National Security and International Affairs Division

B-280539

August 10, 1998

The Honorable Arlen Specter Chairman, Committee on Veterans Affairs United States Senate

The Honorable John D. Rockefeller IV Ranking Minority Member Committee on Veterans Affairs United States Senate

Subject: Role of the Persian Gulf Veterans' Coordinating Board in Scientific

Evaluation of Research Proposals and the Funding Recommendations

Made by its Research Working Group

The formation of the Persian Gulf Veterans' Coordinating Board (PGVCB) was announced in early 1994 for the purpose of coordinating federal research and other activities in response to illnesses reported by Gulf War veterans. PGVCB is co-chaired by the Secretaries of the Department of Veterans' Affairs, the Department of Defense (DOD), and the Department of Health and Human Services and comprises working groups on research, clinical issues, and compensation. The PGVCB's Research Working Group (RWG) describes its charges as: (1) assessing the state and direction of research, identifying gaps in factual knowledge and conceptual understanding; (2) identifying testable hypotheses and potential research approaches; (3) reviewing research concepts as they are developed; (4) collecting and disseminating scientifically peer-reviewed information; and (5) insuring that appropriate peer review and oversight are applied to research conducted and sponsored by the Federal Government.

At your request, we (1) determined the role of PGVCB's RWG in assessing the scientific merit of applications for grants to conduct Gulf War illness-related research and (2) identified the proposals that RWG recommended for funding, those it did not recommend, and the proposals for which funding was eventually announced.

Generally, PGVCB's RWG has not directly solicited or assessed the scientific merit of grant applications. The RWG does comment on draft solicitations, but it is the board's member agencies that solicit research proposals, assess their

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scientific merit with input from panels of experts, and award research grants. After several solicitations issued by PGVCB's member agencies, a RWG subcommittee conducted a supplementary review of the proposals that an agency-sponsored expert panel had given scientific merit scores equal or superior to a specified level (generally 2.5 or 3 on a scale of 1 to 5, with 1 being best). The purpose of this supplementary review was not to reassess scientific merit but to examine programmatic relevance. Based on its review, the subcommittee made recommendations to the member agencies regarding which of the proposals should be funded. Enclosure I identifies the solicitations for which RWG provided this supplementary review. Enclosure II summarizes the scope and results of the supplementary review.

Of the 191 proposals submitted, RWG reviewed 73 that had received scientific review scores superior to a specific criterion, recommending that 38 should be funded. The agencies eventually announced funding for 28 of these recommended proposals with awards totaling about \$24.4 million. The Department of Veterans' Affairs characterizes this amount as less than 25 percent of the total financial investment in research on Gulf War illnesses; the remaining 75 percent includes VA-sponsored projects and others that were not reviewed by RWG in the proposal stage as well as a few projects awarded funds after the close of our review. Enclosure III lists the titles of the proposals submitted under each solicitation subject to RWG supplementary review, the action that RWG took on each that it reviewed, the funds requested by the applicant, and the award (if any) announced by the member agency.

To collect this information, we interviewed officials of PGVCB's RWG and its member agencies. We also reviewed research solicitations issued by the member agencies, public announcements of funding decisions, and internal minutes and other documents related to the supplementary review performed by PGVCB's RWG and the scientific merit review performed by the member agencies. The scope of our review was limited to solicitations for research proposals issued since May 1995 for which awards had been made by March 1998 and which incorporated review by a RWG subcommittee. We did not review the extent to which proposals for which no funding was announced in connection with these competitions eventually received federal funding through other avenues. Our work was conducted between December 1997 and March 1998 in accordance with generally accepted government auditing standards.

The Centers for Disease Control and Prevention, DOD, and the Department of Veterans' Affairs provided comments on a draft of this report. CDC generally concurred with the information in the report. DOD and VA commented that we did not adequately characterize the RWG role in managing research on illnesses among Gulf War veterans. Specifically, they believed that the report should provide a broader description of RWG's functions beyond those related to the review of research proposals and we have incorporated RWG's description of its overall role. In addition, VA believed that the report did not adequately address certain features of RWG's supplementary review process and provided

information to expand on the process, including that material provided for RWG's review is edited to discourage the identification of individual investigators and institutions, and that the RWG receives abstracts of all submitted proposals though its supplementary review focuses only on those with acceptable scientific merit scores. We incorporated or clarified these aspects of the review as appropriate. CDC, DOD, and VA also provided technical comments that we incorporated as appropriate.

Please call me on (202) 512-3652 or Sushil Sharma, Assistant Director, on (202) 512-3460, if you have any questions.

Kwai-Cheung Chan

Director, Special Studies and Evaluations

Enclosures - 3

SOLICITATIONS FOR RESEARCH THAT INCORPORATED SUPPLEMENTARY REVIEW

Between May 1995 and March 1998, the Department of Defense and the Centers for Disease Control and Prevention announced awards in connection with several solicitations for research on Gulf War veterans' illnesses that were subject to supplementary review by the Research Working Group of the Persian Gulf Veterans' Coordinating Board. Each of these solicitations is described in the following table along with the amount of funds that were advertised to be available, the number of proposals submitted, the number of proposals for which funding was announced, and the total amount of the awards that were announced.

