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Federally Sponsored Research on Gulf War Veterans' Illnesses for 2003

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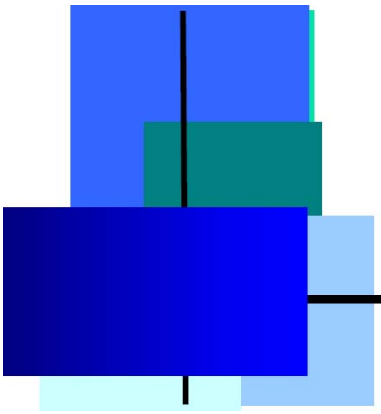

Annual Report to Congress – 2003

Research on Gulf War Veterans' Illnesses

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EXECUTIVE SUMMARY

I. INTRODUCTION

Section 707 of Public Law 102-585 as amended by Section 104 of Public Law 105-368, requires that an annual report be submitted to the Senate and House Veterans' Affairs Committees on the results, status, and priorities of research activities related to the health consequences of military service in the Gulf War. The Research Subcommittee of the interagency Deployment Health Working Group (DHWG) prepared this *2003 Annual Report to Congress*, which is the tenth report on research and research activities. (PGVCB, 1995a; 1996a; 1997; 1998a; 1999a; 2001; MVHCB, 2001a; 2002; DHWG, 2004a; 2004b) The DHWG tracks all federally funded research projects related to Gulf War veterans' illnesses.

This Annual Report is divided into four sections. Section I is an introduction. Section II highlights and summarizes research progress since the last Annual Report. Section III is an analysis of the Federal Government's portfolio of research on Gulf War veterans' illnesses. Section IV highlights significant new research projects and initiatives since the last Annual Report.

II. RESEARCH RESULTS IN 2003

In 2003, numerous research studies have yielded results that provide new and expanded information on the health problems of Gulf War veterans. Section II provides brief summaries of research projects for which results were published from January 2003 to December 2003. As in previous Annual Reports, the research reports summarized in Section II are grouped according to nine focus areas: symptoms and general health status, brain and nervous system function, diagnosis, reproduction, treatment, prevention, chemical weapons, pyridostigmine bromide, and interactions of exposures.

A. Symptoms and General Health Status:

Seven large studies published in 2003 focused on symptoms and general health. (Kang, et al., 2003; Smith, et al., 2003; Stuart, et al., 2003; Wessely, et al., 2003; Hotopf, et al., 2003a; Macfarlane, et al., 2003; Carney, et al., 2003) These publications included the results of studies conducted at three federally funded research centers in San Diego, Iowa, and London, UK. Each of the publications included hundreds to thousands of individuals. Three of these studies relied upon medical evaluations, rather than relying solely on self-administered surveys. (Smith, et al., 2003; Stuart, et al., 2003; Macfarlane, et al., 2003) Six of these studies were population-based, which means that the investigators attempted to broadly sample affected individuals rather study a small, possibly unrepresentative sample. Thus, the results of those six studies may have implications for the overall population of 697,000 Gulf War veterans (all except Stuart, et al., 2003).

The first study studied the prevalence of posttraumatic stress disorder (PTSD) and chronic fatigue syndrome-like illness (CFS) among 11,441 Gulf War veterans and 9,476 non-deployed veterans. Researchers noted that CFS was significantly associated with younger age, single marital status, enlisted rank, service in the Reserve/National Guard vs. active-duty, and service in the Army and Marines vs. the other services. PTSD was significantly associated with female gender, older age, non-white race, enlisted rank, service in the Reserve/National Guard vs. active-duty, and service in the Army vs. the other services. (Kang, et al., 2003)

The second study compared the rates and causes of hospitalizations in 99,614 Gulf War veterans who may been exposed to low-levels of nerve agents due to the demolitions at Khamisiyah, Iraq, in March 1991, with the rates and causes in 318,458 Gulf War veterans who were unlikely to have been exposed. Researchers found no differences in the rates or causes of hospitalizations except for cardiac dysrhythmia (higher in Gulf War veterans). (Smith, et al., 2003)

The third study found that in contrast to veterans who believed they had not been exposed, veterans who believed they had been exposed to chemical weapons were significantly more likely to be: female, older, non-white race, in the Army vs. the other services, to report more symptoms and worse overall health at the time of their evaluations, and to be diagnosed with psychiatric disorders vs. disorders of other organ systems.. (Stuart, et al., 2003)

The fourth and fifth studies were linked, and were based on a comparison of three groups of British veterans at two time points (1997-98 and

2000-2001): 1,089 Gulf War veterans, 638 Bosnia veterans, and 643 non-deployed veterans.

Authors of the fourth study found that "Reporting of military hazards after a conflict is not static, and is associated with current self-rated perception of health. Self-report of exposures associated with media publicity needs to be treated with caution." (Wessely, et al., 2003)

The fifth study found that the health gap between Gulf War veterans and the control groups had narrowed slightly. Gulf War veteran health did not deteriorate between the two time periods, and they did not have a higher incidence of new illnesses compared to the two control groups. Gulf War veterans reported a modest improvement in the prevalence of chronic fatigue and psychological distress. However, they reported a slight worsening of physical functioning. (Hotopf, et al., 2003a)

The sixth study compared the cancer incidence rates in 51,721 British Gulf War veterans, with the rates in 50,755 British non-deployed veterans, from 1991 to 2002. The authors concluded: "Incidence of and mortality from cancer in Gulf War veterans is almost identical to that seen in veterans who were not deployed in the Gulf." (Macfarlane, et al., 2003)

The seventh study compared 129 female Gulf War veterans and 1,767 male Gulf War veterans from the state of Iowa on their combat experiences, environmental exposures, and rates of health care utilization. The authors found: "The frequency with which serious aspects of nearby combat are reported by women confirms that the experience in the U.S. military is clearly becoming more homogeneous." (Carney, et al., 2003)

B. Brain and Nervous System Function:

The 12 studies published in 2003 focused on brain and nervous system function. (Horner, et al., 2003; Haley, 2003; Peckerman, et al., 2003; Nagelkirk, et al., 2003; Vasterling, et al., 2003; Lindem, et al., 2003a; Lindem, et al., 2003b; Lindem, et al., 2003c; Sullivan, et al., 2003; Kang, et al., 2003; Sadler, et al., 2003; Stimpson, et al., 2003) These publications included results of eight studies conducted at four federally funded research centers in New Jersey, Boston, Iowa, and Washington, DC. (Peckerman, et al., 2003; Nagelkirk, et al., 2003; Lindem, et al., 2003a; Lindem, et al., 2003b; Lindem, et al., 2003c; Sullivan, et al., 2003; Kang, et al., 2003; Sadler, et al., 2003) Eight of these studies included hundreds to thousands of individuals. (Horner, et al., 2003; Lindem, et al., 2003a; Lindem, et al., 2003b; Lindem, et al., 2003c; Sullivan, et al., 2003; Kang, et al., 2003; Sadler, et al., 2003; Stimpson, et al., 2003) Nine studies relied upon psychiatric, neuropsychological, or neurological evaluations, rather than relying solely on self-administered surveys (all except Kang, et al., 2003, Sadler, et al., 2003 and Stimpson, et al., 2003)

The first study determined the risk of amyotrophic lateral sclerosis (ALS) was significantly increased among Gulf War veterans compared to the controls, with a relative risk of 1.92. (Horner, et al., 2003)

The second study found the incidence of ALS from 1991 to 1998 that occurred in a subset of Gulf War veterans who were diagnosed with ALS before age 45 was higher than that of the general U.S. population. (Haley, 2003)

The third study compared 16 Gulf War veterans who had CFS and PTSD, 39 Gulf War veterans with CFS only, and 47 healthy Gulf War veterans on cardiovascular responses to a variety of stressors. The authors concluded that: "Comorbid PTSD contributes to dysregulation of cardiovascular responses to mental and postural stressors in Gulf veterans with medically unexplained fatiguing illness, and may provide a physiological basis for increased somatic complaints in Gulf veterans with symptoms of posttraumatic stress." (Peckerman, et al., 2003)

The fourth study evaluated 15 Gulf War veterans with CFS and 19 healthy Gulf War veterans, who were a subset of the veterans in the first New Jersey study, on respiratory and cardiovascular responses to maximal exercise. No differences were observed between the veterans with CFS and healthy veterans with regard to virtually every aspect of the exercise test. The exercise capacity was not different between the groups, and both groups would be considered to be in the lower end of the normal range. (Nagelkirk, et al., 2003)

The fifth study showed no significant differences between Gulf War veterans and non-deployed veterans on the olfactory identification test or on

any of the 11 neurocognitive measures. The authors concluded: "The absence of both olfactory and cognitive performance deficits argues against a neurotoxic etiology for self-reported health and cognitive symptoms." (Vasterling, et al., 2003)

The objectives of the sixth, seventh, and eighth studies were linked and were based on an evaluation of Gulf War veterans from Boston and New Orleans. (Lindem, 2003a; Lindem, 2003b; Lindem, et al., 2003c) These studies did not alter the major conclusions of the 2001 parent study (White, et al., 2001) in which the authors concluded that the rates of PTSD were "quite high in health care seeking veterans who have received the diagnosis of CFS or ICF (idiopathic chronic fatigue). This finding supports, at least in part, the hypothesis that the stress of deployment and combat did play a significant role in producing the alterations in health reported by some Gulf veterans."

The ninth study was to compare cognitive functioning on neuropsychological testing in 207 Gulf War veterans and 53 non-deployed veterans, who were seeking treatment for a variety of health problems. Overall, the Gulf War veterans performed more poorly than the non-deployed veterans on several tests of attention, visuospatial skills, visual memory, mood complaints, and motivation to perform well on the tests. Compared to Gulf War veterans without PTSD, Gulf War veterans diagnosed with PTSD reported increased rates of several mood complaints, but showed no other differences. However, the authors did not adjust for PTSD, depression, or other psychological distress. (Sullivan, et al., 2003)

The tenth study estimated the prevalence of PTSD and chronic fatigue syndrome-like illness (CFS) among 11,441 Gulf War veterans and 9,476 non-deployed veterans who participated in the VA National Health Survey; and to evaluate the relationships between the prevalence rates and deployment-related stress. PTSD was significantly higher in Gulf War veterans (10.1%) compared to non-deployed veterans (4.2%), with an adjusted odds ratio of 2.6. The prevalence of CFS was significantly increased in Gulf War veterans (4.9%) compared to non-deployed veterans (1.2%), with an adjusted odds ratio of 4.2. (Kang, et al., 2003)

The eleventh study used the results of a national study of women veterans to describe characteristics of rape victims and assailants, and to identify workplace environmental factors associated with rape occurring during military service. The authors found that "Military environmental factors were strongly associated with women's risk of rape during military service, even when considered in the context of established risk factors for violence, such as prior victimization and younger age (Sadler, et al., 2003)

The twelfth study consisted of a meta-analysis of published studies that compared the prevalence of psychiatric disorders in Gulf War veterans with the prevalence of those disorders in non-deployed veterans. The authors found Gulf War veterans have consistently been diagnosed with significantly higher rates of PTSD, major depression, and anxiety disorders than non-deployed veterans. Stimpson, et al., 2003

C. Diagnosis:

One study published in 2003 focused on diagnosis of the level of an enzyme, paraoxonase (PON1), which hydrolyzes (breaks down) many classes of chemicals, including organophosphate chemicals, such as nerve agents and pesticides. The authors concluded: "there are no differences in the genotype or PON1 activity between healthy and ill Gulf War veterans; and the participants who were deployed to the Gulf had lower median PON1 values than the other two groups . . . This effect appears to relate to the deployment per se rather than illness." (Hotopf, et al., 2003b)

D. Reproduction:

One study published in 2003 focused on reproduction in Gulf War veterans (GWV). Overall, there were no significant differences in the proportion of infants born with one or more of the 48 birth defects to GWV, compared to the proportion of infants born with one or more of the 48 birth defects to non-deployed veterans (NDV). However, the authors did not control for multiple statistical comparisons. (Araneta, et al., 2003)

E. Treatment:

One study published in 2003 evaluated whether aerobic exercise (AE) and/or cognitive behavior

therapy (CBT) could improve the chronic symptoms and functional status of ill Gulf war veterans. CBT, with or without AE, led to improvements in mental health functioning and cognitive symptoms. AE, with or without CBT, led to improvements in mental health functioning, cognitive symptoms, fatigue, and distress. Neither treatment led to a significant decrease in pain. (Donta, et al., 2003)

F. Prevention:

Two articles published in 2003 focused on the potential health effects of the anthrax vaccine, a preventive measure.

The first study examined all inpatient and outpatient visits of 2 million active-duty servicemembers during a three-year period to identify diagnoses that were more frequent after anthrax vaccination than before. The authors concluded: "the results together with those of other monitoring efforts provide unprecedented oversight of the safety of the AVA program. Results of surveillance efforts to date suggest that AVA has few if any significant adverse health effects." (Lange, et al., 2003)

The second study evaluated a broad range of short-term and longer-term health effects of the anthrax vaccine in a cohort of 601 Army health care personnel, who were followed for two years. The authors did not find any serious adverse events or effects on health (Wasserman, et al., 2003)

G. Chemical Weapons:

Three studies published in 2003 focused on the health effects of chemical weapons, one in human volunteers and two in laboratory animals.

