and bronchitis), fibromyalgia, and alcohol abuse. These

studies should include appropriate clinical evaluation in order to validate the diagnosis, assessment of the course of the illness among PGW veterans, assessment of risk factors, and assessment of the impact of the illness on functional status.

Characterization of illnesses among PGW veterans. Conduct studies focusing on development of a case-definition for illness among PGW veterans. These studies should evaluate whether symptoms reported among PGW veterans represent a unique illness or are better characterized by existing clinical entities. This should include a comparison of data driven case-definitions and use of known clinical diagnoses in order to determine the best way to characterize illness among PGW. It may also include validation of previous data driven case definitions of illnesses among Gulf War veterans.

## Reporting Requirements

An original and two copies of the Financial Status Report (FSR) are due within 90 days after the end of each budget period. An original and two copies of the technical semi-annual reports, using the format below, are due 30 days after the end of each quarter to the CDC Grants Management Officer.

The semi-annual progress report must include the following for each program, function, or activity involved:

### A. Highlights

Discuss issues and activities that had significant impact on the program and that you wish to bring to the attention of CDC.

Discuss any changes in program personnel, especially changes affecting those involved with the grant.

### B. Objectives and Achievements

List major objectives and discuss your progress in meeting these objectives.

Summarize your accomplishments for the period and for the budget year.

Mention anything that either helped or hindered your achieving these objectives.

## Application Content

All applications must be developed in accordance with the instructions that are contained in this program announcement, Form PHS 398, ERRATA sheet, and the instructions outlined in the following section headings. Applicants must identify in a cover letter one of the topics previously outlined under the heading Programmatic Priorities upon which their project is focused.

The following are application requirements:

1. A principal investigator who has conducted research, published the findings, and has specific authority and responsibility to carry out the proposed project.

2. Demonstrate the commitment of veterans service organizations to serve on a Public Advisory Committee by securing letters of support from at least three veterans' service organizations, as described under the heading, "Definitions."

3. The applicant must provide a one page abstract outlining the plans, objectives, and expected outcomes of the proposed research.

Provide a succinct but informative response to each requirement. Your response must not exceed 2 pages (letters of support may be referenced to where they are located in the application). This response must appear as the first 2 pages of the text of your application and be titled "Program Requirements." An affirmative response to each question is required to qualify for further review. Those that do not respond will be determined as non-responsive and will be returned to the applicant.

Applications for these cooperative agreements should include:

### A. Description of the Problem to be Addressed



1. The project's focus that justifies the research need and describes the scientific basis for the research, the expected outcome, and the relevance of the findings to reduce morbidity among PGW veterans.

2. Describe the issues related to requirements, problems, complexities, and interactions required in developing the study.

3. Discuss past experiences with similar projects.

#### B. Goals and Objectives

1. For each of the elements (item C below) provide specific, measurable, and time-framed objectives that are consistent with the applicants proposed theme, purpose, and objectives.

#### C. Program Plan

1. A detailed plan describing the elements of the research project and the methods by which the objectives will be achieved, including their sequence.

2. Discuss the administrative and scientific capacity critical to the development and conduct of the study.

3. A description of the involvement of the State or local Health Department, veteran service organizations, and other affected parties to ensure they have ample input during all phases of the study. It should include commitments of support and a clear statement of their roles.

4. Describe the State agency linkages and support that will be used during the development, conduct, and conclusion of the study.

#### D. Management and Staffing Plan

1. A description of the role and responsibilities of the project's principal investigator. Describe research background, publications, specific authority and responsibilities to carryout the proposed project.

2. A description of all the project staff regardless of their funding source. It should include their title, qualifications, experience, percentage of time each will devote to the project, as well as that portion of their salary to be paid by the grant.

3. A description of all key contractor staff, their role in the study, and their resumes.

4. A description of those activities related to, but not proposed to be supported by the grant.

#### E. Evaluation

Describe how progress toward meeting the study objectives will be evaluated. A comprehensive evaluation plan is an essential component of the application.