Table I.1: Solicitations for Research on Gulf War Illnesses that Incorporated RWG Supplementary Review of Submitted Proposals (Dollars in millions)

Citation and date of solicitation	Issued by	Topics	Funds available ^a	No. of proposals submitted	No. of proposals funded ^b	Total awards announced under the solicitation
Commerce Business Daily PSA-1353 5/24/95	DOD	(1) Epidemiological studies of health consequences of military service in SW Asia during the war, (2) studies of the consequences of use of pyridostigmine bromide, alone and with other chemicals, and (3) clinical studies and other research on health consequences of military service in SW Asia during the Persian Gulf War.	\$8.0 ·	111	14	\$8.6°

Citation and date of solicitation	Issued by	Topics	Funds available ^a	No. of proposals submitted	No. of proposals funded ^b	Total awards announced under the solicitation
Commerce Business Daily PSA-1738 12/10/96	DOD	(1) Feasibility of epidemiological studies of persons near Khamisiyah, Iraq, in the first weeks of March 1991 and (2) animal studies to assess long-term or delayed effects of low level exposures to chemical warfare agents.	\$2.0	topic 1: 0 topic 2: 22	topic 1: 0 ^d topic 2: 4	\$3.2°
Commerce Business Daily PSA-1761 1/14/97	DOD	(1) Causal relationships between illnesses/symptoms and possible exposures to hazardous material and (2) studies of historical war syndromes.	topic 1: \$9.5 topic 2: \$5.0	topic 1: 36 ^f topic 2: 14	topic 1: 8 topic 2: 0 ^g	topic 1: \$9.0 topic 2: \$0.0 ^g
Federal Register CDC Ann. 748 5/5/97	CDC	Research on conditions and symptoms reported to be more prevalent among Gulf War veterans or that assists in development or validation of a case definition of illness among PGW veterans.	\$3.6 ^h	8 ⁱ	2	\$3.6 ^j

^aThese are approximate figures identified in the respective solicitations.

^bThese figures are based on awards publicly announced in connection with the various solicitations or identified by agency officials in comments on our draft report. We did not assess the extent to which

proposals for which no funding was announced under these solicitations eventually received federal funds through other avenues.

^cOf this total, \$1.3 million was not included in the June 20, 1996 public announcement of awards under this solicitation. DOD officials stated that these additional funds were awarded and noted that they were likely excluded from the announcement because contract negotiations were not complete for these awards when the announcement was issued.

^dThe Institute of Medicine's Medical Follow-Up Agency has been approached about conducting this work, for which no proposals were submitted.

^eThis total includes an additional \$0.4 million that DOD officials state was subsequently added to one project.

^fAdditional proposals submitted under an earlier announcement were reconsidered along with the 36 submitted under this one.

Department of Veterans' Affairs officials indicated that awards for 3 projects under this solicitation are pending completion of contract negotiations. DOD records we reviewed indicated that awards of about \$1.8 million are anticipated with \$0.7 million already obligated to one of the projects.

^hCDC's announcement anticipated the availability of \$1.2 million per year for up to 3 years, but noted that award continuation beyond year 1 was subject to satisfactory progress and availability of funds.

'One additional proposal was returned as nonresponsive due to lack of a host institution.

^jAwards of \$1.2 million were made for year 1. The amount shown in the table includes recommended future support subject to satisfactory progress and availability of funds.

COVERAGE AND RESULTS OF SUPPLEMENTARY REVIEW OF SOLICITED PROPOSALS

PGVCB's RWG conducted supplementary reviews of proposals that had been scored for scientific merit by panels of experts administered by CDC or DOD. In the case of proposals to DOD, these expert panels were run by its contractor, the American Institute for Biological Sciences. The responses to the CDC solicitation were rated for scientific merit by a federally chartered expert panel assembled by CDC. RWG normally only provided a supplementary review for those proposals considered scientifically meritorious on the basis of having achieved a scientific merit score equal or superior to a particular criterion (generally 2.5 or 3 on a scale of 1 to 5, with 1 being best). This practice generally eliminated most of the proposals from supplementary review. For the remainder of proposals, which RWG did review, the table lists the number of proposals it recommended for funding and the number it did not recommend.