The human volunteer study evaluated the potential long-term health effects of exposure to chemical warfare agents, including self-reported symptoms of neuropsychological impairment, peripheral neuropathy, sleep disorders, depression, and anxiety. There appeared to be few or no observable long-term effects of nerve agent exposure, to date. This study is unique because the chemical exposures of these volunteers were documented, at known concentrations that were high enough to cause immediate symptoms in many of the experiments. (Page, 2003)

The first laboratory study exposed guinea pigs and marmosets (monkeys) to the lowest quantifiable concentration of sarin vapor and to increase exposure time until the lowest observable effect level (LOEL) became measurable. The authors estimated that the measurement of detectable sarin concentration in plasma was as much as 1000 times more sensitive than the measurement of inhibition of cholinesterase activity, which is the classic method of assessing internal dose of sarin. The study did not actually measure cholinesterase activity or any health effects in the animals; therefore, these results cannot be extrapolated to potential health effects in humans. (van Helden, et al., 2003)

The objective of the second laboratory study was to investigate the toxicokinetics of VX, a non-volatile, persistent nerve agent, in hairless guinea pigs and marmosets (monkeys). Large variations were observed between individual animals in the rate of skin penetration of VX. This study is not directly relevant to Gulf War veterans, however, because there is no evidence that servicemembers were exposed to VX. (van der Schans, et al., 2003)

H. Pyridostigmine Bromide:

One laboratory study published in 2003 focused on the health effects of pyridostigmine bromide (PB). The authors concluded: "A comprehensive investigation [of rodent models] using long-term blood pressure and heart rate monitoring, and behavioral evaluation revealed no changes in any parameters. This occurred concurrent with significant inhibition of blood AChE activity. The results suggest that prolonged low-dose PB treatment itself does not represent a significant risk factor." (Bernatova, et al., 2003)

I. Interactions of Exposures:

Three laboratory studies published in 2003 focused on the effects of pyridostigmine bromide (PB), in combination with stress or other chemicals.

The first study evaluated the effects of forced running stress, low dose paraoxon, or a combination of stress and paraoxon on the short-term toxicity of high-dose PB in male Sprague-Dawley rats. The authors concluded: "These results provide further information that acute physical stress has little effect on PB toxicity and

suggest that pre-exposure to a moderately low dose of an organophosphate anticholinesterase also has little influence on the peripheral and/or central effects of acute PB exposure." (Shaikh and Pope, 2003)

The second study evaluated the effects of 14 days of daily physical stress (treadmill running) or daily exposure to a subclinical dosage of paraoxon on cholinesterase inhibition in the blood and brain of male Sprague-Dawley rats, combined with exposure to PB. The authors concluded: "The results of this study suggest that repeated physical stress (forced running) and daily subclinical paraoxon exposures have relatively little effect on subacute PB toxicity. (Shaikh, et al., 2003)

The third study sought to determine if exposure to low-level sarin exposure and PB, alone or in combination, could lead to cognitive or neurobehavioral abnormalities in male Sprague-Dawley rats. The authors concluded: "This study gives further support to the use of PB as one of the therapeutic resources against nerve agent poisoning and does not support the hypothesis that delayed symptoms experienced by Persian Gulf War veterans could be due to PB, alone or in association, with low-level nerve agent exposure." (Scremin, et al., 2003)

III. RESEARCH FUNDING TRENDS

The Departments of Veterans Affairs (VA), Defense (DoD), and Health and Human Services (HHS) have sponsored 256 projects. The scope of the Federal research portfolio is broad, from small pilot studies to large-scale epidemiology studies involving large populations and major research center programs. From FY94 through FY03, Federal Government funding for the direct costs of Gulf War research exceeded $242.9 million during this period. This funding does not include indirect costs of conducting the research such as facility, administrative and operational costs. Estimates of these indirect costs are $72.9 million. As of September 30, 2003, 185 projects were completed (72% of the 256 projects), and 71 projects were ongoing.

IV. NEW RESEARCH PROJECTS AND INITIATIVES

Besides new research findings appearing in the published scientific literature, VA and DoD funded 13 new projects.

In February 2003, VA joined DoD in funding a study of neuropsychological function in Army soldiers who are deploying to the current war in Iraq. (VA-88/DoD-154) This study is the first of its kind to compare pre- and post-deployment cognitive function.

VA funded an additional 10 projects during FY03. The primary research foci of these projects included treatment (2); pyridostigmine bromide (1); and brain and nervous system (7). DoD funded two other projects in FY03 that focus on interactions.

V. RESEARCH PRIORITIES

These priorities remain unchanged.

I. INTRODUCTION

On August 31, 1993, in response to section 707 of Public Law 102-585, President William J. Clinton named the Secretary of Veterans Affairs (VA) to coordinate research activities undertaken or funded by the Executive Branch of the Federal Government into the health consequences of service in the Gulf War. Section 104 of Public Law 105-368 (1998) expanded the range of activities to be coordinated. VA carries out its coordinating role through the auspices of the Research Subcommittee of the Deployment Health Working Group (DHWG). The DHWG reports, in turn, to the Health Executive Council that VA's Under Secretary of Health and the Department of Defense (DoD) Assistant Secretary for Health Affairs co-chair.

As part of its coordination role, VA is required to submit an annual report on the results, status, and priorities of Gulf War-related research activities to the Senate and House Veterans' Affairs Committees. This document, the 2003 *Annual Report to Congress*, is the tenth report on research and research activities. (PGVCB, 1995a; 1996a; 1997; 1998a; 1999a; 2001; MVHCB, 2001a; 2002; DHWG, 2004a; 2004b) The 2003 *Annual Report to Congress* reports on research funded by Federal and non-federal institutions. All new peer-reviewed reports of high quality research add to existing knowledge, regardless of funding source.

This Annual Report contains three sections in addition to the introduction. Section II highlights and summarizes research progress since the last Annual Report. Section III is an analysis of the Federal Government's portfolio of research on Gulf War veterans' illnesses. Section IV highlights significant research projects and initiatives since the last Annual Report.

II. RESEARCH RESULTS IN 2003

In the past year, there have been numerous research studies that have yielded results that provide new and expanded information on the health problems of Gulf War veterans. This section provides brief summaries of research projects for which results were published from January 2003 to December 2003. Because all scientifically peer-reviewed research must be considered in assessments of Gulf War veterans' illnesses, these summaries are inclusive of both federally funded and non-federally funded research. The Deployment Health Working Group tracks all federally funded research projects related to Gulf War veterans' illnesses. These are described in Appendix A.

All research studies have strengths and limitations. The presence of limitations in a particular study does not necessarily invalidate its findings or conclusions, but must be taken into account in evaluating a study's overall validity and importance. For this reason, the strengths and limitations of each of the new reports of study findings are cited as a guide for the reader. Among the limitations, epidemiological studies are frequently subject to a variety of biases. For example, studies that rely on self-reported symptoms and exposures are subject to recall bias, which can result in misclassification as to whether an individual truly experienced an outcome of interest or incurred exposure to a specific agent or other circumstance. Such misclassification can produced erroneous results. Another form of bias results when individuals are enrolled in a study solely because they attend a specific clinic or because they have certain characteristics rather being chosen at random. This can create selection bias that can produce conclusions that are erroneous or which apply to only a segment of the overall population of affected individuals. Other factors that can affect the validity or reliability of a study's conclusion include sample size and response rate.

Research using animal models is subject to limitations in its applicability to humans. Sources of limitations include extrapolation of biological processes from one animal species to another, and extrapolation of experimental dosing regimens (route of administration, amount, and duration) from animal experiments to real human exposure situations. Experiments utilizing whole laboratory animals are less difficult to extrapolate to humans than studies performed in test tubes; therefore, studies of whole animals are emphasized in this report.

As in previous reports to Congress, studies have been categorized according to the particular focus of the research. The research reports summarized below are grouped in nine focus areas: symptoms and general health status, brain and nervous system function, diagnosis, reproduction, treatment, prevention, chemical

weapons, pyridostigmine bromide, and interactions of exposures.

A. Symptoms and General Health Status

Overview:

Seven large studies published in 2003 focused on symptoms and general health. (Kang, et al., 2003; Smith, et al., 2003; Stuart, et al., 2003; Wessely, et al., 2003; Hotopf, et al., 2003a; Macfarlane, et al., 2003; Carney, et al., 2003) These publications included the results of studies conducted at three federally funded research centers in San Diego, Iowa, and London, UK. Each of the publications included hundreds to thousands of individuals. Three of these studies relied upon medical evaluations, rather than relying solely on self-administered surveys. (Smith, et al., 2003; Stuart, et al., 2003; Macfarlane, et al., 2003) Six of these studies were population-based, which means that the investigators attempted to broadly sample affected individuals rather than study a small, possibly unrepresentative sample. Thus, the results of these six studies may have implications for the overall population of 697,000 Gulf War veterans (all except Stuart, et al., 2003).

Kang, et al. (2003) included two objectives. The first objective was to estimate the prevalence of posttraumatic stress disorder (PTSD) and chronic fatigue syndrome-like illness (CFS) among 11,441 Gulf War veterans and 9,476 non-deployed veterans who participated in the VA National Health Survey. The second was to evaluate the relationships between the rates of these conditions and deployment-related stress.

The objective of Smith, et al. (2003) was to compare the rates and causes of hospitalizations in 99,614 Gulf War veterans who may been exposed to low-levels of nerve agents due to the demolitions at Khamisiyah, Iraq, in March 1991, with the rates and causes in 318,458 Gulf War veterans who were unlikely to have been exposed, from 1991 to 2000.

The objective of Stuart, et al. (2003) was to evaluate data from 44,168 veterans enrolled in the DoD Gulf War registry program to determine possible predictors of belief in exposure to nerve agent or mustard agent during the Gulf War, including demographic factors, military service factors, environmental exposures, combat exposures, reported symptoms, and medical diagnoses, in order to identify risk factors for belief in exposure to a potential terrorist weapon.

The objectives of Wessely, et al. (2003) and Hotopf, et al. (2003a) were linked, and were based on a comparison of three groups of British veterans at two time points. Time I was 1997-98 and Time III was 2000-2001. The authors did not use an intermediate Time 2 for these particular studies. Participants included 1,089 Gulf War veterans, 638 Bosnia veterans, and 643 non-deployed veterans. The objectives of the Wessely, et al. were to compare the consistency of reporting of military traumatic events and environmental exposures at Time I versus Time III; and to compare consistency of reporting between Gulf War veterans and Bosnia veterans. The objectives of Hotopf, et al. were to compare the prevalence of several health outcomes over time (Time I to Time III), among the three cohorts; and to determine if differences in prevalence at follow-up among the three cohorts could be explained by greater incidence or greater persistence of disorders.

The objective of Macfarlane, et al. (2003) was to compare the cancer incidence rates in 51,721 British Gulf War veterans, with the rates in 50,755 British non-deployed veterans, from 1991 to 2002.

The objective of Carney, et al. (2003) was to compare 129 female Gulf War veterans and 1,767 male Gulf War veterans from the state of Iowa on their combat experiences, environmental exposures, and rates of health care utilization.

Individual Study Results:

Kang, et al. (2003) examined the results of the VA National Health Survey to determine whether differences existed between Gulf War veterans who were diagnosed with chronic fatigue syndrome (CFS) or posttraumatic stress disorder (PTSD) compared with healthy Gulf War veterans. Researchers noted that CFS was significantly associated with younger age, single marital status, enlisted rank, service in the Reserve/National Guard vs. active-duty, and service in the Army and Marines vs. the other services. PTSD was significantly associated with female gender, older age, non-white race, enlisted rank, service in the Reserve/National Guard vs. active-duty, and service in the Army vs. the other services.

Smith, et al. (2003) evaluated the health effects of potential exposure to very low levels of sarin and cyclosarin due to the demolition of munitions in Khamisiyah, Iraq in March 1991. (Smith, et al., 2003) In particular, the study sought to identify rates, causes, and risk factors associated with hospitalization. Researchers found several factors associated with an increased risk of hospitalization. These included: female gender, older age, enlisted rank, service in the Reserve/National Guard vs. active-duty, service in the Army vs. the Air Force, and hospitalization in the twelve months preceding the war.

Rates and causes of hospitalizations were compared between 99,614 veterans who were potentially exposed to nerve agents, and 318,458 veterans with no exposure, from 1991 to 2000. There were no differences in the rates or causes of hospitalizations, with one exception. The rate of cardiac dysrhythmia was higher in Gulf War veterans. The authors concluded that these results "may be reassuring to those veterans concerned about other health effects associated with possible exposure to munitions destruction at Khamisiyah, Iraq."

Stuart, et al. (2003) evaluated data from 44,168 veterans enrolled in the DoD Gulf War registry program to determine possible predictors of belief in exposure to nerve agent or mustard agent during the Gulf War, including demographic factors, military service factors, environmental exposures, combat exposures, reported symptoms, and medical diagnoses. (Stuart, et al., 2003) In contrast to veterans who believed they had not been exposed, veterans who believed they had been exposed to chemical weapons were significantly more likely to be: female, older, non-white race, in the Army vs. the other services, to report more symptoms and worse overall health at the time of their evaluations, and to be diagnosed with psychiatric disorders vs. disorders of other organ systems.

The objective of Wessely, et al. (2003) was to evaluate the reliability of recall of traumatic events and environmental exposures during the Gulf War. (Wessely, et al., 2003) This study focused on two groups of British veterans who have been evaluated at three time points (Time I was 1997-98 and Time III was 2000-2001), including 1,089 Gulf War veterans and 638 Bosnia veterans. The objectives of this study were to compare the consistency of reporting of military traumatic events and environmental exposures at Time I versus Time III; and to compare consistency of reporting between Gulf War veterans and Bosnia veterans. A questionnaire that included 28 potential traumatic experiences and environmental exposures was used at both time points. The reliability of the reporting over time was good for some exposures, but was very low for others. Gulf War veterans reported a higher number of exposures over time, but Bosnia veterans did not. Among Gulf War veterans only, reporting new exposures for the first time at Time III was associated with worsening of health perception. Conversely, not reporting exposures that were previously reported at Time I was associated with improvement of health perception. The authors concluded: "Stability of recall of hazardous exposures during military operations differs according to the nature of the exposure-those extensively publicized in the media are particularly problematic. Reporting of military hazards after a conflict is not static, and is associated with current self-rated perception of health. Self-report of exposures associated with media publicity needs to be treated with caution."

The results of this 2003 British study were consistent with several previous studies that evaluated the recall of traumatic events and environmental exposures during the Gulf War. These have included studies of traumatic events among Gulf War veterans in New Haven (CT) and Boston. (Southwick, et al., 1997; King, et al., 2000) They also included studies of environmental exposures among Gulf War veterans in Portland, Boston, Iowa, and the United Kingdom. (Wolfe, et al., 1998; McCauley, et al., 1999a; Wolfe, et al., 2002; Lange, et al., 2002; Greenberg, et al., 2003) These studies systematically evaluated the potential problem of recall bias in questionnaire studies of Gulf War veterans, and each study supported the view that self-reported information on exposures could be unreliable and subject to change over time.