#### F. Budget

1. A detailed first year budget for the project with future annual projections.

2. A budget projection that clearly separates and distinguishes direct and indirect costs.

An applicant organization has the option of having specific salary and fringe benefit amounts for individuals omitted from the copies of the application which are made available to outside reviewing groups. To exercise this option: on the original and five copies of the application, the applicant must use asterisks to indicate those individuals for whom salaries and fringe benefits are not shown; the subtotals must still be shown. In addition, the applicant must submit an additional copy of page four of Form PHS-398, completed in full, with the asterisks replaced by the salaries and fringe benefits. This budget page will be reserved for internal staff use only.

#### Evaluation Criteria

Upon receipt, applications will be screened by CDC staff for completeness and responsiveness. Incomplete applications and applications that are not responsive will be returned to the applicant without further consideration. Applications which are complete and responsive will be evaluated by an independent Special Emphasis Panel (SEP) according to the following criteria:

1. Understanding the Problem (5 points).

The background of the proposal, i.e., the basis for the present proposal, the critical evaluation of existing knowledge, and specific identification of the knowledge gaps which the proposal is intended to fill.

2. Measurable Objectives (10 points).

Specific, measurable, and time-framed objectives that are consistent with the applicants proposed theme, purpose, and hypotheses to be tested.

3. Proposed Plan (75 points).

- a. The significance and originality from a scientific or technical standpoint of the specific aims of the proposed research, including the adequacy of the theoretical and conceptual framework for the research.

(5 points)

b. The overall match between the applicant's proposed theme and research objectives, and the program priorities as described under the heading "Programmatic Priorities." (15 points)

c. The adequacy of the proposed research design, approaches, and methodology to carry out the research, including quality assurance procedures, plan for data management, and statistical analysis plans. The degree to which the applicant has met the CDC Policy requirements regarding the inclusion of women, ethnic, and racial groups in the proposed research. This includes: (a) The proposed plan for the inclusion of both sexes and racial and ethnic minority populations for appropriate representation; (b) the proposed justification when representation is limited or absent; (3) a statement as to whether the design of the study is adequate to measure differences when warranted; and (4) a statement as to whether the plans for recruitment and outreach for study participants include the process of establishing partnerships with community(ies) and recognition of mutual benefits will be documented. (25 points)

d. The degree of commitment and cooperation of other interested parties as evidenced by letters of commitment detailing the nature and extent of the involvement. (10 points)

e. Qualifications, adequacy, and appropriateness of personnel to accomplish the proposed activities. Demonstrated experience in conducting, evaluating, and publishing research on the health effects of military service on the applicants project team. (10 points)

f. Adequacy of existing and proposed facilities and resources. (10 points)

4. Proposed Evaluation Plan (10 points).

The extent to which the evaluation plan will allow for the measurement of progress toward the achievement of the stated objectives.

5. Budget (Not Scored).

The reasonableness of the proposed budget to the proposed research. Continuation awards within the project period will be made on the basis of the availability of funds and the following criteria:

1. The accomplishments reflected in the progress report of the continuation application indicate that the applicant is meeting previously stated objectives and timelines contained in the project proposal and satisfactory progress has been demonstrated through monitoring work-in-progress.

2. The objectives for the new budget period are realistic, specific, and measurable.

3. The methods described will clearly lead to achievement of these objectives.

4. The evaluation plan will allow management to monitor whether the methods are effective.

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5. The budget request is clearly explained, adequately justified, reasonable and consistent with the intended use of cooperative agreement funds.

Executive Order 12372 Review

Applications are not subject to the review requirements of Executive Order 12372.

Public Health System Reporting Requirements

This program is not subject to the Public Health System Reporting Requirements.

Catalog of Federal Domestic Assistance Number

The Catalog of Federal Domestic Assistance Number is 93.283.

Other Requirements

Paperwork Reduction Act

Projects that involve the collection of information from 10 or more individuals and funded by these cooperative agreements will be subject to approval by the Office of Management and Budget (OMB) under the Paperwork Reduction Act.