Table II.1: Coverage and Results of Supplementary Review of Solicited Proposals by the PGVCB RWG and the Relationship of RWG's Recommendations to the Agencies' Announced Funding Decisions

Date and solicitation (topics, if separately	reported	Proposals submitted	No. not reviewed by RWG	No. RWG reviewed and recommended for funding	No. for which funding was announced and recommended by RWG	No. RWG reviewed and did <u>not</u> recommend for funding	No. for which funding was announced but not recommended by RWG ^a
5/24/95 DOD		111	74	15	14 ^b	22	0
12/10/96 DOD	Feasibility of epidemiological studies of persons near Khamisiyah, Iraq, in the first weeks of March 1991.	0	0	0	0	0	0

Date and s solicitation (topics, if separately	reported	Proposals submitted	No. not reviewed by RWG	No. RWG reviewed and recommended for funding	No. for which funding was announced and recommended by RWG	No. RWG reviewed and did <u>not</u> recommend for funding	No. for which funding was announced but not recommended by RWG ^a
12/10/96 DOD	Animal studies to assess long-term or delayed effects of low level exposures to chemical warfare agents.	22	14	4	4	4	0
1/14/97 DOD	Causal relationships between illnesses or symptoms and possible exposures to hazardous material.	36 (40)°	22 (23)	12 (14)	8	2 (3)	0
	Studies of historical war syndromes.	14	8	3	O ^d	3	0
5/5/97 CDC		8	0	2	2°	6 ^e	0

^aWe did not assess the extent to which proposals that did not receive funds under this solicitation (or substantially similar applications) eventually received federal funds through other avenues.

bVA officials indicated that an additional proposal recommended by RWG was subsequently withdrawn by the investigator. Only 12 of these projects were incorporated in DOD's announcement of awards under this solicitation; DOD officials indicated that this was probably because contract negotiations for these projects were not complete at the time the remaining awards were announced.

Four proposals that had been submitted under the previous announcement were evaluated again under this announcement, bringing the total number of proposals reviewed to 40. The numbers in parentheses refer to the results of the review incorporating these four additional proposals.

^dVA officials note that formal announcements of awards for all three of the recommended proposals are awaiting final contract negotiations.

^eCDC notes that RWG was informed that only two proposals would be funded under this solicitation and might otherwise have recommended additional ones.

PROPOSALS BY SUPPLEMENTARY REVIEW STATUS WITH FUNDS REQUESTED AND FUNDING ANNOUNCED

For each solicitation incorporating some supplementary review from RWG, the following tables list the titles of submitted proposals according to whether RWG reviewed them and, if so, the action RWG took. The tables also show the funds requested at the time of submission and the award, if any, publicly announced by DOD or CDC in connection with the solicitation. We did not review the extent to which proposals received federal funding through other avenues.

Table III.1: Actions Taken Toward Proposals Submitted Under DOD's 1995 Solicitations (Commerce Business Daily, 1995, Issue No. PSA-1353)

Proposals RWG reviewed and recommended for funding ^a	Funds requested ^b	Award DOD announced ^c
Markers of A Persian Gulf War Syndrome With Fatigue	\$470,300	None ^d
The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment	2,228,386	\$700,000°
Investigation of Seminal Plasma Hypersensitivity Reactions	633,669	633,669°
Dysregulation of the Stress Response in the Persian Gulf Syndrome	970,578	971,000
Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin and DEET in Males and Females	970,426	934,000
Evaluation of Muscle Function in Persian Gulf Veterans	874,401	906,000
Clinical and Epidemiological Studies Into Persian Gulf War Illnesses	781,945 ^f	865,000
Persian Gulf Women's Health Linkage Study	780,633	779,000
Diagnostic Antigens of Leishmania Tropica	693,160	611,000
Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms	487,375	554,000

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Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War	\$467,279	\$427,000
Effects of Pyridostigmine in Flinders Differing in Cholinergic Sensitivity	355,224	354,000
Neuropsychological Functioning in Persian Gulf War Era Veterans	346,896	353,000
Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents	284,531	283,000
Psychological and Neurobiological Consequences of the Gulf War Experience	264,000	264,000
Proposals RWG reviewed but did not recommend for funding ^a		
Effects of Pyridostigmine Under Various Conditions on Cognitive and Pulmonary Function	622,525	None
Pulmonary and General Health Survey of Persian Gulf War Veterans	390,691	None
Identifying Potential Carcinogenic Effects of Combined Exposures to Lead, Quartz, DEET, and Pyridostigmine	756,488	None
Illness in Persian Gulf War Veterans	2,734,073	None
Nonassociative and Associative Learning in Persian Gulf Veterans: Implications for Neurological Damage	655,660	None
Molecular Identification of Microbial Pathogens in Persons with Persian Gulf-Associated Illnesses	369,451	None
Immune Consequences of Multiple Exposures Unique to the Persian Gulf War: The Role of Lead and Pyridostigmine Bromide in Bacterial-Induced Autoimmunity	456,001	None