Hotopf, et al. (2003a) compared three groups of British veterans at two time points. Participants of this longitudinal study consisted of 1,089 Gulf War veterans, 638 Bosnia veterans, and 643 non-deployed veterans, and the authors compared data taken at Time I (1997-98) and at Time III (2000-2001) of the study. The authors did not use an intermediate Time II for this particular

study. Their objectives were to compare the prevalence of several health outcomes over time among the three cohorts (Time I to Time III); and to determine if differences in prevalence at follow-up could be explained by greater incidence or greater persistence of disorders. Gulf War veterans continued to report worse health on all health outcomes at Time III compared to the two control groups. However, the health gap between the Gulf War veterans and the control groups had narrowed slightly. Gulf War veterans did not deteriorate from Time I to Time III, and they did not have a higher incidence of new illnesses at Time III, compared to the two control groups. Gulf War veterans reported a modest improvement in the prevalence of chronic fatigue and psychological distress at Time III compared to Time I; however, they reported a slight worsening of physical functioning. Bosnia veterans and non-deployed veterans also reported a slight worsening of physical functioning at Time III compared to Time I, probably due to aging. The higher rates of illnesses in Gulf War veterans at Time III were explained by both higher incidence of symptoms at Time I and greater persistence of symptoms from Time I to Time III. This was the first population-based study to evaluate whether Gulf War veterans were getting better, staying the same, or getting worse over time.

The objective of Macfarlane, et al. (2003) was to compare the cancer incidence rates in the entire population of 51,721 British Gulf War veterans, with the rates in 50,755 British non-deployed veterans, from 1991 to 2002. Cancer of all types was diagnosed in a total of 270 Gulf War veterans (0.52%) and 269 non-deployed veterans (0.53%). In addition, there was no increase in the rates of specific types of cancer in Gulf War veterans. After adjustment for lifestyle factors (smoking and alcohol use), there were no changes in the results. The authors concluded: "Incidence of and mortality from cancer in Gulf War veterans is almost identical to that seen in veterans who were not deployed in the Gulf." This was the first study of the cancer incidence in Gulf War veterans, and its results were quite consistent with the results of six earlier studies (four studies of cancer mortality and two studies of hospitalization for cancer). (Macfarlane, et al., 2000; Kang, et al., 1996; Kang, et al., 2001; Kang, et al., 2002; Gray, et al., 1996; Gray, et al., 2000)

Carney, et al. (2003) focused on the potential differences in experiences of female and male Gulf War veterans. Seven percent of Gulf War troops were women, the highest proportion in any major conflict, to date. In 1995-96, a telephone survey was performed of a randomly selected sample of military personnel, whose home state of residence was Iowa. A total of 3,695 Gulf War veterans and non-deployed veterans completed the survey. (Iowa, 1997; Doebbeling, et al., 2000) The objective of this particular analysis was to compare 129 female Gulf War veterans and 1,767 male Gulf War veterans on their combat experiences, environmental exposures, and rates of health care utilization. Women and men were similar on age, race, and rank. Women were more likely to be: better educated; single or divorced; married to a spouse who was also in the military; in the reserve or National Guard vs. active-duty; and in the Army vs. the other services. Military occupational specialties were similar in women and men. Participation in combat was defined as: the subject was deployed during the air war or ground war and the subject reported three or more of nine-combat related exposures (for example, "came under small arms fire" or "saw any dead bodies"). Men were significantly more likely to have participated in combat than women (28% vs. 19%). Men reported a significantly higher number of the nine combat exposures (an average of 2.0 vs. 1.0 exposures). A total of 31 combat and environmental exposures were included in the survey (for example, smoke from oil well fires or pesticides). Women and men both reported an average of 10.0 of these 31 exposures. Men were significantly more likely to report three of the 31 exposures. Women and men reported the other 28 exposures at about the same rates. Women reported significantly higher rates of outpatient visits and hospitalizations in the previous year (including visits for gynecology and pregnancy). Seventeen percent of women had been hospitalized in the previous year, compared with 5% of men. Women also reported higher rates of receiving VA disability compensation, compared to men (17% vs. 7%). The authors stated: "The frequency with which serious aspects of nearby combat are reported by women confirms that the experience in the U.S. military is clearly becoming more homogeneous."

There has only been one other population-based study that focused specifically on the health of female Gulf War veterans. (Unwin, et al., 2002)

This British study showed only a few differences in the health of female and male veterans. The authors stated: "women are neither more nor less vulnerable to the physical and psychological stressors of active service;" and they found nothing to suggest "any special considerations be made on health grounds for service women in future deployments."

B. Brain and Nervous System Function

Overview:

Twelve studies published in 2003 focused on brain and nervous system function. (Horner, et al., 2003; Haley, 2003; Peckerman, et al., 2003; Nagelkirk, et al., 2003; Vasterling, et al., 2003; Lindem, et al., 2003a; Lindem, et al., 2003b; Lindem, et al., 2003c; Sullivan, et al., 2003; Kang, et al., 2003; Sadler, et al., 2003; Stimpson, et al., 2003) These publications included results of eight studies conducted at four federally funded research centers in New Jersey, Boston, Iowa, and Washington, DC. (Peckerman, et al., 2003; Nagelkirk, et al., 2003; Lindem, et al., 2003a; Lindem, et al., 2003b; Lindem, et al., 2003c; Sullivan, et al., 2003; Kang, et al., 2003; Sadler, et al., 2003) Eight of these studies included hundreds to thousands of individuals. (Horner, et al., 2003; Lindem, et al., 2003a; Lindem, et al., 2003b; Lindem, et al., 2003c; Sullivan, et al., 2003; Kang, et al., 2003; Sadler, et al., 2003; Stimpson, et al., 2003) Nine studies relied upon psychiatric, neuropsychological, or neurological evaluations, rather than relying solely on self-administered surveys (all except Kang, et al., 2003, Sadler, et al., 2003, and Stimpson, et al., 2003).

Two 2003 studies evaluated the incidence of amyotrophic lateral sclerosis (ALS; also known as Lou Gehrig's disease) in Gulf War veterans. (Horner, et al., 2003; Haley, 2003) ALS is a rapidly fatal neuromuscular disease of unknown etiology. The objective of the first study was to compare the incidence of ALS in Gulf War veterans from 1990 to 2000 with the incidence of ALS in non-deployed veterans. (Horner, et al., 2003) The objective of the second study was to determine the incidence of ALS in 1991 to 1998 in a subset of the Gulf War veterans, who were diagnosed with ALS before age 45, and who were also included in the first study. (Haley, 2003)

Two studies in New Jersey evaluated autonomic nervous system control of cardiovascular function in ill and healthy Gulf War veterans. (Peckerman, et al., 2003; Nagelkirk, et al., 2003) The objective of the first study was to compare 16 Gulf War veterans who had CFS and PTSD, 39 Gulf War veterans with CFS only, and 47 healthy Gulf War veterans on cardiovascular responses to a variety of stressors. (Peckerman et al., 2003) The objective of the second study was to evaluate 15 Gulf War veterans with CFS and 19 healthy Gulf War veterans, who were a subset of the veterans in the first New Jersey study, on respiratory and cardiovascular responses to maximal exercise. (Nagelkirk, et al., 2003)

The objective of the fifth study was to evaluate olfactory identification performance and neuropsychological functioning in 72 Gulf War veterans and 33 non-deployed veterans in New Orleans. (Vasterling, et al., 2003)

The objectives of the sixth, seventh, and eighth studies were linked and were based on an evaluation of Gulf War veterans from Boston and New Orleans. (Lindem, 2003a; Lindem, 2003b; Lindem, et al., 2003c) In 1994-96, neuropsychological testing was performed on 142 members of the Fort Devens cohort, 51 members of the New Orleans cohort, and 47 comparison veterans who had deployed to Germany. The overall results of this evaluation were previously published. (White, et al., 2001) In 2003, sub-analyses of three different aspects of this neuropsychological evaluation were published, as a series. (Lindem, 2003a; Lindem, 2003b; Lindem, et al., 2003c)

The objective of the ninth study was to compare cognitive functioning on neuropsychological testing in 207 Gulf War veterans and 53 non-deployed veterans, who were seeking treatment for a variety of health problems. (Sullivan, et al., 2003)

The objectives of the tenth study were to estimate the prevalence of PTSD and chronic fatigue syndrome-like illness (CFS) among 11,441 Gulf War veterans and 9,476 non-deployed veterans who participated in the VA National Health Survey; and to evaluate the relationships between the prevalence rates and deployment-related stress. (Kang, et al., 2003)

The objectives of the eleventh study were to use the results of a national study of women veterans to describe characteristics of rape victims and assailants, and to identify workplace environmental factors associated with rape occurring during military service. (Sadler, et al., 2003)

The objective of the twelfth study was to review all published studies that compared the prevalence of psychiatric disorders in Gulf War veterans with the prevalence in non-deployed veterans. (Stimpson, et al., 2003)

Neurology and Neurophysiology Studies

Two 2003 studies evaluated the incidence of amyotrophic lateral sclerosis (ALS; also known as Lou Gehrig's disease) in Gulf War veterans. (Horner, et al., 2003; Haley, 2003) ALS is a rapidly fatal neuromuscular disease of unknown etiology.

The objective of Horner, et al. (2003) was to compare the incidence of ALS in Gulf War veterans with the incidence of ALS in non-deployed veterans, from August 1990 to July 2000. This study used several active and passive ascertainment methods nationwide, to follow-up the entire population of military personnel who were on active-duty in 1990. Over ten years, 107 cases of ALS were identified and medically confirmed among approximately 2.5 million veterans. Forty cases were diagnosed among 696,118 Gulf war veterans, and 67 cases were diagnosed among 1,786,215 non-deployed veterans. The risk of ALS was significantly increased among Gulf War veterans compared to the controls, with a relative risk of 1.92. In addition, the risks were significantly elevated among Gulf War veterans who were in the Air Force or the Army, compared to their non-deployed counterparts (relative risks of 2.68 and 2.04, respectively). This study included detailed interviews to obtain medical, military, and environmental exposure histories. These data are being analyzed to determine if specific factors can be identified in Gulf War veterans that are associated with an elevated risk of ALS, and the results should be published in 2004. In addition, VA determined that systematic identification and tracking of veterans with ALS was a high research priority. In 2002, VA funded a National Registry of Veterans with ALS, to provide a data resource for future studies on the causes and treatment of ALS (Project VA-89).

The objective of Haley (2003) was to determine the incidence of ALS in 1991 to 1998 in a subset of the Gulf War veterans, who were diagnosed with ALS before age 45, and who were also included in the Horner, et al. study. The incidence rate of ALS in Gulf War veterans was compared with the rate in the same age group in the general U.S. population. Seventeen cases of ALS were identified and medically confirmed among young Gulf War veterans, who were diagnosed when they were less than age 45. The author commented that this number probably reflected an undercount, because of incomplete methods of ascertainment. From 1991 to 1994, four young Gulf War veterans were diagnosed with ALS, which is approximately 6% less than expected in the general population. From 1995 to 1998, thirteen young Gulf War veterans were diagnosed with ALS, which is 2.27 times higher than expected in the general population, which was statistically significant. The author commented: "These findings indicate the need for active surveillance to determine whether the excess incidence of ALS in young Gulf War veterans continues and for case-control studies to define potentially etiologic risk factors."

An invited editorial accompanied the two ALS studies. (Rose, 2003) It highlighted some methodological limitations of the studies, and it expressed doubt about whether further Gulf War studies would reveal much about the etiology of ALS, as follows: "Although these researchers are to be congratulated for their thorough and painstaking work, there is still the concern that this excess risk is not convincing, especially given the small number of ALS cases, and a number of potential methodological flaws." The editorial noted that "subgroup analysis to determine which of the many Gulf War-specific environmental factors might trigger ALS is unreliable in such a small group of cases. It seems unlikely that more research into Gulf War-related environmental factors will disclose a reliable trigger factor when applied to an ALS cluster with a still controversial twofold excess risk."

Two studies in New Jersey evaluated autonomic nervous system control of cardiovascular function in ill and healthy Gulf War veterans. The objective of Peckerman, et al. (2003) was to compare 16 Gulf War veterans who had CFS and PTSD, 39 Gulf War veterans with CFS only, and 47 healthy Gulf War veterans on cardiovascular

responses to a variety of stressors. (Peckerman et al., 2003) In 1995-96, scientists at the East Orange VA Medical Center performed a survey of 1,161 Gulf War veterans who had participated in the VA Gulf War Registry exam. One hundred Gulf War veterans who reported severe fatigue were invited to participate in a clinical evaluation to determine if they met the diagnostic criteria for CFS. Fifty-five veterans who met the criteria for CFS were invited to participate in more detailed evaluations, as well as 47 healthy Gulf War veterans. (Pollet, et al., 1998; Natelson, et al., 2001) This particular study evaluated if altered control of cardiovascular responses during stress could be part of the underlying mechanism of fatigue in some Gulf War veterans with CFS. (Peckerman et al., 2003) PTSD can also cause significant changes in autonomic function, and could possibly alter cardiovascular responses. The 16 veterans with CFS and PTSD demonstrated abnormal responses in cardiovascular regulation, but the 39 veterans with CFS only did not. The 16 veterans with CFS and PTSD demonstrated a significantly reduced ability to regulate blood pressure, whether it was in response to a mental effort that called for an increase in blood pressure, or in response to the normal reflex response of recovery of blood pressure after standing up. The authors concluded: "Comorbid PTSD contributes to dysregulation of cardiovascular responses to mental and postural stressors in Gulf veterans with medically unexplained fatiguing illness, and may provide a physiological basis for increased somatic complaints in Gulf veterans with symptoms of posttraumatic stress."