#### Human Subjects

If the proposed project involves research on human subjects, the applicant must comply with the Department of Health and Human Services Regulations, 45 CFR Part 46, regarding the protection of human subjects. Assurance must be provided to demonstrate that the project will be subject to initial and continuing review by appropriate institutional review committees. The applicant will be responsible for providing assurance in accordance with the appropriate guidelines and forms provided in the application kit.

#### Women and Minority Inclusion Policy

It is the policy of the CDC to ensure that women and racial and ethnic groups will be included in CDC supported research projects involving human subjects, whenever feasible and appropriate. Racial and ethnic groups are those defined in OMB Directive No. 15 and include American Indian, Alaskan Native, Asian, Pacific Islander, Black and Hispanic. Applicants shall ensure that women, racial and ethnic minority populations are appropriately represented in applications for research involving human subjects. Where clear and compelling rationale exist that inclusion is inappropriate or not feasible, this situation must be explained as part of the application.

In conducting the review of applications for scientific merit, review groups will evaluate proposed plans for inclusion of minorities and both sexes as part of the scientific assessment and assigned score. This policy does not apply to research studies when the investigator cannot control the race, ethnicity and/or sex of subjects. Further guidance to this policy is contained in the Federal Register, Vol. 60, No. 179, Friday, September 15, 1995, pages 47947-47951.

#### Application Submission and Deadlines

##### A. Pre-application Letter of Intent

Although not a prerequisite of application, a non-binding letter of intent-to-apply is requested from potential applicants. The letter should be submitted to the Grants Management Specialist (whose address is reflected in section B, "Applications"). It should be postmarked no later than June 2, 1997. The letter should identify the announcement number, name the principal investigator, and specify the priority area of study the proposal addresses as outlined under the section Programmatic Priorities. The letter of intent does not influence review or funding decisions, but it will enable CDC to plan the review more efficiently, and will ensure that each applicant receives timely and relevant information prior to application submission.

##### B. Applications

Applicants should use Form PHS-398 (OMB No. 0925-0001 Revised 5/95) and adhere to the ERRATA Instruction Sheet for Form PHS-398 contained in the Grant Application Kit.

Please submit an original and five copies, on or before July 8, 1997 to: Lisa G. Tamaroff, Grants Management Specialist, Grants Management Branch, Procurement and Grants Office, Centers for Disease Control and Prevention (CDC), 255 East Paces Ferry Road, NE., Room 321, Atlanta, Georgia 30305, telephone (404) 842-6796 or internet: lgt1.cdc.gov.

##### C. Deadlines

1. Applications shall be considered as meeting a deadline if they are either:
  - A. Received at the above address on or before the deadline date, or

B. Sent on or before the deadline date to the above address, and received in time for the review process. Applicants should request a legibly dated U.S. Postal Service postmark or obtain a legibly dated receipt from a commercial carrier or the U.S. Postal Service. Private metered postmarks shall not be acceptable as proof of timely mailings.

2. Applications which do not meet the criteria above are considered late applications and will be returned to the applicant.

#### Where to Obtain Additional Information

To receive a complete program description, information on application procedures and application forms call (404) 332-4561. You will be asked to leave your name, address, and the telephone number and will need to refer to Announcement 748. Business management technical information may be obtained from Lisa Tamaroff, Grants Management Specialist, Grants Management Branch, Procurement and Grants Office, Centers for Disease Control and Prevention (CDC), 255 East Paces Ferry Road, NE., Mailstop E-13, Atlanta, GA 30305, telephone (404) 842-6796 or internet: lgt1.cdc.gov.

Programmatic technical assistance may be obtained from Phillip M. Talbot, Project Officer, Veterans' Health Activity, Division of Environmental Hazards and Health Effects, National Center for Environmental Health, Centers for Disease Control and Prevention (CDC), Mailstop F-28, 4770 Buford Highway, NE., Atlanta, Georgia 30341-3724, telephone (770) 488-7347, internet: pmt0.cdc.gov.

This and other CDC announcements are also available through the CDC homepage on the Internet. The address for the CDC homepage is <http://www.cdc.gov>.