The Effect of Pyridostigmine on the Human Immune System	\$309,200	None
Role of Respirable Saudi Arabian Sand in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?	1,006,608	None
Development of Strategies for Restoring Protective Immunity in Leishmaniasis and Molecular Methods for Guiding Treatment	763,632	None
Role of Cholinesterase Inhibitors or Pesticides in Persian Gulf Syndrome	428,002	None
Performance Assessment and Symptom Presentation in Gulf War Veterans: An Experimental Multidisciplinary Study	587,778	None
Reproductive Dysfunction in Male Gulf War Veterans	869,782	None
Epidemiological Studies Persian Gulf War Illnesses	7,689,222	None
Pyridostigmine Bromide and Persian Gulf War Illnesses Studies	1,351,143	None
Pyridostigmine Bromide Studies Persian Gulf War Illnesses	7,689,222	None
Persistent Airway Inflammation in Persian Gulf War Veterans: A Novel Syndrome	732,086	None
Investigating the Persian Gulf War Illness	727,183	None
Reproductive Health Survey of Persian Gulf War Veterans	680,774	None
Mechanism of Action of Pyridostigmine Bromide	427,257	None
Electrophysiological Investigation of Persian Gulf War Veterans	444,821	None
Prevalence and Characterization of Leishmania in the Persian Gulf Area	1,044,800	None

Proposals RWG did not review ^a		
Research on Psychological and Biological Markers Associated with Gulf War Illnesses	\$2,066,120	None
Alterations in Central Processing of Visceral and Somatic Sensory Information in Patients with Persian Gulf War Syndrome (PGWS)	617,100	None
Epidemiological Studies: Etiology of Persian Gulf War Illnesses	828,037	None
Toxic Interactions: Pyridostigmine/DEET/Permethrin on Antioxidant, Immune and Cholinergic Systems During Exercise in Rats	534,624	None
Mycoplasma Infections in Persian Gulf War Illnesses	1,735,496	None
Birth Defects in Iowa Persian Gulf War Veterans: A Population-Based Evaluation	343,182	None
A Study of Persian Gulf War Illness to Investigate if Sand Inhalation Has Caused Silica/Silicate Specific Immune Reactivity, and the Symptoms of PGWI	4,769,457	None
Epidemiological Studies Persian Gulf War Illnesses	1,898,434	None
Effect of Pyridostigmine in a Learned Helplessness Animal Model of Depression	175,700	None
An Epidemiologic Survey of Military Personnel During the Persian Gulf War	844,412	None
Clinical Research and Other Studies of Persian Gulf War Illnesses	413,375	None
International Health Survey of Persian Gulf Veterans	677,650	None

A Controlled Study of Serotonin/Dopamine Agonists for Persian Gulf Illness, Fibromyalgia, Chronic Fatigue Syndrome	\$1,251,300	None
A Longitudinal Study of the Biobehavioral Responses of Members of the Air National Guard to the Persian Gulf War	499,410	None
Gulf War and Vietnam Veterans with Post-Deployment Illnesses	799,286	None
Perceived Stress, Mood, and Social Support as Predictors of Health Complaints of Veterans Reporting Persian Gulf War Illnesses, their Spouses, and a Matched Control Group	370,919	None
A Non-Human-Primate Model to Explore Potential Multiple-Organ Toxicity of Chronically Administered Pyridostigmine Bromide Alone and in Combination with Organophosphate and Carbamate Pesticides	243,100	None
Persian Gulf War Veterans: Assessment of the Stress-Response System and Biological and Genetic Risk Factors for Symptom Development Following Treatment with Pyridostigmine	570,663	None
Toxicological Effects of Pyridostigmine and its Combinations with DEET, Permethrin and Ciprofloxacin	2,867,896	None
Xenobiotics in Persian Gulf War Veterans	499,700	None
Studies on the Immunopathogenesis of Symptomatic Persian Gulf War Veterans	454,203	None
Genetic Predisposition for Susceptibility to Cholinergic Deficits Under Anticholinesterase Treatment	551,625	None
Pyruvate Kinase, Chemical Sensitivity, and Chronic Disease	479,257	None

Injected Aniline Derivative Etiology for Persian Gulf Veterans	\$1,914,952	None
Injected Aniline Derivative Etiology for Persian Gulf Veterans	1,914,952	None
Injected Aniline Derivative Etiology for Persian Gulf Veterans	1,914,952	None
Pyridostigmine Bromide Studies Persian Gulf War Illnesses	2,690,117	None
A Cytologic Study of Operation Desert Shield/Storm Female Veterans	36,271	None
A Morphologic Study of Operation Desert Shield/Storm Veterans	299,920	None
Cellular Mechanisms of Pyridostigmine Toxicity: Potential Interactions with Stress	463,141	None
Toxicity Evaluation of Multiple Chemical Exposures as a Potential Cause of Persian Gulf War Illnesses	1,235,871	None
Effects of Pyridostigmine on Hormonal and Behavioral Responses in Healthy and Depressed Subjects	1,198,097	None
Application of Ultraviolet Blood Irradiation for Inactivation of Bloodborne Pathogens (as Applied to Treatment of GWS)	341,388	None
Title Unknown	1,644,758	None
Potential Interactions of Pyridostigmine Bromide, Stress and Pesticides in Persian Gulf War Illnesses	717,865	None
Epidemiological Studies of Persian Gulf War Illnesses	1,086,459	None
Sarcoidosis in U.S. Gulf War Veterans	324,717	None
Toxicity Evaluation of Multiple Chemical Exposures as a Potential Cause of Persian Gulf War Illnesses	1,235,871	None