The objective of Nagelkirk, et al. (2003) was to evaluate 15 Gulf War veterans with CFS and 19 healthy Gulf War veterans, who were a subset of the veterans in the first New Jersey study, on respiratory and cardiovascular responses to maximal exercise. (Nagelkirk, et al., 2003) Previous studies of civilians with CFS have indicated reduced aerobic capacity. Cardiorespiratory and metabolic responses were recorded during a maximal exercise test on a bicycle ergometer. Several indices were examined at both maximal and submaximal intensities to evaluate physiological responses to aerobic exercise. No differences were observed between the veterans with CFS and healthy veterans with regard to virtually every aspect of the exercise test. The exercise capacity was not different between the groups, and both groups would be considered to be in the lower end of the normal range. The authors concluded: "the present results do not support an explanation for CFS in Gulf veterans as an impaired muscular function or a deficiency in the ability of the cardiopulmonary system to meet metabolic demands of strenuous physical exertion."

Neuropsychology Studies

Several populations of Gulf War veterans and non-deployed veterans have demonstrated consistent results on neuropsychological testing. Self-reports of memory and concentration problems have been more common among the Gulf War veterans than among control subjects in several studies. However, on objective testing, performance was the same on most neuropsychological tests in Gulf War veterans and controls. In a small proportion of tests, such as attention or response speed, Gulf War veterans performed significantly more poorly than controls. After adjustment for PTSD, depression, or other psychological distress, the differences on the tests between the two groups diminished or disappeared. Similarly, in some studies that included many tests, the differences on the tests between the two groups diminished or disappeared, after adjustment for multiple statistical comparisons. These results were consistent in studies in New Orleans, Portland, New Jersey, Boston, and the U.K. (Vasterling, et al., 1997; Vasterling, et al., 1998; Anger, et al., 1999; Binder, et al., 1999; Storzbach, et al., 2000; Storzbach, et al., 2001; Lange, et al., 2001; White, et al., 2001; David, et al., 2002)

The objective of Vasterling, et al. (2003) was to evaluate olfactory identification performance and neuropsychological functioning in 72 Gulf War veterans and 33 non-deployed veterans in New Orleans. (Olfactory function was added to a standardized neuropsychological test battery to increase sensitivity of detection of possible neurotoxic effects. The authors evaluated the health of 844 Gulf War veterans and 326 non-deployed veterans from southern Louisiana in 1992 (Time 1). Some of these veterans were re-evaluated in 1993 (Time 2), 1995-96 (Time 3), and 2000 (Time 4). The 105 veterans in this particular analysis were a random subset of the veterans evaluated at Time 4. Twenty-eight of the 72 Gulf War veterans (39%) were diagnosed with Axis I psychiatric disorders, which was significantly higher than the rate in the 33 non-deployed veterans (9%). Gulf War veterans

were diagnosed with PTSD at significantly higher rates (15% vs. 0%). In addition, Gulf War veterans were diagnosed more frequently with depressive disorders and with anxiety disorders. The numbers of reported physical health symptoms were significantly associated with: the reported levels of war-zone stressor exposure; the number of depression symptoms; and the severity of PTSD symptoms. Olfactory identification was assessed with a widely used, 40-item "scratch and sniff" test that is sensitive to decreased ability to smell. A brief neuropsychological test battery was used, including 11 standardized measures (attention, fine motor skills, executive functioning, and memory). Gulf War veterans and non-deployed veterans showed no significant differences on the olfactory identification test or on any of the 11 neurocognitive measures. The authors concluded: "The absence of both olfactory and cognitive performance deficits argues against a neurotoxic etiology for self-reported health and cognitive symptoms."

The objectives of the second, third, and fourth neuropsychological studies in 2003 were published, as a series. (Lindem, 2003a; Lindem, 2003b; Lindem, et al., 2003c) They represent sub-analyses of three different aspects of neuropsychological testing conducted in 1994-96. Test participants consisted of 140 members of the Fort Devens cohort, 53 members of the New Orleans cohort, and 47 comparison veterans who had deployed to Germany. The overall results of this evaluation were previously published, and the authors concluded that their findings "do not suggest a widespread pattern of neurobehavioral deficits in Gulf War-deployed veterans, but rather there may be subgroups of veterans with subtle impairments." (White, et al., 2001)

The objective of the first sub-analysis was to evaluate the relationships between the severity of PTSD symptoms, self-reported exposure to chemical weapons, and neuropsychological functioning, through the use of objective neuropsychological tests. (Lindem, et al., 2003a) The objective of the second sub-analysis was to investigate the relationship between the level of reported cognitive symptoms, such as problems with memory, and objective neuropsychological test performance. (Lindem, et al., 2003b) The objectives of the third sub-analysis were to assess motivation to perform well on neuropsychological testing and to assess the relationship between motivation to perform well and objective neuropsychological test performance. (Lindem, et al., 2003c) These three sub-analyses did not alter the major conclusions of the 2001 parent study. (White, et al., 2001) The authors had concluded that the rates of PTSD were "quite high in health care seeking veterans who have received the diagnosis of CFS or ICF (idiopathic chronic fatigue). This finding supports, at least in part, the hypothesis that the stress of deployment and combat did play a significant role in producing the alterations in health reported by some Gulf veterans. Finding a large rate of PTSD in Gulf veteran patients with medically unexplained somatic symptoms is consistent with epidemiological data indicating that Gulf veterans with PTSD report significantly more symptoms than Gulf veterans who received a medical diagnosis for their complaints."

The objective of Sullivan, et al. (2003) was to compare cognitive functioning on neuropsychological testing in 207 Gulf War veterans and 53 non-deployed veterans, who were seeking treatment for a variety of health problems. Eighty-seven of the Gulf War veterans and all 53 of the controls were randomly selected from lists of patients who were seeking diagnostic evaluation or treatment for any type of health complaint at any of the Boston area VA clinics. In addition, 120 of the Gulf War veterans were referred specifically for neuropsychological evaluation because of cognitive symptoms or physical symptoms. The symptoms of both groups of Gulf War veterans included memory and concentration difficulties, headaches, mood disorder, joint pains, and fatigue. No information was given on the symptoms of the control group. 28 Gulf War veterans (14%) met diagnostic criteria for current PTSD, compared to none of the controls. 44% of the 207 Gulf War veterans stated they had used pyridostigmine bromide (PB) during the war. Overall, the Gulf War veterans performed more poorly than the non-deployed veterans on several tests of attention, visuospatial skills, visual memory, mood complaints, and motivation to perform well on the tests. Compared to Gulf War veterans without PTSD, Gulf War veterans diagnosed with PTSD reported increased rates of several mood complaints, but showed no other differences. Gulf War veterans who reported using PB showed a difference on only one isolated test of executive function, compared to veterans who

did not use PB. This study had two substantial limitations. Other than PTSD, no information was provided on the actual diagnoses of the Gulf War veterans and controls, and whether the two groups had similar types of diagnoses, at similar levels of severity. It was possible that the overall level of medical or psychiatric disability was more severe in the Gulf War veterans, which secondarily affected their cognitive functioning. Also, in the comparison of the Gulf War veterans and the controls, there was no adjustment for PTSD, depression, or other psychological distress.

Psychiatry and Psychology Studies

Three 2003 studies examined the prevalence of PTSD, chronic fatigue syndrome-like illness, and psychiatric disorders as well as the prevalence of sexual assault in the military. (Kang, et al., 2003; Sadler, et al., 2003; Stimpson, et al., 2003)

The objectives of Kang, et al. (2003) were to estimate the prevalence of PTSD and chronic fatigue syndrome-like illness (CFS) in deployed and non-deployed Gulf War era veterans, and to evaluate the relationships between the prevalence rates and deployment-related stress. Researchers used data obtained in VA's "National Health Survey of Gulf War Era Veterans and Their Families," a project conducted in 1995-98. A total of 11,441 Gulf War veterans and 9,476 non-deployed veterans participated. For this particular analysis, rates of current PTSD and CFS were calculated, during the month before the survey. The rate of PTSD was determined with the PTSD Checklist. Veterans were considered to have "CFS-like illness," rather than CFS, because the 1994 CDC (Centers for Disease Control and Prevention) case definition of CFS requires a medical evaluation. Stressor severity was estimated among Reserve/National Guard troops only. Severity was defined as follows: veterans with minimal stress were non-deployed; veterans with moderate stress were deployed to a location other than the Gulf War; and veterans with high stress were deployed to the Gulf War. Also, the high stress group was stratified on the basis of three types of reported combat exposure: "wore chemical protective gear, other than for training, or heard chemical alarms sounding;" "involved in direct combat duty;" or "witnessed any deaths."

The rates of PTSD were significantly higher in Gulf War veterans (10.1%) compared to non-deployed veterans (4.2%), with an adjusted odds ratio of 2.6. (Kang, et al., 2003) The prevalence of PTSD was significantly associated with stress level, as follows: minimal stress, 3.3%; moderate stress, 6.1%; and high stress (with zero combat exposures), 7.0%. Increasing numbers of reported combat exposures were also significantly associated with PTSD rates: zero exposures, 7.0%; one exposure, 11.9%; two exposures, 18.4%; and three exposures, 22.6%. Therefore, the relative odds of PTSD increased monotonically across six stressor intensities, from 3.3% in the least stressful situation to 22.6% in the most stressful situation. The prevalence of CFS was significantly increased in Gulf War veterans (4.9%) compared to non-deployed veterans (1.2%), with an adjusted odds ratio of 4.2. The likelihood of CFS was significantly associated with stress level, as follows: minimal stress, 0.8%; moderate stress, 1.7%; and high stress (with zero combat exposures), 5.4%. The authors stated: "The results suggest that PTSD and CFS may account for a substantial portion of Gulf veterans who complain of a medically unexplained constellation of symptoms. The DoD should include screening for PTSD/CFS as part of post-deployment clinical examinations for troops returning from future military conflicts and appropriate follow-up health care should be planned by both DoD and VA."

Sadler, et al. (2003) used a national study of women veterans in 2003 to describe characteristics of rape victims and assailants, and to identify workplace environmental factors associated with rape occurring during military service. In three previous studies of women seeking VA medical care, there were frequent reports of sexual assault during military service (23 to 29% of respondents). In November 1996 to May 1997, a telephone survey was performed, which included a national sample of 558 women veterans. 26% of the women served in the Vietnam era (1961-May 7, 1975); 47% of the women served in the post-Vietnam era (May 8, 1975 to July 1990); and 27% of the women served in the Gulf War era (August 1990 to 1996). The average age was 40 years, 49% had been in the Army, 10% held officer rank, and 19% had served in a combat zone. The legal definition of rape was used, which includes attempted or completed sexual penetration, without the woman's consent. Sexual harassment was defined by several factors indicating a hostile environment. 79% of the

participants reported experiences of sexual harassment during their military service. 30% reported one or more attempted or completed rapes during military service; and 11% reported two or more rapes. Rape occurred more frequently on base, during off-duty hours, and in living quarters (barracks). There were no significant differences in the reported rates by era (Vietnam era, 24%; post-Vietnam era, 30%; and Gulf War era, 23%). 66% of the women had a service-connected disability: 49% had medical disabilities, 7% had psychiatric disabilities, and 10% had both medical and psychiatric disabilities. The authors concluded: "Military environmental factors were strongly associated with women's risk of rape during military service, even when considered in the context of established risk factors for violence, such as prior victimization and younger age. Consistent rates of rape across eras of service indicate that violence towards military women remains an unresolved problem."

The objective of a meta-analysis in 2003 was to review all published studies that compared the prevalence of psychiatric disorders in Gulf War veterans with the prevalence in non-deployed veterans. (Stimpson, et al., 2003) The authors searched the medical literature from January 1990 to May 2001 for studies of Gulf War veterans, and they eventually reviewed 409 relevant articles. They identified 20 studies that focused on the prevalence of PTSD and "common mental disorders," which the authors defined as depression and anxiety. In all 20 studies, the prevalence rates of PTSD and common mental disorders were higher in Gulf War veterans than in non-deployed veterans. A meta-analysis of the combined data from 9 of the 20 studies demonstrated that the prevalence of PTSD was 3.2 times higher in Gulf War veterans than in controls. A meta-analysis of the combined data from 11 of the 20 studies demonstrated that the prevalence of common mental disorders was two times higher in Gulf War veterans than in controls. Based on the aftermath of previous conflicts, the authors pointed out: "An increased rate of psychiatric disorders would therefore be expected in Gulf War veterans, although this does not diminish the importance of this morbidity in affecting veterans many years after returning from the conflict." The authors concluded: "These findings are attributable to the increase in psychologically traumatic events in wartime."

In summary, Gulf War veterans have consistently been diagnosed with significantly higher rates of PTSD, major depression, and anxiety disorders than non-deployed veterans. These higher rates have been demonstrated in several different populations of Gulf War veterans, through structured psychiatric interviews, as well as through self-administered questionnaires. Long-term follow-up evaluations of physical and psychological symptoms are continuing in five studies that include about 18,000 Gulf War veterans and non-deployed veterans, in Boston, New Orleans, New Jersey, Iowa, and the United Kingdom. In addition, the health of about 30,000 Gulf War veterans and non-deployed veterans will be re-evaluated as follow-up to the VA National Survey. This longitudinal research will provide a better understanding of the mind/body connection and how stress may have placed Gulf War veterans at increased risk for adverse health outcomes, ultimately leading to improved treatment and prevention strategies in the future.

C. Diagnosis

The one study published in 2003 focused on diagnosing the level of paraoxonase, an enzyme that hydrolyzes (breaks down) many classes of chemicals such as the organophosphate chemicals nerve agents and pesticides. The primary objective of this study was to compare the serum activity levels and genetic variants of the enzyme paraoxonase (PON1) in Gulf War veterans, Bosnia veterans, and non-deployed veterans. (Hotopf, et al., 2003b) Two smaller studies of ill Gulf War veterans had previously demonstrated some differences in the PON1 activity levels (Mackness, et al., 2000); or differences in the levels of genetic variants (polymorphisms) of the enzyme (Haley, et al., 1999). Low serum PON1 activity is associated with several diseases with an inflammatory component, such as coronary heart disease, diabetes, and renal disease. Therefore, the secondary objective was to determine if PON1 activity was associated with proinflammatory cytokine levels.