CDC will not send application kits by facsimile or express mail.

Please refer to Announcement Number 748 when requesting information and submitting an application.

Potential applicants may obtain a copy of Healthy People 2000 (Full Report, Stock No. 017-001-00474-0) or Healthy People 2000 (Summary Report, Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC, 20402-9325, telephone (202) 512-1800.

Dated: April 29, 1997.

Joseph R. Carter,

Acting Associate Director for Management and Operations, Centers for Disease Control and Prevention (CDC).

[FR Doc. 97-11573 Filed 5-2-97; 8:45 am]

BILLING CODE 4163-18-P

## Appendix C-3

### VA Solicitations for Multi-Site Trials

VA CENTRAL OFFICE  
WASHINGTON, D.C.

PRIORITY

1/9/98

JOE GOUGH, M.A. 273-8248

DIRECTORS (00/151) ALVAMC

SUBJ: OFFICE OF RESEARCH AND DEVELOPMENT - PRIORITY ANNOUNCEMENT  
VA COOPERATIVE STUDIES PROGRAM (CSP)

JANUARY 9, 1998

OFFICE OF RESEARCH AND DEVELOPMENT LETTER

VA COOPERATIVE STUDIES PROGRAM  
REQUEST FOR APPLICATIONS - PERSIAN GULF WAR VETERANS' ILLNESSES RESEARCH

PURPOSE. THIS PROGRAM ANNOUNCEMENT IS TO SOLICIT SUBMISSION OF PLANNING REQUEST LETTERS FOR HYPOTHESIS-DRIVEN, MULTI-SITE, RANDOMIZED CLINICAL TRIALS TO EVALUATE PROPOSED TREATMENTS FOR ILLNESSES AMONG GULF WAR VETERANS RIGOROUSLY AND SYSTEMATICALLY. EMPHASIS IS PLACED ON WELL-DEFINED, CLINICALLY DIAGNOSED SUBPOPULATIONS OF GULF WAR VETERANS. THERAPEUTIC APPROACHES SHOULD EMPHASIZE THERAPIES OF POTENTIAL BENEFIT AND KNOWN RISK. PLANNING REQUEST SUBMISSIONS ARE OPEN TO ALL VA INVESTIGATORS BUT MUST BE RESPONSIVE TO THE CONTENT AREAS AND PARAMETERS OUTLINED IN THIS ANNOUNCEMENT.

BACKGROUND. IN AUGUST 1990, THE UNITED STATES BEGAN DEPLOYMENT OF TROOPS TO THE PERSIAN GULF AREA. APPROXIMATELY 697,000 MILITARY PERSONNEL SERVED IN SAUDI ARABIA, KUWAIT, IRAQ AND OTHER COUNTRIES IN THE PERSIAN GULF AREA. THE FIGHTING THAT TOOK PLACE FROM THE MIDDLE OF JANUARY 1991 UNTIL THE CEASE FIRE ON FEBRUARY 28, 1991 INCLUDED 40 DAYS OF AIR WARFARE AND FIVE DAYS OF GROUND COMBAT. WHILE THERE WERE RELATIVELY FEW COMBAT CASUALTIES AND LESS THAN 200 BATTLE DEATHS, GULF WAR VETERANS WERE SUBJECT TO A VARIETY OF ENVIRONMENTAL EXPOSURES, BOTH NATURAL AND MAN-MADE, THAT COULD HAVE POTENTIALLY HARMFUL EFFECTS ON EXPOSED INDIVIDUALS.

WITHIN MONTHS OF THEIR RETURN, A NUMBER OF GULF WAR VETERANS BEGAN TO EXPERIENCE A VARIETY OF SYMPTOMS, WHICH DO NOT EASILY FIT INTO WELL UNDERSTOOD DIAGNOSTIC CATEGORIES. THESE SYMPTOMS INCLUDE FATIGUE, MUSCULOSKELETAL PAIN, AND MEMORY PROBLEMS.