Petroleum Toxicity and Petroleum Induced Illness	\$90,000	None
Pyridostigmine Bromide Studies	936,422	None
A Longitudinal Study of War-Related Stress and Somatic Symptoms in Gulf War Veterans	109,600	None
Microphysiometry Studies of Pyridostigmine Bromide	409,006	None
Design for Epidemiological Study for Persian Gulf War Illnesses	875,661	None
A Cohort Study of Health Consequences of Participation in the Persian Gulf War	790,502 - 3,312,259	None
The Neurobiological Correlates and Consequences of Trauma in Military Personnel	1,785,000	None
The Cell Cycle and Autogenous Lymphocytic Factor (ALF) in the Diagnosis and Treatment of the Gulf War Illnesses	315,000	None
Toxicity and Interactions of Pyridostigmine, DEET and Chlorpyrifos Oxon in the Swine Model	2,035,725	None
Chronic Organophosphorous Exposure and Cognition: Effect of Pyridostigmine Pretreatment	160,917	None
A Clinical Demonstration of Effectiveness of Comprehensive Nutritional Parenteral and Oral Therapy in Gulf War Veterans	400,000	None
Study of Mycoplasma Infections in Veterans with Gulf War Illness	635,829	None
Effects of Combined Pyridostigmine Bromide and Pesticides on Cholinergically-Regulated Cytokines and Hormones – A Potential Etiology for Persian Gulf War Illnesses	727,585	None

Bovine Respiratory Disease: Model of Stress-Related Disease	\$306,385	None
Investigation into Complaints of Reproductive Problems of Persian Gulf Veterans and their Partners	959,119	None
Psychiatric and Psychological Correlates of Persian Gulf War Related Symptomatology: Assessing the Contributions of Somaticization Disorder, Substance Abuse, Axis II Cluster B Disorders, and Specific Psychological Styles to Illness Presentation	564,830	None
Pyridostigmine Bromide as a Risk Factor for Sleep Disturbance in Persian Gulf War Veterans	257,437	None
Pyridostigmine Bromide as a Risk Factor for Sleep Disturbance in Persian Gulf War Veterans	257,437	None
Determining Whether Gulf War Veterans are Sensitive to Chemicals, Via Challenge Tests in an Environmental Medical Unit	2,461,836	None
Physiologic and Behavioral Parameters of Low-Level Chemical Sensitivities in Double-Blind Provocation Chamber Challenges	819,463	None
Effects of Persian Gulf War Service on Military Working Dogs	209,876	None
Clara Cell Protein in Pulmonary and Reproductive Toxicity	372,376	None
Gulf War Veterans: Psychophysiological and Psychiatric Assessment	597,171	None
Leishmania Tropica: Studies on the Zoonotic Cycle, Vector Habitat and Diagnosis of Infections	784,987	None
Toxicology of Combinations of Possible Toxic Agents in Desert Storm	309,593	None

Balance and Cognitive Function in Persian Gulf Veterans	\$800,355	None
A Case Control Family Study of Ill and Non-Ill Persian Gulf War Veterans	856,334	None
Case-Control Study of Gulf War Veterans/Genetic, Immunologic, and Infectious Disease Markers, Psychological Factors, and Occupational Exposures	1,200,641	None
Pyridostigmine Bromide: Effects on CNS Control of Behavioral State	1,078,395	None
Clinical Research and Other Studies Persian Gulf War Illnesses	7,689,222	None
Persian Gulf War Illnesses/Clinical Research and Other Studies	2,090,720	None
The Role of the Frontal Cortex in the Generation of Stress Symptoms	Not Provided	None
An Evaluation of Alpha-Theta Brainwave Biofeedback Therapy for Post Traumatic Stress Disorder Using Measurements of Self-Reported Symptoms and the Acoustic Startle Response	Not Provided	None
Sleep Abnormalities and Persian Gulf Illnesses	330,000	None
Eye Findings Among Gulf War Veterans	156,824	None
Pharmacokinetics and Specific Biological Effects of Lead Inhaled By Rats That Ingest Pyridostigmine Bromide	627,845	None

There were occasionally multiple submissions under the same title. As these were assigned separate control numbers in the review process, we have listed them here as distinct proposals.

^bThis refers to the amount of funds requested under the proposal at the time of submission. Unless otherwise noted, all figures are in current U.S. dollars.

^cAll funds are in current U.S. dollars. The award amounts are those publicly announced by the agency in connection with the solicitation or identified by agency officials. We did not review the extent to which submitted proposals (or substantially similar proposals) received federal funds through other avenues or were funded as intramural efforts before or after their submission.