This study was the fifth of five publications based on so-called Time II medical exams. (Ismail, et al., 2002; David, et al., 2002; Sharief, et al., 2002; Higgins, et al., 2002; Hotopf, et al., 2003b) In Time I of this study, a mail survey was completed by more than 8,000 British Gulf War veterans, Bosnia veterans, and non-

deployed veterans. Time II of this study was performed in 1999-2000 and it involved thorough medical evaluations, including evaluation of PON1 levels. Subjects at Time II were selected on the basis of reported level of physical disability (illness) at Time I, including 115 ill Gulf War veterans, 95 healthy Gulf War veterans, 52 ill Bosnia veterans, and 85 ill non-deployed veterans.

There were significant differences in the PON1 activity levels among the four groups: both groups of ill and healthy Gulf War veterans had lower levels than the two ill control groups. (Hotopf, et al., 2003b) There were no statistical differences between the levels of genetic variants among the four groups. There were no associations between PON1 activity and gender or age. At Time I, the ill Gulf War veterans reported significantly higher numbers of physical symptoms and higher levels of psychological distress, than the other three groups. After adjusting for physical symptoms and psychological distress, there were still significant differences in the PON1 activity levels among the four groups. There were no associations found between PON1 activity levels and levels of several intracellular cytokines. The authors concluded: "there are no differences in the genotype or PON1 activity between healthy and ill Gulf War veterans; and the participants who were deployed to the Gulf had lower median PON1 values than the other two groups . . . This effect appears to relate to the deployment per se rather than illness." This British study had two advantages: a larger and more representative study population. The findings in this study were not consistent with the two previous studies because there were no differences in PON1 related to illness in Gulf War veterans.

D. Reproduction

One study published in 2003 focused on reproduction in Gulf War veterans. The primary objective of this study was to identify infants of military personnel born in six states, between January 1, 1989 and December 31, 1993. (Araneta, et al., 2003) Since the 1980s, active case ascertainment has been conducted for all major congenital anomalies in three states, Arizona, Hawaii, and Iowa, and in particular counties of Arkansas, California, and Georgia. The secondary objective was to compare the prevalence of major congenital anomalies in infants of Gulf War veterans (GWV), with the prevalence in infants of non-deployed veterans (NDV). Linked data from 2,271,747 military personnel and 2,314,908 live births in the six states identified 45,013 infants who were born to individuals who served on active-duty in February 1991. Twenty-seven percent of these infants were born to Gulf War veterans, and 10% were born to women veterans. There were no differences in the rates of low birth weight or preterm delivery in the infants born to GWV vs. infants born to NDV. Infants were identified who were diagnosed with birth defects in 48 categories, including 45 birth defect categories that are frequent or have important public health significance, according to CDC. Three additional defects were included, because of concerns of GWV families: dextrocardia, Goldenhar syndrome, and chromosomal anomalies (other than trisomies 13, 18, and 21). (Araneta, et al., 1997)

Overall, there were no significant differences in the proportion of infants born with one or more of the 48 birth defects to GWV, compared to the proportion of infants born with one or more of the 48 birth defects to NDV. These results were consistent with two large studies, which demonstrated that there were no significant differences in the rates of birth defects in infants born to GWV and NDV. (Cowan, et al., 1997; Araneta, et al., 2000)

Before the Gulf War, 0.7% of 142 infants born to female GWV had a birth defect, compared to 2.3% of 2,007 infants born to female NDV (not significant [NS]). (Araneta, et al., 2003) After the Gulf War, 2.9% of 308 infants born to female GWV had a birth defect, compared to 1.7% of 1,959 infants born to female NDV (NS). Before the Gulf War, 1.6% of 6,863 infants born to male GWV had a birth defect, compared to 1.8% of 17,922 infants born to male NDV (NS). After the Gulf War, 1.6% of 4,648 infants born to male GWV had a birth defect, compared to 1.6% of 11,164 infants born to male NDV (NS). There were no cases of Goldenhar syndrome among the 45,013 infants in this study. There were no significant differences in the rates of dextrocardia or chromosomal anomalies in infants of GWV, compared to infants of NDV.

After the Gulf War, the rate of one of the 48 birth defects, hypospadias, was significantly higher in sons of female GWV, compared to the prevalence in sons of female NDV (2.6% vs. 0.4%). After the Gulf War, the rates of two of

the 48 birth defects were significantly higher in infants of male GWV, compared to the rates in infants of male NDV. The prevalence of congenital tricuspid valve insufficiency or regurgitation was 0.22% in infants of male GWV, vs. 0.08% in infants of male NDV. The prevalence of aortic valve stenosis was 0.11% in infants of male GWV, vs. 0.02% in infants of male NDV. There was no control for multiple statistical comparisons. Hundreds of comparisons were made, and it would be expected that a certain number of apparent positive associations would be observed on the basis of chance alone. The authors commented: "We did not have the ability to determine if the excess was caused by inherited or environmental factors, or was due to chance because of myriad reasons, including multiple comparisons." Naval Health Research Center scientists have criticized this study because of concern about multiple comparisons. (Ryan, et al., 2004)

E. Treatment

VA and DoD determined that the development of treatments for medically unexplained symptoms was a research priority in 1998. That year, VA funded five treatment demonstration projects (VA-56, VA-57, VA-58, VA-59, and VA-60). A key goal was to test new and innovative clinical approaches for treating Gulf War veterans who have medically unexplained symptoms. The results of three projects have been published. (Everson, et al., 2002; Baker, et al., 2001; Richardson, et al., 2001; Hunt, et al., 2002; Richardson, et al., 2002) Final progress reports for all five projects are accessible at www.va.gov/health/environ/persgulf.htm.

VA also funded an Institute of Medicine study to identify effective treatments for health problems in Gulf War veterans. This study started in 1999, and it was published in July 2001. IOM concluded that difficult-to-diagnose symptoms experienced by some Gulf War veterans have a large overlap with the following seven diagnoses: chronic fatigue syndrome, depression, fibromyalgia, headache, irritable bowel syndrome, panic disorder, and PTSD. (IOM, 2001) In response to the report, VA and DoD jointly funded a treatment trial in FY02 for PTSD in women active-duty personnel and veterans (VA-74/DoD-125). This study was described in the *Annual Report for 2001*. (MVHCB, 2002) In FY03, VA funded two studies designed to improve the treatment of depression (VA-86 and VA-87).

In 1999, VA and DoD jointly funded two multi-site treatment trials. These were the Exercise Behavioral Therapy Trial (EBT) (VA-62 and DoD-115) and the Antibiotic Treatment Trial (VA-55 and DoD-119). (Donta, et al., 2003; Collins, et al., 2002) Details on these trials were provided in Section IV.C.1 of the *Annual Report for 1999*. (PGVCB, 2001) VA and DoD funded these two trials for more than $9.6 million and $5.6 million, respectively.

The EBT results were published in 2003. The objective of this study was to evaluate if aerobic exercise (AE) and/or cognitive behavior therapy (CBT) could improve the chronic symptoms and functional status of ill Gulf war veterans. (Donta, et al., 2003). The symptoms experienced by some ill Gulf War veterans resemble two chronic multi-symptom illnesses, chronic fatigue syndrome (CFS) and fibromyalgia (FM). Two treatments, cognitive behavior therapy and aerobic exercise, have been effective in improving the symptoms and functional status of individuals with CFS and FM. A randomized, multi-center, controlled trial was conducted at 18 VA Medical Centers and 2 military hospitals from April 1999 to September 2001. One thousand ninety two patients were randomized into the trial, and 998 patients (91%) completed the trial. 271 patients received usual care; 286 received CBT only; 269 received AE only; and 266 received CBT and AE.

To be eligible, veterans had to report the current presence of at least two of three symptoms: fatigue that limited usual activity; musculoskeletal pain, involving two or more regions of the body; and/or cognitive symptoms, including memory, concentration, or attention difficulties. Symptoms had to have begun after August 1990, and had to have lasted more than six months. Eligibility required a score of less than 40 on the Physical Component Summary (PCS) of the Medical Outcomes Survey SF-36. Patients were a mean age of 41 years, 85% male, 53% white, and 81% reported the presence of all three symptoms, for a mean duration of 6.7 years. 42% were currently receiving disability benefits, and another 24% had applied for benefits. Their mean score on the PCS was 33.7, 1.6 standard deviations below the mean in the general U.S. population. Their mean score on the Mental Component Summary (MCS) on the

SF-36 was 37.5, 1.3 standard deviations below the mean in the general population. Treatment lasted for 12 weeks. Patients were evaluated at baseline, 3 months, 6 months, and 12 months. CBT consisted of 12 weekly group sessions that were 60-90 minutes long. The goal was to learn behavioral skills to improve physical functioning, gradually and safely. AE consisted of 12 weekly one-hour sessions with an exercise therapist. The goal was to increase activity level, by setting the intensity of exercise based on the level of symptoms.

The primary outcome measure was the proportion of patients who showed more than a 7-point increase in the PCS at 12 months. At 12 months, the proportions with more than a 7-point increase were: 18.4% of patients in the CBE+AE group; 18.5% of patients in the CBT only group; 11.7% of patients in the AE only group; and 11.5% of the patients in the usual care group. The odds ratio of a 7-point increase in the groups receiving CBT (18.3% of 552 patients) vs. the groups without CBT (11.6% of 535 patients) was 1.71 (C.I.=1.15, 2.53). CBT, with or without AE, led to improvements in mental health functioning and cognitive symptoms. AE, with or without CBT, led to improvements in mental health functioning, cognitive symptoms, fatigue, and distress. Neither treatment led to a significant decrease in pain. Patients were not very compliant with either therapy, attending only 50% of the 12 weekly sessions, on average. However, patients who attended 8 or more of the 12 weekly sessions reported significantly greater improvement in physical function than patients who attended fewer sessions.

F. Prevention

Two articles published in 2003 focused on the potential health effects of the anthrax vaccine, a preventive measure. (Lange, et al., 2003; Wasserman, et al., 2003) The objective of the first study was to examine all inpatient and outpatient visits of 2 million active-duty servicemembers during a three-year period to identify diagnoses that were more frequent after anthrax vaccination than before. (Lange, et al., 2003) The objective of the second study was to evaluate a broad range of short-term and longer-term health effects of the anthrax vaccine in a cohort of 601 Army health care personnel, who were followed for two years. (Wasserman, et al., 2003)

In early 2002, the Institute of Medicine (IOM) published a report, entitled *The Anthrax Vaccine: Is It Safe? Does It Work?* (IOM, 2002) This report is based on hundreds of scientific studies and is 265 pages long. On page 2, its major conclusions on the adverse health effects of the anthrax vaccine (AVA) were: "The [IOM] committee found no evidence that vaccine recipients face an increased risk of experiencing life-threatening or permanently disabling adverse events immediately after receiving AVA, when compared with the general population. Nor did it find any convincing evidence that vaccine recipients face elevated risk of developing adverse health effects over the longer term, although data are limited in this regard (as they are for all vaccines)."

Since the IOM report was published in early 2002, several large epidemiological studies have been published that evaluated the potential adverse health effects of AVA. These studies have focused on military members who were vaccinated in 1998 or later years. Several studies included follow-up of months or years after vaccination. In general, there were no differences in the long-term health of servicemembers who were vaccinated with AVA, compared to those who were not vaccinated. (Sato, et al., 2002; Sever, et al., 2002; Rehme, et al., 2002; Wiesen and Littell, 2002; Lange, et al., 2003; Wasserman, et al., 2003) A review article was published in November 2003 that incorporated most of these 2002 and 2003 studies. (Grabenstein, 2003)

The objective of the first study in 2003 was to examine all inpatient and outpatient visits of 2 million active-duty servicemembers during a three-year period to identify diagnoses that were more frequent after anthrax vaccination than before. (Lange, et al., 2003) Individuals who were on active-duty at any time between January 1, 1998 and December 31, 2000 were included in this study (total of 2,013,179). This was defined as the pre-vaccination cohort. The Defense Medical Surveillance System was the source of all the data in the study, including all anthrax vaccinations (AVA), and all hospitalizations and outpatient visits in military facilities during that time period. Rates of hospitalizations and outpatient visits were calculated for 14 major ICD-9 categories, and for 843 specific illness and injury diagnoses. During the three-year period, 23% of servicemembers (454,145) received one or more AVA (defined as the post-

vaccination cohort). There were 136,314 hospitalizations and 15,465,744 outpatient visits. Overall rates for both outcomes were significantly higher in the pre-vaccine cohort than in the post-vaccine cohort. This was also true for each of the 14 major ICD-9 categories.

Three specific diagnoses out of 843 (0.4%) were significantly more frequent in the hospitalization data in the post-vaccine cohort, compared to the pre-vaccine cohort. (Lange, et al., 2003) Twenty-three specific diagnoses out of 843 (2.7%) were significantly more frequent in the outpatient data in the post-vaccine cohort, compared to the pre-vaccine cohort. During 1998-2000, AVA was required before assignments to certain regions that had higher risks of possible use of anthrax as a biological weapon. Therefore, some diagnoses were significantly higher in the post-vaccine cohort because of the risks inherent to certain locations rather than to the adverse effects of the vaccine itself. For example, malaria was the only diagnosis that was significantly increased in the post-vaccine cohort, in both the hospitalization and outpatient data. The strong association between AVA and subsequent malaria was due to confounding because servicemembers received AVA prior to deploying to Korea. The authors concluded: "the results together with those of other monitoring efforts provide unprecedented oversight of the safety of the AVA program. Results of surveillance efforts to date suggest that AVA has few if any significant adverse health effects."

The objective of the second study in 2003 was to evaluate a broad range of short-term and longer-term health effects of the anthrax vaccine in a cohort of 601 Army health care personnel, who were followed for two years. (Wasserman, et al., 2003) In 1998, DoD initiated a program to immunize military personnel with the anthrax vaccine absorbed (AVA). Health care personnel stationed at Tripler Army Medical Center (TAMC) in Honolulu were enrolled in this prospective study, if they started the six-vaccine AVA series between September 12 and October 16, 1998. Individuals completed a survey at 7 to 14 days after each of the six vaccines. The survey included several symptoms, such as localized injection-site reactions, fever, and muscle aches, including severity and duration. Six hundred one individuals received 3,069 AVA, and completed 2,849 surveys (93%). After the vaccine, an average of 4% of men and 6% of women reported that they could not perform one or more of their normal duties because of a symptom. The most common symptoms that affected performance of duties were muscle aches, headaches, joint aches, and fatigue. The most common localized site reactions were subcutaneous nodules (reported by more than 60% of men and more than 80% of women); localized muscle soreness; localized itching; and redness that was more than 5 cm in diameter. Women reported rates of these localized reactions 1.4 to 2.3 times more often than men.