CONTENT AREAS. LISTED BELOW ARE GULF WAR ILLNESSES RESEARCH CONTENT AREAS APPROPRIATE FOR SUBMISSION OF A VA COOPERATIVE STUDY PLANNING REQUEST LETTER.

- TREATMENT TRIALS FOR DISORDERS INCLUDING CHRONIC FATIGUE SYNDROME (CFS) AND FIBROMYALGIA (FM) OR OTHER CLEARLY DEFINED MEDICAL SYNDROMES OR ILLNESSES AMONG SUBGROUPS OF GULF WAR VETERANS.

- TREATMENT TRIALS OF SUBGROUPS OF GULF WAR VETERANS WITH A DIAGNOSIS OF POST TRAUMATIC STRESS DISORDER (PTSD), SOMATOFORM DISORDER, OR OTHER PSYCHIATRIC DISORDERS.
- CANDIDATE TREATMENTS FOR RANDOMIZED CONTROLLED TRIALS OF OTHER WELL-DEFINED SUBPOPULATIONS OF GULF WAR VETERANS FOR WHOM PROOF OF POTENTIAL EFFICACY AND SAFETY HAVE BEEN DEMONSTRATED IN EITHER SINGLE OR MULTI-SITE EXPERIMENTAL TRIALS.

#### SPECIFICATIONS.

- THE PROPOSED STUDY MUST BE DRIVEN BY A SCIENTIFICALLY PLAUSIBLE RESEARCH HYPOTHESIS.
- THE STUDY MUST ADDRESS THE THERAPY OF INDIVIDUALS WHO MEET PUBLISHED CASE CRITERIA FOR THE DIAGNOSIS OF CHRONIC FATIGUE SYNDROME, FIBROMYALGIA, PTSD, OR OTHER CONDITIONS.
- AT LEAST 50% OF THE STUDY POPULATION MUST BE GULF WAR VETERANS.
- TREATMENT STRATEGIES MUST BE DEFINED EXPLICITLY, BE REPLICABLE BY OTHER HEALTH CARE PROVIDERS, AND POTENTIALLY AVAILABLE AT PARTICIPATING VA MEDICAL CENTERS. INTERVENTIONS INVOLVING DRUGS OR BIOLOGICS SHOULD INCLUDE ONLY AGENTS THAT ARE ALREADY LICENSED BY THE FDA.
- TREATMENT STRATEGIES MUST BE EVALUATED USING EXPERIMENTAL RESEARCH METHODS, INCLUDING RANDOMIZED ALLOCATION OF STUDY PATIENTS TO COMPETING THERAPIES.
- EXPLICIT PATIENT FOCUSED OUTCOMES MUST BE PROPOSED AND, FOR NON-FATAL OUTCOMES, VALIDATED INSTRUMENTS EMPLOYED.

#### APPLICATION PROCESS.

1. INTERESTED INVESTIGATORS SHOULD CONTACT JOE GOUGH, MA, COOPERATIVE STUDIES PROGRAM ANALYST AT (202) 273-8248 TO REQUEST A COPY OF INSTRUCTIONS FOR SUBMISSION OF A CSP PLANNING REQUEST. CSP PLANNING REQUESTS MAY BE SUBMITTED AT ANY TIME.
2. SUBMIT FIVE COPIES OF THE CSP PLANNING REQUEST AND CURRICULUM VITAE TO: VA HEADQUARTERS, COOPERATIVE STUDIES PROGRAM (124D), 810 VERMONT AVENUE, NW, WASHINGTON, DC 20420. ALL CSP PLANNING REQUESTS WILL BE REVIEWED BY AD HOC EXPERTS IN THE FIELD OF RESEARCH PROPOSED. NOTIFICATION OF THE PLANNING REQUEST REVIEW DISPOSITION WILL BE PROVIDED IN APPROXIMATELY ONE MONTH.
3. INVESTIGATORS WITH AN APPROVED CSP PLANNING REQUEST WILL BE ASSIGNED BY VA CSP HEADQUARTERS TO ONE OF THE FOUR VA COOPERATIVE STUDIES COORDINATING CENTERS FOR TECHNICAL ASSISTANCE AND GUIDANCE IN DEVELOPMENT OF A FULL STUDY PROTOCOL.