^dDOD and VA officials indicated that this proposal was withdrawn by the investigator.

Funding for this proposal was not included in the public announcement we reviewed. According to a DOD official, this was probably because the contract with the investigator had not been formally completed at the time the public announcement was issued.

The budget request for this project was provided in British pounds. We have used an exchange rate of \$1.71 per £1.00 to convert the request to dollars. This may not have been the exchange rate at the time that funds were awarded for this project.

Table III.2: Actions Taken Toward Proposals Submitted Under DOD's 1996 Solicitation for Animal Studies to Assess Long-term or Delayed Effects of Low Level Exposures to Chemical Warfare Agents (announced in <u>Commerce Business Daily</u>, 1996, Issue Number PSA-1738)

Proposal withdrawn before agency review	Funds requested ^a	Award DOD announced ^b		
Assessment of Delayed Effects of Low-Level Exposure to Chemical Warfare Agents Sarin, and Mustard in Rats and Sheep	\$299,431	Not applicable		
Proposals RWG reviewed and recommended for funding ^a				
Low-level Sarin Neurotoxicity and its Modulation by Pyridostigmine	932,287	\$785,000		
Low Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation and Possible Delayed Effects	1,585,807	630,000		
Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposures	466,317	414,000		
Long-term Effects of Subclinical Exposures to Sarin	1,777,677	1,394,420°		
Proposals RWG reviewed but did not recommend for funding ^a				
Low-level Exposure to Sarin: Persistently Exaggerated Startle Responses in Rats	782,533	None		
Indicators of Human Disease from Persian Gulf War Service: A Study of Military Working Dogs	308,461	None		
An Animal Model of Gulf War Toxicants and Sarin Exposure	1,108,190	None		

Long-term Effects of Subchronic Exposure to Sarin, Alone and in Combination with Stress and Other Chemicals	\$1,481,390	None ^d
Proposals RWG did not review ^a		
Persistent Startle Sensitization in Rats: Effects of Stress, Sarin and Pyridostigmine Bromide	782,533	None
Oxidative Damage in Stress-Related Disease	513,763	None
Long-term Neurochemical, Behavioral, Neurological, and Physiological Effects in Rats Exposed to Subsymptomatic Doses of Sarin	687,126	None
Animal Model of Persian Gulf War Illness: A Progressive Response to Pyridostigmine, Sarin, Insecticide, and Diesel Exhaust Exposure?	1,166,319	None
Long-term Effects Following Prolonged, Low Level Sarin Exposure in Rodents: Stress, Strain Differences and Chemical Interactions	1,420,700	None
Neurotoxicity of Low Doses of DFP, an Organophosphate Acetylcholinesterase Inhibitor, and Potential Enhancement by Exposure to PB, DEET, and/or Stress	546,860	None
An Investigation of Possible Long-term Effects of Exposure to Sub-Lethal Effects of Nerve Agents	1,000,000	None
Delayed Neurotoxic Effects of Low Dose Sarin in Mice	196,165	None
Animal Model of Persian Gulf War Illness: A Progressive Response to Multiple Toxicants?	999,942	None

Long-term Neurobehavioral Consequences in Rats from Exposure to Low Levels of Sarin and Other Persian Gulf War Chemical Toxicants and Stressors	\$1,000,000	None
Isopropyl-Methylphosphofluoridate: Effects on CNS Control of Behavioral State	960,965	None
Cognitive and Electromyographic Studies of Delayed Toxicity to Chronic Low Level Anticholinesterase Exposure	1,049,997	None
Experimental Models of Gulf War Syndrome	1,274,019	None
Neurological and Immunological Impact of Exposure to Sarin, Pyridostigmine, Permethrin, and DEET in a Rat Model	965,900	None

^aThis refers to the amount of funds requested under the proposal at the time of submission. Unless otherwise noted, all figures are in current U.S. dollars.

^bAll funds are in current U.S. dollars. The award amounts are those publicly announced by the agency in connection with the solicitation or identified by agency officials. We did not review the extent to which submitted proposals (or substantially similar proposals) received federal funds through other avenues or were funded as intramural efforts before or after their submission.

'The March 1998 records that we reviewed and the public announcement issued by DOD indicated that \$1,000,000 was initially awarded and obligated to this project. DOD officials told us that, with RWG's concurrence, an additional \$394,420 was eventually awarded to fund supplementary work on heat stress.

^dDOD officials told us that this project was not funded under the above-referenced competition, but that it was later awarded \$996,000.