Among the 601 soldiers who received the AVA in 1998, 301 soldiers completed the Health Enrollment Assessment Review Survey HEARS) in 2000. (Wasserman, et al., 2003) This survey is a standardized, validated health risk appraisal tool that DoD uses to provide health risk education and feedback. No reference to the anthrax vaccine was made during the HEARS. 26 health questions, related to current health problems or problems during the past 12 months, were selected from the 156-question HEARS, based on their relevance to this study, including overall health status, chronic headaches, neurologic disease, asthma, muscle, joint, or back problems, and depression. 639 soldiers served as a comparison group, who were stationed at TAMC in September 1998, who never received the AVA, and who completed the HEARS in 2000. There were no significant differences between the 301 vaccinated soldiers and 639 unvaccinated soldiers on any of the 26 HEARS questions.

The rates of hospitalizations and outpatient visits were evaluated from October 1, 1998 to September 30, 2000, focusing on all diagnoses, and on broad ICD-9 categories (such as, musculoskeletal, mental, digestive, and injury). (Wasserman, et al., 2003) Due to the relatively small sample size, the rates of individual diagnoses could not be evaluated. The rates in the 601 vaccinated health care personnel were compared to the rates in 637 soldiers who were stationed at TAMC in October 1998 and who did not receive the vaccine. There were no significant differences in the rates of inpatient or outpatient diagnoses between vaccinated and unvaccinated groups, with one exception. The rate of outpatient visits for mental disorders was significantly lower in the vaccinated group. The 601 vaccinated soldiers were also compared with the 637 unvaccinated soldiers on the rates of

voluntarily leaving the service, medical discharge, and retirement before September 30, 2000. The unvaccinated group left the service at 1.7 times the rate of the vaccinated group. There were no differences in the rates of medical discharge or retirement. The authors concluded: "The findings of this study support the relative reactogenicity [ability to cause injection-site reactions] of AVA immunization but do not reveal any serious adverse events or effects on health."

G. Chemical Weapons

Four studies published in 2003 focused on the health effects of chemical weapons. One consisted of a review of 160 studies, one evaluated exposures in human volunteers and two examined exposures to laboratory animals. (Riddle, et al., 2003; Page, 2003; van Helden, et al., 2003; van der Schans, et al., 2003) The objective of the human volunteer study was to evaluate the potential long-term health effects of exposure to chemical warfare agents, including self-reported symptoms of neuropsychological impairment, peripheral neuropathy, sleep disorders, depression, and anxiety. (Page, 2003) The objective of the first laboratory study was to expose guinea pigs and marmosets (monkeys) to the lowest quantifiable concentration of sarin vapor and to increase exposure time until the lowest observable effect level (LOEL) became measurable. (van Helden, et al., 2003) The objective of the second laboratory study was to investigate the toxicokinetics of VX, a non-volatile, persistent nerve agent, in hairless guinea pigs and marmosets (monkeys). (van der Schans, et al., 2003)

A comprehensive review was published in 2003 on the potential health effects of chemical warfare agent exposure in Gulf War veterans, based on 160 studies. (Riddle, et al., 2003) The major conclusions were: "It is unlikely that Gulf War veterans are suffering chronic effects from illnesses caused by chemical warfare nerve agent exposure. Extensive investigation and review by several expert panels have determined that no evidence exists that chemical warfare nerve agents were used during the Gulf War. At no time, before, during, or after the war was there confirmation of symptoms among anyone, military or civilian, caused by chemical warfare nerve agent exposure." Regarding the demolition of munitions at Khamisiyah, the authors pointed out: "The findings of U.N. inspections and investigations following the Gulf War indicate that some U.S. troops potentially may have exposed to trace levels of sarin and cyclosarin." They summarized many previous reviews of human and laboratory studies, as follows: "Reviews of the literature indicate that long-term health effects from exposures do not occur unless there are symptoms immediately following exposure."

Between 1955 and 1975, service members volunteered for controlled experimental exposures to chemical warfare agents in Edgewood, Maryland. (Page, 2003) The levels of parenteral or inhalation exposures were high enough in many of the experiments to cause immediate symptoms, according to existing records. Exposure levels were described as follows: "Rarely did intravenous or intramuscular doses exceed 1.5 times the incapacitating dose, and although inhalation doses were higher, their potencies were lower. Acute effects were seen in some volunteers." The definition of the incapacitation dose is a concentration sufficient to cause immediate, disabling symptoms, which require medical treatment. Some soldiers were exposed to one of 15 chemical nerve agents that inhibit acetylcholinesterase, including sarin, VX, and eserine. Some soldiers were exposed to other types of chemicals, including anticholinergics, such as atropine; cholinesterase reactivators, such as pralidoxime (2-PAM); psychoactive chemicals, such as LSD; irritants, such as tear gas; or blister agents, such as mustard gas. Some soldiers participated in experiments that only tested equipment, without exposure to chemicals. In 1985, the National Academy of Science evaluated three groups of these volunteers to determine the potential long-term health effects of the exposures. (National Academy of Sciences, 1985) This study demonstrated no marked health differences among men who were exposed to chemical nerve agents, men who were exposed to other types of chemicals, and men who were not exposed to chemicals.

The objective of the 2003 study was to evaluate the potential long-term health effects in human volunteers exposed to chemical warfare agents, including self-reported symptoms of neuropsychological impairment, peripheral neuropathy, sleep disorders, depression, and anxiety. (Page, 2003) In addition, the prevalence of chronic medical conditions was assessed using items from the National Health

Interview Survey. Telephone interviews were performed in 2000-2001. There was a 62% participation rate, including subjects who could not be located. Eight-hundred fifty-five subjects had been exposed to nerve agents in at least one experiment; 871 subjects had been exposed to other types of chemicals in at least two experiments; and 752 subjects had participated in equipment testing only. The questionnaire included several questions about disabilities related to activities of daily living, and several questions about major medical and neurological conditions diagnosed by a physician, including cancer, diabetes, stroke, Parkinson's disease, epilepsy, and carpal tunnel syndrome. There were almost no significant differences in the rates of disabilities and major medical conditions among the three groups.

At the time of the testing, healthier men were selected for exposure to chemicals, and less healthy men were selected for equipment testing only. The group with exposure to other chemicals was likely to be the healthiest, the group with no chemical exposure was likely to be the least healthy, and the group exposed to nerve agents was in between. In the analyses, the initial health fitness of individual subjects was estimated using two sets of data: exposure to psychoactive chemicals, and total number of tests participated in. The authors noted that selection bias was a potential limitation: "To deal with these issues, two measures of health fitness-exposure to psychochemicals and number of tests administered-were introduced to correct for some of these biases."

The Neuropsychological Impairment Scale was used to measure two subscales: the attention scale and the memory scale. The total number of peripheral nerve symptoms was determined, as well as the score on the Sleep Disturbance Index. Diagnoses of depression and generalized anxiety disorder were determined using the gold standard, the Structured Clinical Interview for DSM-III Revised (SCID). In a multivariate analysis, adjustments were made for age at testing, race, the two measures of initial health fitness, and self-reported chemical exposures outside of Edgewood. After adjustment, there were almost no differences among the three groups on the mean scores of the two neuropsychological subscales, the mean numbers of peripheral neuropathy symptoms, the mean sleep disturbance scores, or the rates of depression or anxiety. One exception was a significant increase in the number of reported attention problems in the group exposed to other chemicals, compared to the group exposed to nerve agents. The only other exception was a significant increase in the number of reported sleep problems in the group exposed to nerve agents, compared to the group with no exposure to chemicals. This study is unique because the chemical exposures of these volunteers were documented, at known concentrations that were high enough to cause immediate symptoms in many of the experiments. There appeared to be few or no observable long-term effects of nerve agent exposure, to date.

The objective of the first laboratory study in 2003 was to expose guinea pigs and marmosets (monkeys) to the lowest quantifiable concentration of sarin vapor and to increase exposure time until the lowest observable effect level (LOEL) became measurable. (van Helden, et al., 2003) A system was developed for exposing animals to extremely low concentrations of sarin: 0.05 to 1.0 micrograms of sarin per cubic meter of air (8 to 160 parts per trillion). The air concentration was measured semi-continuously, at 4-minute time intervals, by gas chromatography. Each animal was exposed for one five-hour period, and blood samples were taken every 30 minutes for internal dose assessment. The internal dose was assessed by the analysis of sarin concentration in plasma, after release of the sarin from binding sites with fluoride ions. These sites were primarily the enzyme butyrylcholinesterase. The LOEL was defined as the air concentration of sarin that led to a detectable level of sarin in the plasma. For a five- hour exposure, the LOEL for guinea pigs was a concentration of 0.01 mg of sarin per cubic meter of air, per minute of exposure. The LOEL for marmosets was 0.04 mg of sarin per cubic meter of air, per minute of exposure (four times higher). The authors estimated that the measurement of detectable sarin concentration in plasma was as much as 1000 times more sensitive than the measurement of inhibition of cholinesterase activity, which is the classic method of assessing internal dose of sarin. The study did not actually measure cholinesterase activity or any health effects in the animals; therefore, these results cannot be extrapolated to potential health effects in humans.

The objective of the second laboratory study in 2003 was to investigate the toxicokinetics of VX, a non-volatile, persistent nerve agent, in hairless

guinea pigs and marmosets (monkeys). (van der Schans, et al., 2003) This was the first detailed investigation of the absorption rate and elimination rate of VX, which has had very little evaluation in the past. The toxicokinetics were measured in guinea pigs and marmosets at intravenous doses that corresponded to 1 X LD50 and 2 X LD50 in guinea pigs (LD50 is the amount of a material, given all at once, that causes the death of 50% of a group of test animals). Deaths of the animals occurred within 15 minutes. A method to measure blood levels of VX at very low concentrations was developed, using gas chromatography. In addition, the toxicokinetics of VX were measured after percutaneous exposure to guinea pigs at a skin dose that corresponded to 1 x LD50 (death of the animals occurred within 24 hours). Large variations were observed between individual animals in the rate of skin penetration of VX. After skin exposure, blood levels of VX increased gradually over a 6-hour period. After a seven-hour skin penetration period, the blood VX concentration corresponded to 2.5% bioavailability when compared to IV exposure. The period of time in which toxicologically relevant levels of VX persisted in the body was 10 to 20 hours with IV exposure, and probably much longer with skin exposure. These time periods were much longer than those of sarin or soman, which would be 2 hours at most for an IV dose. Skin exposure to VX could involve a substantial lag period between the time of exposure and the appearance of first symptoms of poisoning. Also, VX was substantially more persistent in the blood, compared to soman, which might adversely impact the effectiveness of treatment of VX poisoning. This study is not directly relevant to Gulf War veterans, however, because there is no evidence that servicemembers were exposed to VX.

H. Pyridostigmine Bromide

One laboratory study published in 2003 focused on the health effects of pyridostigmine bromide (PB). The objective was to determine the effect of PB treatment on blood acetylcholinesterase activity, cardiovascular function, and behavior in male mice. (Bernatova, et al., 2003) PB was administered subcutaneously for 7 days using implanted osmotic pumps. There were two doses: 1 and 3 mg PB per kg body weight per day (low-dose and moderate-dose, respectively). There was no change in blood acetylcholinesterase (AChE) activity level at the lower dose. At the higher dose, blood AChE activity level was decreased by 85% on day 7. At both doses, PB treatment did not cause a decrease in plasma butyrylcholinesterase activity level. Using implanted carotid artery catheters, blood pressure and heart rate were measured continuously for 24 hours before treatment and on days 3 and 7 of treatment. At both doses, PB treatment had no effect on mean arterial pressure or heart rate. At both doses, PB treatment did not alter the open field behavior of the mice (including locomotor activity, rearing, distance traveled, rest time, number of entries, and pokes). The authors concluded: "A comprehensive investigation using long-term blood pressure and heart rate monitoring, and behavioral evaluation revealed no changes in any parameters. This occurred concurrent with significant inhibition of blood AChE activity. The results suggest that prolonged low-dose PB treatment itself does not represent a significant risk factor."