JOHN R. FEUSSNER, M.D.  
CHIEF RESEARCH AND DEVELOPMENT OFFICER

## Appendix C-4

### VA/DoD Request for Stress Related Proposals





DEPARTMENT OF VETERANS AFFAIRS  
Veterans Health Administration  
Washington DC 20420

IL 12-97-009

In Reply Refer To: 12

May 28, 1997

RESEARCH AND DEVELOPMENT LETTER

REQUEST FOR PROPOSALS FOR A VA - DOD COLLABORATIVE RESEARCH  
PROGRAM ON MILITARY OPERATIONAL STRESS-RELATED ILLNESSES

1. The Veterans Health Administration (VHA) announces a cooperative research program with the Department of Defense (DOD) for studies on the biological basis of Military Operational Stress-related Illnesses. Research proposals will be accepted from Department of Veterans Affairs (VA) investigators, DOD investigators, and VA - DOD collaborating investigators.
2. Chronic stress-related illness may be a consequence of military operations in which current and former active duty and reserve personnel have been involved such as activities in the Persian Gulf. Reported symptoms in operationally exposed individuals have included fatigue, headache, joint pain, and psychological conditions. Military operational stress-related disorders include, but are not limited to, post-traumatic stress disorder (PTSD) and fibromyalgia. In order to advance the treatment and prevention of stress-related illnesses, an understanding of the biological or chemical basis for stress disorders is essential. Therefore, further research is needed on the etiology, pathogenesis, and pathophysiology of traumatic and non-traumatic stress-related disorders. Treatment studies are not appropriate for submission in response to this solicitation. Topics which may be appropriate for proposals submitted in response to the Military Operational Stress-related Illnesses initiative include, but are not limited to:
  - a. The role of neurotransmitter, immunologic, and neuroendocrine dysregulation in the pathophysiology of stress related illnesses.
  - b. Neurotransmitter, immunologic, and neuroendocrine receptor dysregulation in stress related illnesses.
  - c. Characterization of heritability or identification of polymorphic markers associated with the control of stress response and PTSD.
  - d. Psychological and biomedical measurements for early identification of individuals at risk for stress related disorders.
  - e. Animal models to identify etiologic and pathogenic processes contributing to human chronic stress response disorders.
  - f. Imaging studies, including magnetic resonance imaging (MRI), magnetic resonance spectroscopy (MRS), functional magnetic resonance imaging (fMRI), magnetoencephalograph (MEG), single photon emission computed tomography (SPECT), and positron emission

IL 12-97-009

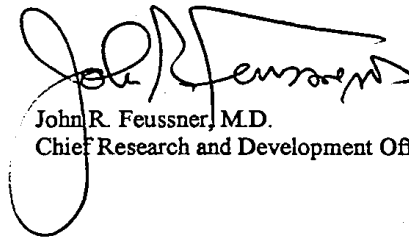
May 28, 1997

tomography (PET), to localize and quantify abnormal brain structure, function, and neurochemistry associated with stress response and PTSD.

3. Qualified independent VA and DOD investigators are invited to submit a Letter of Intent (LOI) for Merit Review proposals on military operational stress-related illnesses. VA investigators must be eligible for Medical Research Service funding before proposal submission. Investigators whose LOIs satisfy the criteria for the initiative will be invited to submit full proposals. Attachment A includes instructions for LOI preparation, general information about proposal submission, and a timetable for submission and funding.

4. Duration of proposals is up to 3 years. The total proposal budget for a 3 year proposal is limited to a maximum of \$300,000 for investigators at a single research site. Collaborative proposals with co-principal investigators at more than one site may request a maximum of \$600,000 for 3 years.

5. Questions may be directed to Peggy T. Swoveland, Ph.D., Coordinator, VA/DOD Collaborative Research Program, at 410-605-7132 or e-mail [pswovela@umabnet.ab.umd.edu](mailto:pswovela@umabnet.ab.umd.edu).