Table III.3: Actions Taken Toward Proposals Submitted Under DOD's 1997 Solicitation for Research on Causal Relationships between Illnesses/Symptoms and Possible Exposures to Hazardous Material (announced in <u>Commerce Business Daily</u>, 1997, Issue No. PSA-1761)^a

Proposals RWG reviewed and recommended for funding	Funds requested ^b	Award DOD announced ^c	
PGW Illness Research	\$2,352,944	None	
Biobehavioral Health Outcomes of PGW Veterans	2,498,063	None	
Clinical, Neurophysiologic and Immunologic Studies Into Persian Gulf War Illness	750,000	None	
Physiologic Effects of Stress in GWV	1,210,308	\$908,000	
PB-induced Neurodegeneration: Role of Neuronal Apoptosis	624,727	617,000	
Sarin and PB Interaction Under Physical Stress: Neurotoxic Effects in Mice	200,833	200,000	
Illness Among Persian Gulf War Veterans: Case Validation Studies	2,042,635	2,200,000	
Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness	125,000	125,000	
Individual Differences in Neurobehavioral Effects of PB	2,769,819	1,900,000	
PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity	2,302,329	1,600,000	
Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, PB, Pesticides and Botulinum Toxoid	1,660,834	1,500,000	
A Controlled Clinical Study of Neuromuscular Symptoms Experienced by Servicemen and Women of the U.K. Armed Forces with Reference to PGW Service	329,184	None	

Proposals RWG reviewed but did not recommend for funding		
Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?	\$663,779	None
Interaction of Chronic Stress and Pyridostigmine on Physiology and Behavior as Assessed Using a Rodent Model of Sustained Operations	315,944	None
Proposals RWG did not review		·
Investigating the Relationship of Toxic Exposure to Muscle Joint Pain in Persian Gulf War Veterans	3,341,668	None
Military Medical Record Review to Examine Outpatient Service Utilization and Complaints Among Gulf War Veterans	999,827 None	
Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War-related Syndromes Leading to Diagnosis and Treatment	13,815,792	None
A Randomized Controlled Trial of a Multicomponent Therapy for Patients with Persian Gulf Syndrome	1,107,199	None
An Evaluation of the Hypothesis of Brain/Nerve Damage in Khamisiyah Veterans	4,219,778	None
Regulation of Central Stress Pathways in an Animal Model Relevant to Gulf War Illness	616,247	None
Pyridostigmine Bromide and Persian Gulf War Illnesses: Effects of Drug Metabolism	868,661	None
Assessment of Neuromuscular Fatigue in Gulf War Veterans	1,084,200	None
Functional and Structural Neuroimaging of Central Nervous System Abnormalities in Symptomatic Persian Gulf Veterans	856,941	None

Evaluation of the Neurological, Psychological and Physical Work Performances of Gulf War Veterans Stationed in the Khamisiyah Theater	\$4,523,535	None
Biochemical and Molecular Markers for Gulf War Syndrome	1,218,581	None
A Study of Persian Gulf War Illness to Investigate if Sand Inhalation Has Caused Innate and Specific Immune Reactivity, and the Symptoms of PGWI	604,882	None
Psycho-biological Assessment of High Intensity Military Training	365,534	None
Pathogenesis of Gulf-War Related Pulmonary Disease	1,496,284	None
Mechanisms of Interactions Between Pyridostigmine (PB) and DEET, Adrenergic Effects, Caffeine, and Stress	1,247,939	None
Stress-Enhanced Toxicity of Gulf War Chemicals in Sedentary and Well-Trained Male and Female Rats	3,270,942	None
Persian Gulf War Illness Research	633,361	None
Persian Gulf War Illness Research: Prophylaxis and Treatment	1,620,305	None
Gulf War Illness: Evaluation of a Treatment Protocol for a Subset of Veterans Who Had Chemical Exposures	1,371,350	None
A Comprehensive Neurological Evaluation of Khamisiyah and Non-Khamisiyah Gulf Veterans	4,219,778	None
A Quantification Diagnosis for Persian Gulf War Illness Using Two-Dimensional Electrophoresis Protein Analysis	1,287,858	None
Stealth Virus Infection in Veterans with the Persian Gulf War Illness	864,030	None

^aIn addition to the 36 proposals that were submitted under this announcement (as listed in table III.3), RWG incorporated reconsideration of 4 proposals that had been submitted under the previous announcement (see table III.2) but were not funded as a result of that competition. The review that occurred in connection with this announcement led RWG to recommend funding for 2 of these 4 additional proposals – "An Animal Model of Gulf War Toxicants and Sarin Exposure," and "Long-term Effects of Subchronic Exposure to Sarin, Alone and in Combination with Stress and Other Chemicals." The latter was awarded \$996,000. A third proposal was carried over but not recommended for funding, while the fourth received no further review because its scientific merit score did not meet the criterion RWG established for this round of review.

^bThis refers to the amount of funds requested by the proposal's authors at the time of submission. All figures are in current U.S. dollars.

'All funds are in current U.S. dollars. The award amounts are those publicly announced by the agency in connection with the solicitation. We did not review the extent to which submitted proposals (or substantially similar proposals) received federal funds through other avenues or were funded as intramural efforts before or after their submission.