I. Interactions of Exposures (Pyridostigmine Bromide in Combination with Stress or Other Chemicals)

Overview:

Three laboratory studies published in 2003 focused on the effects of pyridostigmine bromide (PB), in combination with stress or other chemicals. (Shaikh and Pope, 2003; Shaikh, et al., 2003; Scremin, et al., 2003)

Two studies in 2003 focused on the effects of PB in combination with stress. The objective of the first study was to evaluate the effects of forced running stress, low dose paraoxon, or a combination of stress and paraoxon on the short-term toxicity of high-dose PB in male Sprague-Dawley rats. (Shaikh and Pope, 2003) The objective of the second study was to evaluate the effects of 14 days of daily physical stress (treadmill running) or daily exposure to a subclinical dosage of paraoxon on cholinesterase inhibition in the blood and brain of male Sprague-Dawley rats, combined with exposure to PB. (Shaikh, et al., 2003)

One study in 2003 focused on the effects of PB in combination with sarin. The objective of this study was to determine if exposure to low-level sarin exposure and PB, alone or in combination, could lead to cognitive or neurobehavioral

abnormalities in male Sprague-Dawley rats. (Scremin, et al., 2003)

Stress alone has been shown to induce significant changes in blood-brain barrier (BBB) permeability in young rats and mice, but little or no changes in adults. Reports in rodents have shown effects of exogenous stressors like forced swim, restraint, or heat stress on the entry of radioactive tracers, dyes, or viruses into the central nervous system (CNS). These studies have been conducted primarily in young, immature animals. (Sharma, et al., 1991; Sinton, et al., 2000; Song, et al., 2002) The overall conclusion in a recent study was: "There is no evidence that exogenous stress increases BBB permeability in mature rodents." (Sinton, et al., 2000)

The one exception, regarding adult rodents, was a study by Friedman that suggested that pyridostigmine bromide (PB) could enter the brain of adult mice subjected to forced swimming stress. (Friedman, et al., 1996) Friedman demonstrated that the dose of PB required to produce 50% inhibition of brain acetylcholinesterase (AChE) activity in stressed FVB/n mice was only 1% of the dose of PB required to produce 50% inhibition in non-stressed mice. However, there is some experimental evidence that the FVB/n mouse strain may have an unusually permeable BBB. (Telang, et al., 1999) Furthermore, the intensity of the reported effect in Friedman's study (more than 50% inhibition) could not be easily explained by the limited and localized changes in BBB permeability that had previously been reported to be induced by stress. (Sharma, et al., 1991, Telang, et al., 1999)

Several recent studies have evaluated whether stress can increase BBB permeability, and can therefore enhance penetration of PB into the brain. If PB does not cross the BBB, it is unlikely to cause long-term changes in brain function. These studies have included several species and strains of animals:

- guinea pigs (Lallement, et al., 1998);
- 3 different strains of mice (Telang, et al., 1999; Chaney, et al., 1999; Grauer, et al., 2000); and
- 3 strains of rats (Sinton, et al., 2000; Chaney, et al., 2000; Kant, et al., 2001; Tian, et al., 2002; Song, et al., 2002; Abou-Donia, et al., 2002; Shaikh and Pope, 2003; Shaikh, et al., 2003; Scremin, et al., 2003).

These studies have included several types of stressors:

- forced swimming stress (Telang, et al., 1999; Grauer, et al., 2000; Sinton, et al., 2000; Tian, et al., 2002);
- forced running stress (Tian, et al., 2002; Shaikh and Pope, 2003; Shaikh, et al., 2003);
- heat stress (Lallement, et al., 1998; Sinton, et al., 2000);
- severe cold stress (Grauer, et al., 2000);
- restraint stress (Sinton, et al., 2000; Kant, et al., 2001; Song, et al., 2002);
- foot shock stress (Kant, et al., 2001);
- chemical stress (coadministration of sarin) (Abou-Donia, et al., 2002; Scremin, et al., 2003);
- chemical stress (coadministration of high doses of DEET) (Chaney, et al., 1999; Chaney, et al., 2000); and
- chemical stress (coadministration of an organophosphate, paraoxon) (Shaikh and Pope, 2003; Shaikh, et al., 2003).

All of these recent studies have reached the conclusion that stress does not increase BBB permeability to PB, and that PB does not penetrate the brain, even at very high doses. For example, the conclusion of a 2001 study was "The preponderance of the evidence by a number of laboratories now points to some unknown experimental artifact associated with the original positive report [Friedman, et al., 1996]." (Kant, et al., 2001) Another study by Sinton, Haley, and colleagues concluded "to the extent that cross-species comparisons are valid" between humans and rodents, "the effects of stress on BBB permeability to PB are unlikely to explain the chronic CNS symptoms reported by some Gulf War veterans." (Sinton, et al., 2000) The conclusion in this 2000 study was particularly noteworthy because one of the authors, Robert Haley, previously reported an association between a history of PB use and long-term CNS symptoms, based on a questionnaire administered to a small group of Gulf War veterans. (Haley, et al., 1997c)

The authors of a 2002 study reviewed these published studies and concluded: "The results from our study as well as a number of other recent reports indicate that stress does not generally increase the anticholinesterase actions of PB in the central nervous system. (Lallement,

et al., 1998; Telang, et al., 1999; Grauer, et al., 2000; Sinton, et al., 2000; Kant, et al., 2001; Tian, et al., 2002) While stress may in some way alter the toxicity of PB under some conditions, the overall data available to date do not support a link between stress and enhanced cholinesterase inhibition/cholinergic toxicity following PB exposure in the etiology of Gulf War illnesses." (Song, et al., 2002)

The authors of a 2003 study of PB and sarin concluded: "This study gives further support to the use of PB as one of the therapeutic resources against nerve agent poisoning and does not support the hypothesis that delayed symptoms experienced by Persian Gulf War veterans could be due to PB, alone or in association, with low-level nerve agent exposure." (Scremin, et al., 2003)

Individual Study Results:

The objective of the first study in 2003 was to evaluate the effects of forced running stress, low dose paraoxon, or a combination of stress and paraoxon on the short-term toxicity of high-dose pyridostigmine bromide (PB) in male Sprague-Dawley rats. (Shaikh and Pope, 2003) Paraoxon is an organophosphate that causes cholinesterase inhibition. Cholinesterase inhibition was measured in blood and in different regions of the brain (cerebral cortex, cerebellum, hypothalamus, and hippocampus). Rats were injected intramuscularly with saline or paraoxon (0.1 milligram of paraoxon per kilogram body weight). Half of the rats were forced to run on a treadmill for 60 minutes. PB or saline was given orally 60 minutes after dosing with paraoxon. Rats were evaluated for cholinergic toxicity before sacrifice, which was 60 minutes after PB exposure. There were two doses of PB, both of which elicited signs of toxicity, such as tremors, convulsions, or diarrhea (10 and 30 milligrams PB per kilogram of body weight). No signs of toxicity were noted following dosing with paraoxon. PB caused extensive inhibition of blood cholinesterase activity (decrease of 88 to 94%), but no significant effect on brain cholinesterase activity. Paraoxon caused moderate cholinesterase inhibition in the blood and in the brain (decrease of 23 to 46%). PB and paraoxon combined did not lead to further reduction of cholinesterase activity, compared to paraoxon alone. Forced running stress did not alter cholinesterase activity, following PB alone, paraoxon alone, or PB and paraoxon together. The authors concluded: "These results provide further information that acute physical stress has little effect on PB toxicity and suggest that pre-exposure to a moderately low dose of an organophosphate anticholinesterase also has little influence on the peripheral and/or central effects of acute PB exposure." The authors commented that these results were consistent with several other studies, as follows: "Using various acute stressors in a number of species (mice, rats, and guinea pigs), a number of research groups have failed to find an effect of acute stress on PB entry into the brain or central cholinergic deficits. (Lallement, et al., 1998; Grauer, et al., 2000; Sinton, et al., 2000; Ovadia, et al., 2001; Song, et al., 2002; Tian, et al., 2002) Together, these data suggest that acute physical stress does not generally alter the ability of PB to enter the central nervous system and lead to increased neurotoxic consequences."

The objective of the second study in 2003 was to evaluate the effects of 14 days of daily physical stress (treadmill running) or daily exposure to a subclinical dosage of paraoxon on cholinesterase inhibition in the blood and brain of male Sprague-Dawley rats, combined with exposure to PB. (Shaikh, et al., 2003) Paraoxon is an organophosphate that causes cholinesterase inhibition. In the stress experiments, rats ran on a treadmill for 90 minutes each day for 14 days. Immediately afterwards, they were dosed orally with saline, a moderate dose of PB, or a high dose of PB (3 or 10 milligram of PB per kilogram body weight per day). In the paraoxon experiments, the rats were injected intramuscularly with saline or paraoxon for 14 days (0.05 or 0.1 milligram of paraoxon per kilogram body weight per day). One hour after paraoxon dosing, the rats were dosed with PB or saline. The rats were sacrificed one hour after the last dose of PB on day 14. Rats given the high dose of PB exhibited signs of toxicity (involuntary movements) for the first 6 days of treatment, which subsided. Paraoxon did not cause overt signs of toxicity at the two doses used in this study. Rats exposed to PB alone demonstrated significant inhibition of cholinesterase activity in the blood (decrease of 56 to 79%). PB alone did not cause any significant changes in regional brain cholinesterase activity. The combination of PB and running stress did not significantly alter the cholinesterase activity in the blood or brain regions, compared to PB alone. Paraoxon alone caused a significant inhibition of blood and

regional brain cholinesterase activity (decrease of 29 to 82%). PB and paraoxon combined did not lead to further reduction of brain cholinesterase activity, compared to paraoxon alone. The authors concluded: "The results of this study suggest that repeated physical stress (forced running) and daily subclinical paraoxon exposures have relatively little effect on subacute PB toxicity. Though daily stress may alter the subacute toxicity of PB under some conditions, the degree of alteration of PB toxicity appears minimal. Such changes may indeed be through alteration of peripheral instead of central cholinergic mechanisms."

The objective of the third study in 2003 was to determine if exposure to low-level sarin exposure and PB, alone or in combination, could lead to cognitive or neurobehavioral abnormalities in male Sprague-Dawley rats. (Scremin, et al., 2003) This study has the advantage that there was an effort to use exposure levels and durations of exposure to sarin and PB that were relevant to those experienced by Gulf War veterans. The optimal dose of sarin was defined as the highest dose that was not associated with toxic signs during the three weeks of exposure. The optimal dose of PB was defined as the dose that produced 20 to 30% of butyrylcholinesterase inhibition during the three weeks of exposure. Compared to most previous studies, this study has another advantage, in that it followed the health of the rats for up to 16 weeks after cessation of exposure. PB was provided in drinking water (80 milligrams of PB per liter water). Sarin was injected subcutaneously three times a week, at a dose of 0.5 X LD50 (62.5 micrograms sarin per kilogram of body weight). PB alone caused an inhibition of blood acetylcholinesterase activity (AChE) (decrease of 46%). Sarin alone and sarin plus PB caused an inhibition of AChE activity (decrease of 65% and 73%, respectively). By the second week after cessation of exposure, blood AChE activity levels had returned to normal. Brain AChE activity levels remained at normal levels at all times after cessation of exposure. Animals were tested for passive avoidance, nociceptive threshold, acoustic startle, and open field activity at 2, 4, and 16 weeks after cessation of exposure. Two weeks after exposure, sarin alone caused an increase in acoustic startle and decrease in distance explored in the open field. PB alone or sarin plus PB did not cause any behavioral effects at two weeks. Sarin alone, PB alone, and sarin plus PB did not cause any behavioral effects at four weeks. Minimal behavioral effects were noted after 16 weeks of follow-up. The authors concluded: "This study gives further support to the use of PB as one of the therapeutic resources against nerve agent poisoning and does not support the hypothesis that delayed symptoms experienced by Persian Gulf War veterans could be due to PB, alone or in association, with low-level nerve agent exposure."

III. RESEARCH FUNDING TRENDS

A. Overview

Appendix A provides information on the projects that VA, DoD, and HHS have funded. The appendix reflects data as of the end of Fiscal Year 2003. Research projects are grouped according to the Department that is responsible for their funding.

Two descriptors categorize each research project. The first descriptor is a series of **Research Focus Areas**. The research focus areas are categorized as follows:

- Prevalence and risk factors for symptoms and alterations in general health status
- Brain and nervous system function
- Chemical weapons
- Environmental toxicology (e.g. studies focused on specific environmental toxicants such as pesticides, oil well fires, etc.)
- Reproductive health
- Depleted uranium
- Leishmaniasis
- Immune function
- Pyridostigmine bromide
- Mortality experience
- Interactions of exposures (chemical, biological, pharmacological, physiological, etc.)
- Prevention of diseases (i.e. studies that will produce knowledge that could lead to disease prevention strategies)
- Treatment
- Diagnosis (i.e. studies that will improve the ability to diagnose previously unexplained conditions, or to better refine diagnoses with new tools)

Each project is assigned up to three focus areas as categorical descriptors. This allows accounting for projects that cover multiple focus areas. For example, a project on the neurophysiological effects of exposure to sarin in animals would have a focus on the brain and nervous system, and a focus on chemical weapons. The number of focus areas (between one and three) assigned to a project depends on the project itself.

The second descriptor for each project is **Research Type**. The Federal Government defines **Research** as systematic investigation designed to develop or contribute to generalizable knowledge. Each research project on Gulf War veterans' illnesses uses a method of approach to test a specific research hypothesis. Approaches range in type from mechanistic research, addressing potential biological mechanisms of causation, to clinical and epidemiological research that attempt to determine illness prevalence and risk factors. Although precise categorization of research types can be difficult because of overlapping methodologies, research projects can be divided into the following general types:

MECHANISTIC RESEARCH: Research into underlying mechanisms of diseases and illnesses using in vitro and in vivo models.

CLINICAL RESEARCH: Application of an intervention, such as in a controlled drug trial, or use of methodologies such as case-control studies to define risk factors for disease.

EPIDEMIOLOGY RESEARCH: Study of the distribution and determinants of disease in human populations. It includes population-based studies focused on outcomes such as mortality, symptoms, hospitalizations, etc., using devices such as postal surveys, telephone interviews, and reviews of medical records.

In addition to the research on Gulf War veterans' illnesses, the Deployment Health Working Group (DHWG) also tracks development activities. In general, development is the systematic use of the knowledge or understanding gained from research directed toward the production of materials; devices; systems; or methods, including design, development, and improvement of prototypes and new processes. Within the context of Gulf War veterans' illnesses, the DHWG categorizes activities as development as follows:

DEVELOPMENT: An activity that satisfies the general definition of development described above, and is directed toward new biologically based prevention, intervention, and treatment measures.

The research database on Gulf War veterans' illnesses catalogs only research and development activities that either directly involve Gulf War veterans or have been initiated to answer specific questions about risk factors. An example of the latter is a research project using animal models

to determine health effects of low-level chemical warfare agents. The database does not account for the vast accumulated knowledge derived from the nation's investment in biomedical research over the past 50 years.

The research database on Gulf War veterans' illnesses contains research that is Federally sponsored only. This includes research conducted by Federal scientists, as well as that by non-federal scientists supported by Federal research funds through grants, contracts, and cooperative agreements. It is not possible to accurately track research efforts that fall within the private sector or otherwise outside of the purview of the Federal government.

Nonetheless, the DHWG attempts to stay abreast of all research relevant to Gulf War veterans' illnesses. The DHWG accomplishes this by monitoring the peer reviewed published scientific literature, attending scientific meetings, and even using newspaper reports and personal accounts of researchers.