John R. Feussner, M.D.  
Chief Research and Development Officer

Attachment

DISTRIBUTION: CO: E-mailed 5/28/97  
FLD: VISN, MA, DO, OC, OCRO and 200 - FAX 5/28/97  
EX: Boxes 104, 88, 63, 60, 54, 52, 47 and 44 - FAX 5/28/97

ATTACHMENT A

FORMAT FOR PROPOSALS

1. **Instructions for Submission of Letter of Intent (LOI)**. The LOI is limited to two single-spaced typed pages providing an overview and description of the proposed project. Use only letter-quality print; do not use a dot matrix printer. Do not use photo reduction or small fonts.

a. **First Page**. The first page should begin with the following information, listed in the order specified:

(1) LOI-Military Operational Stress-related Illnesses.

(2) Proposed project title.

(3) Principal Investigator(s) name, degree, title, mailing address, telephone and FAX numbers.

(4) Name of Department of Veterans Affairs (VA) or Department of Defense (DOD) research facility.

(5) Administrative contact name and telephone number.

(6) Name, title, address, and signature of Associate Chief of Staff or Coordinator for Research and Development ( for VA) or DOD equivalent.

b. **Remainder of LOI**. The remainder of the letter should follow the format and incorporate the subheadings specified below:

(1) **Background**. Indicate the scientific basis (rationale) for the research and its relationship to other major research findings. Describe the significance of the research for military operational stress-related illnesses, and its relevance to the mission of VA and/or DOD.

(2) **Research Objectives**. Outline precisely and clearly the goals of the planned project, including the hypothesis to be tested and the specific objectives of the project.

(3) **Project Design and Methods**. Briefly define and describe the approach to the research.

c. **Submission**. Submit the original plus eight copies of the letter of intent to:

VA - DOD Collaborative Research Program Medical Research Service (121E)  
Department of Veterans Affairs  
810 Vermont Avenue, NW  
Washington, DC 20420

**IL 12-97-009**  
**May 28, 1997**

*NOTE: The telephone number for FEDEX purposes is: (202) 273-8291.*

d. **Due Date.** LOIs must be received by August 1, 1997. LOIs received after this date will not be reviewed.

e. **Review Process.** Representatives of the VA and DOD will review LOIs for scientific merit, adherence to the goals of the program, and responsiveness to the solicitation.

## **2. Information for Submission of Proposals**

a. Merit Review proposal submissions are appropriate for established investigators. Proposals may be submitted by VA and DOD investigators with approved LOI. The proposed studies must not overlap with other concurrently funded research studies. Proposals approved for funding under this solicitation will be considered as additions to ongoing Merit Review programs and will not require resubmission of a VA investigator's entire program.

b. An investigator may be Principal Investigator (PI) or Co-Principal Investigator (Co-PI) on only one application submitted in response to this solicitation. Each PI and Co-PI must be affiliated with the VA or DOD.

c. Duration of proposals is a maximum of 3 years. Each proposal budget must not exceed \$300,000 in 3 years for investigators at a single research site. Collaborative proposals with Co-PIs at more than one site may request up to \$600,000 for 3 years. Proposals of shorter duration than 3 years should reduce the budget cap proportionately. Equipment requests are included within the funding cap.

d. The proposal narrative is limited to 15 pages, and includes statement of the problem, hypothesis(es), specific objectives, current status of research in the area, significance, relevance, background and work accomplished, work proposed, resources, and collaborations. The proposal must conform to the form and format described in M-3, Part II, Chapter 4, dated October 30, 1989.

*NOTE: Application instructions will be sent to each investigator with an approved LOI.*

e. The deadline for proposals is January 15, 1998.