Table III.4: Actions Taken Toward Proposals Submitted Under DOD's 1997 Solicitation for Studies of Historical War Syndromes (announced in <u>Commerce Business Daily</u>, Jan. 14, 1997, Issue No. PSA-1761)

Proposal withdrawn before agency review	Funds requested	Award DOD announced ^b	
Susceptibility to Pyridostigmine Toxicity from Phenotypic and Genotypic Differences in Cholinergic Functioning	\$877,445	None	
Proposals RWG reviewed and recommended for funding			
A Comparison of Post-Deployment Hospitalization Incidence Between Vietnam and Gulf War Veterans	656,000	Pending contract negotiation ^c	
War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes	656,859 ^d	Pending contract negotiation ^e	
Stress, Behavior and Health: Developing a Model for Predicting Post-deployment Morbidity, Mortality, and Other Adverse Outcomes	2,433,087	Pending contract negotiation ^f	
Proposals RWG reviewed but did not recommend for funding			
Medical and Cost Effectiveness of Multidisciplinary Treatment for Persistent Post-Deployment Symptoms: A Randomized Trial	914,979	None	
Studies of the Effects of Chronic Stress on Brain Function: Augmentation of Stress-Induced Neurotoxicity and Decrements in Learning by Anticholinesterase Agents	642,217	None	
Neuroimaging of Memory and Attention in Gulf War Syndrome	617,820	None	

Proposals RWG did not review		
War Syndromes: Autonomic Etiology	\$1,275,286	None
Investigating Cell Mediated Immune Characteristics in Veterans with Post Traumatic Stress Disorder	2,021,114	None
Historical Patterns and Development of Chronic, Non-Specific Symptoms Following War: A Comprehensive Evaluation	2,056,868	None
The Construction of Authoritative Knowledge About Combat Fatigue	52,250	None
The Long-term Effects of Combat Zone Stressors and Events on US Army Gulf War Veterans: Case Matched CCEP to MilPsych Data	64,481	None
Trench Fever: A Comparison of Syndromes from the First and Second World Wars to Gulf War Illnesses	75,260	None
The Stresses of War, Sleep Disturbance, and the Development of Chronic, Non-Specific Cognitive, Emotional and Physical Symptoms	800,209	· None
Integrated Analyses of Gulf War Illnesses Based on GIS and PBPK/PD Modeling	1,279,861	None

^aThis refers to the amount of funds requested under the proposal at the time of submission. All figures are in current U.S. dollars.

^bAll funds are in current U.S. dollars. We did not review the extent to which submitted proposals (or substantially similar proposals) received federal funds through other avenues or were funded as intramural efforts before or after their submission.

^{&#}x27;March 1998 records from DOD's Extramural Research Management System indicate that \$566,000 was committed on November 25, 1997, but do not show any obligation of funds.

^aThe budget request for this project appears to have been made in British pounds. We have used an exchange rate of \$1.71 per £1 to convert the request to U.S. dollars. This may not have been the exchange rate at the time awards were made.

^eMarch 1998 records from DOD's Extramural Research Management System indicated that \$734,687 has been obligated to this project.

^fAs of March 1998, a commitment of \$500,000 to this project was recorded in DOD's Extramural Research Management System.

Table III.5: Actions Taken Toward Proposals Submitted Under CDC's Announcement 748

Proposals RWG reviewed and recommended for funding	Funds requested ^a	CDC award ^b	
Cognitive Function and Symptom Patterns in Gulf War Veterans	\$1,092,073	\$1,800,000°	
Defining Persian Gulf War Illness	1,722,426	1,800,000	
Proposals RWG reviewed but did not recommend for funding ^d			
Is Gulf War Syndrome Correlated with MHC/HLA (Major Histocompatibility Locus/Human Leukocyte Antigen) Alleles?	597,839	None	
Behavioral and Psychological Assessment of Persian Gulf War Veterans	1,797,110	None	
Assessment of Asthma in Persian Gulf War Veterans	1,769,262	None	
An Evaluation of the Hypothesis of Brain/Nerve Damage in Khamisiyah Veterans	1,934,895	None	
Illness in Persian Gulf Veterans: Case Definition Studies	1,800,000	None _.	
Development and Definition of Illnesses Among Persian Gulf War Women Veterans	1,026,487	None	

^aThis refers to the amount of funds requested under the proposal at the time of submission. All figures are in current U.S. dollars.

^bAll funds are in current U.S. dollars. The award amounts are those identified by the agency in connection with the solicitation, including recommended future support. We did not review the extent to which submitted proposals (or substantially similar proposals) received federal funds through other avenues or were funded as intramural efforts before or after their submission.

^cAt the time the proposal was submitted, two years of funding were requested. During budget negotiations, CDC granted three years of funding. As with other CDC awards, funding after year one is subject to evidence of satisfactory progress.

^dCDC commented that RWG was informed that only two proposals would receive funding under this solicitation and that RWG might otherwise have recommended additional proposals.

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