### **f. Timetable for Submission and Funding**

LOIs due	August 1, 1997
Response to LOIs	September, 1997
Proposals due at VA Headquarters	January 15, 1998
Committee Review of proposals	April, 1997
Start date	July 1, 1998

Appendix C-5

DoD Call for Proposals for Gulf War Health Risk Issues

[Commerce Business Daily: Posted November 18 , 1997]  
From the Commerce Business Daily Online via GPO Access  
[cbdnet.access.gpo.gov]

PART: U.S. GOVERNMENT PROCUREMENTS

SUBPART: SERVICES

CLASSCOD: A-- Research and Development

OFFADD: Director, USAMRAA, 820 Chandler St, Fort Detrick, MD 21702-5014

SUBJECT: A-- GULF WAR ILLNESS RESEARCH PROGRAM

SOL CBD &&&- 9711 - 0001

POC CRAIG D. LEBO, Contracting Officer 301-619-2036

DESC: GULF WAR ILLNESSES RESEARCH PROGRAM - The USAMRMC announces an FY 98 competition for the Gulf War Illnesses Research Program. The Department of Defense solicits research proposals for studies on the possible health risks associated with service in the Gulf War. The goals of this research are to discover the pathogenesis of unexplained illnesses of Gulf War veterans, to use this understanding of basic mechanisms to help veterans, and to avoid or reduce the occurrence of such unexplained illnesses in future military deployments. Proposals may be submitted only by U.S. institutions of higher education (other than federal government) with degree-granting programs in science and/or engineering (~universities~), or by consortia led by such institutions. This solicitation is specifically for research in three areas of focus: (1) Investigation of the confluence of cognitive, emotional and physical factors which produce chronic, non-specific symptoms and physiological outcomes typical of the undiagnosed illnesses of some Gulf War veterans. Examples of studies sought range from sociological studies of the stress manifestations of military deployment to basic studies of psychoneuroimmunological mechanisms which elucidate physical symptoms such as muscle weakness, fatigue, and joint pain; (2) Studies of toxicity and toxic interactions of environmental chemicals, prophylactic drugs, and military materiel. Examples of studies sought in this topic include, but are not limited to, improved understanding of health effects of combinations of exposures specific to the Gulf War (including jet fuel vapor, pesticides and insect repellents, and pyridostigmine bromide), studies of biomarkers to denote individual exposure to toxic substances, and the development of near-real time bioassays and bioelectronic sensor technologies for assessment of toxicological hazards in future deployments. This latter research should emphasize identification of fundamental physiological endpoints in bioassays which could be applied to bioelectronic sensor development to identify hazards from unidentified chemicals and chemical mixtures; (3) Studies of long-term health consequences associated with exposure to subclinical levels of chemical warfare agents. Examples include epidemiological studies of soldiers who may have been exposed to chemical warfare agent without acute symptoms, and epidemiological studies on the health consequences of exposure in populations, such as passengers present during the Tokyo subway attack and individuals who participated in chemical agent research or worked in production plants or storage facilities. Full proposals must be prepared in accordance with USAMRMC Broad Agency Announcement 95-1. This is accessible on the Internet at <http://www-usamraa.army.mil>. USAMRMC will issue no other version of this program description; no paper copy will be available from USAMRMC. No preproposals are necessary, all are encouraged to submit if the proposal content addresses any of

the three studies above. Proposals typically average 2-4 years in duration and typically range in cost between \$200K and \$1.5M. Funds available for this solicitation total approximately \$8M. Full proposals are due to Commander, U.S. Army Medical Research and Materiel Command, ATTN: MCMR-AAA (GWI), Fort Detrick, MD 21702-5014, by 4:00 p.m. EST on 4 February 1998. The primary evaluation criteria will be (1) scientific and technical merits of the proposed research as determined by external (non-DOD) peer review, and (2) relevance and potential contributions of the research to Gulf War illnesses as determined by the Research Working Group of the Persian Gulf Veterans' Coordinating Board. Collaboration with DOD laboratories and other organizations involved in medical research for defense applications is encouraged but not required.

EMAILADD : craig\_lebo@ftdetrck-ccmail.army.mil

EMAILDESC : craig\_lebo@ftdetrck-ccmail.army.mil to contact the Contracting Officer via e-mail.

CITE : (W-322 SN143548)