An interim assessment of the nature and causes of illnesses in Gulf War veterans was included in Appendix C of the Annual Report to Congress for 2000. (MVHCB, 2001a) In 1996, the Persian Gulf Veterans Coordinating Board identified 21 major research questions. The comprehensive Gulf War research portfolio has addressed each of these questions, and relevant results have been published on each one.

The following sections provide a quantitative overview of the current research portfolio on Gulf War veterans' illnesses and the evolution of the portfolio over time since 1994. Topics that are covered include overall research expenditures from 1994-2003, and the types and areas of research in which the Federal Government has invested.

B. Research Funding

From FY 1994 through FY 2003, three departments (VA, DoD, and HHS) have sponsored 256 distinct research projects on Gulf War veterans' illnesses.

Appendix A lists all of the research and development projects and programs supported now or in the past by the Federal government. The appropriated funds, centrally distributed to each program or project, are shown in the fiscal years that funds were obligated. Many extramural projects are multi-year efforts for which funds are obligated at the beginning of the project period.

Table III-1 is a summary of research expenditures by DoD, VA, and HHS between FY94 and FY03. Federal Government funding for the direct costs of Gulf War research totaled $242.9 million during this period. This funding does not include indirect costs of conducting the research such as facility, administrative and operational costs. Estimates of these indirect costs are $72.9 million. As of September 30, 2003, 185 projects were completed (72% of the 256 projects), and 71 projects were ongoing. Both totals are expected to rise by the end of FY04.

Table III-2 is a year-by-year account of new and completed projects.

Table III-1. Funding for Research FY'94-02 in $Millions

Department	FY'94	FY'95	FY'96	FY'97	FY'98	FY'99	FY'00	FY'01	FY'02	FY'03	Direct Costs FY'94-03	Indirect Costs FY'94-03	Total Costs FY'94-03
DoD	$6.5	$11.0	$11.9	$28.9	$13.2	$22.6	$23.8	$28.8	$18.8	$12.4	$178.0	$53.4	$231.4
VA	$1.2	$2.3	$3.9	$2.8	$4.7	$9.0	$12.0	$8.5	$4.1	$4.6	$53.2	$16.0	$69.2
HHS	$0.0	$2.5	$1.6	$0.0	$1.6	$1.6	$1.6	$1.0	$0.8	$1.0	$11.7	$3.5	$15.2
Total	**$7.7**	**$15.8**	**$17.4**	**$31.7**	**$19.5**	**$33.2**	**$37.5**	**$38.6**	**$23.9**	**$18.1**	**$242.9**	**$72.9**	**$315.8**

Table III-1. Direct costs cover the actual research such as testing and lab supplies. Indirect costs cover expenses for administration, infrastructure, utilities etc. These expenses are estimated because indirect costs can be computed only by facility and not by project. Historical data suggest indirect costs equal 30% of direct costs. Table III-1 does not include funding for activities performed by members of the DHWG (salaries, travel, etc.).

Table III-2. Number of New and Completed Projects by Year*

Fiscal Year	New	Completed
1992 – 1994	45	3
1995	39	9
1996	20	3
1997	31	11
1998	17	16
1999	33	21
2000	21	44
2001	25	27
2002	12	46
2003	13	5

IV. NEW RESEARCH PROJECTS AND INITIATIVES

This section highlights the new research projects that have been approved since last year's *Annual Report to Congress*. The three departments did not initiate new funding initiatives in FY03 although VA has a special Request for Applications planned for FY04.

In February 2003, VA joined DoD in funding a study of neuropsychological function in Army soldiers who are deploying to the current war in Iraq, "Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study." (VA-88/DoD-154) This study is the first of its kind to compare pre- and post-deployment cognitive function.

VA funded an additional 10 projects during FY03. The primary research foci of these projects included treatment (2); pyridostigmine bromide (1); and brain and nervous system (7). DoD funded two other projects in FY03 that focus on interactions.

VA-80, "Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress," seeks to determine the nature and the functional significance of reduced acetylcholinesterase (AChE) activity in the brain of rodents when administered pyridostigmine bromide (PB) under conditions of intense stress.

VA-81, "Stress, Pro-Inflammatory Cytokines and Coping Behavior," will attempt to further elucidate the relationship between stress, pro-inflammatory cytokines and coping behavior in Sprague-Dawley rats.

VA-89, "National Registry of Veterans with Amyotrophic Lateral Sclerosis," will systematically identify and track veterans with ALS.

VA-90A, "Neuronal Hyperexcitability and Motor Neuron Regeneration," is a pilot study is to examine the effects of electrical stimulation on motor neuron gene expression (both RNA and protein) during the axonal regeneration process. This will help to identify a list of potential candidate genes that are responsible for faster preferential motor reinnervation.

VA-90B, "Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders," will use state of the art-techniques such as laser capture microdissection (LCM), gene expression microarray approaches, and surface enhanced laser desorption/ionization (SELDI) coupled with mass spectrometry (MS) to conduct gene expression and protein characterization of brain tissue.

VA-90C, "Developmental Differences in Alcohol Withdrawal Sensitivity," will assess changes in hippocampal function and gene expression after chronic ethanol exposure during adolescence and adulthood in rats using the LCM/Gene expression core resources; and characterize the excitability of hippocampal circuits after chronic ethanol exposure using in-vitro electrophysiological and behavioral techniques.

VA-90D, "Seizures and Neuroplasticity: Physiology and Biochemistry," will explore the underlying mechanisms by which seizures disrupt neuroplasticity and alter memory processing using a combination of electrophysiological, biochemical and molecular studies.

VA-91, "The Role of Dietary Choline in Neuroprotection," will test the hypothesis that dietary choline is neuroprotective in a rat model of neurotoxicity: N-methyl-D-aspartate (NMDA) antagonist-induced neurotoxicity in the cingulated and retrosplenial cortices (C/RSC).

VA-92, "Acetylcholinesterase Activity In Gulf War Veterans," seeks to determine whether mood and anxiety disorders or motor neuron diseases are related to serum levels of Acetylcholinesterase (AChE), Butyryl-cholinesterase (BuChE), and/or Paraoxonase (PON) among Gulf War deployed and era veterans.

VA-93, "HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans," will evaluate basal Hypothalamic-Pituitary Adrenal (HPA) axis activity in GWVs with PTSD and comparison subjects. Based on preliminary data, the investigator hypothesizes that adrenocorticotropic hormone (ACTH) levels will be higher in individuals with PTSD.

DoD-155, “Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide” will further evaluate the role of pesticides in the development of central nervous system (CNS) symptoms reported by GW veterans and to assess the additive and/or synergistic effects of combinations of chemical exposures and stress. This will be accomplished by assessing a group of military pesticide applicators with known chemical exposures.

DoD-156, “The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant” will test a model for chemical sensitivity in GW veterans. Researchers will evaluate responses to acute exposures to diesel exhaust both with and without simultaneous exposures to an acute psychological stressor. Subjects will include volunteers who possess either low or high susceptibility to chemical intolerance.

V. RESEARCH PRIORITIES

VA, DoD, and HHS created the Persian Gulf Veterans Coordinating Board (PGVCB) to coordinate research on Gulf War veterans' illnesses. In 1995, the PGVCB decided to provide a contextual framework for the results of completed and ongoing studies and also to develop an approach for the interpretation of research results. To that end, the PGVCB identified 19 major research questions and subsequently added two additional questions in 1996. (PGVCB, 1996b) The comprehensive Gulf War research portfolio has addressed each of these 21 questions, and relevant results have been published on each one. The Medical and Veterans Health Coordinating Board (MVHCB), the successor organization to the PGVCB, conducted a comprehensive assessment of the progress made on each of these 21 questions in the *Annual Report to Congress for 2000*. (MVHCB, 2001a) The Research Subcommittee of the DHWG is currently conducting a second comprehensive assessment of these questions.

A. Twenty-One Research Questions

1. What is the prevalence of symptoms/illnesses in the Persian Gulf veteran population? How does this prevalence compare to that in an appropriate control group?

2. What was the overall exposure of troops to Leishmania tropica?

3. What were the exposure concentrations to various petroleum products, and their combustion products, in typical usage during the Persian Gulf conflict?

4. What was the extent of exposure to specific occupational/environmental hazards known to be common in the Persian Gulf Veterans experience? Was this exposure different from that of an appropriate control group?

5. What were the potential exposures of troops to organophosphorus nerve agent and/or sulfur mustard as a result of allied bombing at Muhammadiyat and Al Muthanna, or the demolition of a weapons bunker at Khamisiyah?

6. What was the extent of exposure to chemical agent, other than at Khamisiyah, Iraq, in the Persian Gulf as a function of space and time?

7. What was the prevalence of PB use among Persian Gulf troops?

8. What was the prevalence of various psychophysiological stressors among Gulf War veterans? Is the prevalence different from that of an appropriate control population?

9. Are Persian Gulf veterans more likely than an appropriate comparison group to experience non-specific symptoms and symptom complexes?

10 Do Persian Gulf veterans have a greater prevalence of altered immune function or host defense when compared with an appropriate control group?

11 Is there a greater prevalence of birth defects in the offspring of Persian Gulf veterans than in an appropriate control population?

12. Have Persian Gulf veterans experienced lower reproductive success than an appropriate control population?

13. Is the prevalence of sexual dysfunction greater among Persian Gulf veterans than among an appropriate comparison population?

14. Do Gulf War veterans report more pulmonary symptoms, or diagnoses, than persons in appropriate control groups?

15. Do Gulf War veterans have a smaller baseline lung function in comparison to an appropriate control group? Do Gulf War veterans have a greater degree of non-specific airway reactivity in comparison to an appropriate control group?

16. IS THERE A GREATER PREVALENCE OF ORGANIC NEUROPSYCHOLOGICAL AND NEUROLOGICAL DEFICITS IN PERSIAN GULF VETERANS COMPARED TO APPROPRIATE CONTROL POPULATIONS?

17. CAN SHORT-TERM, LOW-LEVEL EXPOSURES TO PYRIDOSTIGMINE BROMIDE, THE INSECT REPELLANT DEET, AND THE INSECTICIDE PERMETHRIN, ALONE OR IN COMBINATION, CAUSE SHORT-TERM AND/OR LONG-TERM NEUROLOGICAL EFFECTS?

18. DO PERSIAN GULF VETERANS HAVE A SIGNIFICANTLY HIGHER PREVALENCE OF PSYCHOLOGICAL SYMPTOMS AND/OR DIAGNOSES THAN DO MEMBERS OF AN APPROPRIATE CONTROL GROUP?

19. WHAT IS THE PREVALENCE OF LEISMANIASIS AND OTHER INFECTIOUS DISEASES IN THE GULF WAR VETERAN POPULATION?

20. DO GULF WAR VETERANS HAVE A GREATER RISK OF DEVELOPING CANCERS OF ANY TYPE WHEN COMPARED WITH AN APPROPRIATE CONTROL POPULATION?

21. ARE GULF WAR VETERANS EXPERIENCING A HIGHER MORTALITY RATE THAN THAT OF AN APPROPRIATE CONTROL POPULATION? ARE SPECIFIC CAUSES OF DEATH RELATED TO SERVICE IN THE PERSIAN GULF REGION?

B. Longitudinal Follow-Up Studies of Gulf War Veterans' Illnesses

In 1998, the PGVCB concluded that research approaches to determine the long-term health of veterans be made a high priority. Several research projects funded by the Federal Government have longitudinal components built into them. These projects are directed toward understanding the progress of Gulf War veterans' illnesses over time. In 2003, investigators in Boston, New Orleans, East Orange, New Jersey, Iowa, and the United Kingdom continued to conduct studies that included longitudinal follow-up.

Scientists in Boston and New Orleans have studied their cohorts four times. British scientists have studied their cohort three times, and the Iowa and New Jersey scientists have studied their cohorts twice. Results for follow-up of the Boston cohort of veterans were included in three publications in 2003. (Lindem, et al., 2003a; Lindem, et al., 2003b; Lindem, et al., 2003c)

Results for follow-up of the New Orleans and British cohorts also were published in 2003 (Lindem, et al., 2003a; Lindem, et al., 2003b; Lindem, et al., 2003c; Time 4: Vasterling, et al., 2003; Hotopf, et al., 2003b; Time 3: Wessely, et al., 2003; Hotopf, et al., 2003a)

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Appendix A

Federally Funded Research Projects

Appendix A 1

Project Index By Department

DEPARTMENT OF DEFENSE PROJECTS

DoD-1	Naval Health Study Program
DoD-1 A	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees
DoD-1 B	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not
DoD-1 C	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among Gulf War veterans and other active-duty personnel
DoD-1 D	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in Gulf War Veterans
DoD-1 E	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study
DoD-1 F	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: GWV vs. NDV
DoD-1G	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian Gulf War Veterans
DoD-2	Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET
DoD-4	The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey
DoD-7 A	Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling
DoD-7 B	Carcinogenicity of Depleted Uranium Fragments
DoD-8 A	Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL)
DoD-8 B	Development of a Leishmania Skin Test Antigen (LSTA)
DoD-9	Identification of the Genetic Factors Which Control Tropism in Leishmania
DoD-10	Pyridostigmine Synergistic Toxicity Study

DoD-11	Male/Female Differential Tolerances to Pyridostigmine Bromide
DoD-13	Effects of Persian Gulf War Service on Military Working Dogs
DoD-14	Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry
DoD-15	Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm
DoD-16	Kuwait Oil Fire Health Risk Assessment
DoD-17	Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning
DoD-18	Kuwait Oil Fires Troop Exposure Assessment Model (TEAM)
DoD-19	Persian Gulf Veterans Health Tracking System
DoD-21	Study of Variability In Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals With Symptoms Following Participation in Operation Desert Storm
DoD-22	Chronic Organophosphorus Exposure and Cognition
DoD-23	Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families
DoD-30	Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study
DoD-31	Dysregulation of the Stress Response in the Persian Gulf Syndrome
DoD-32	Neuropsychological Functioning in Persian Gulf Era Veterans
DoD-33	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity
DoD-34	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents
DoD-35	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War.
DoD-36	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms
DoD-37	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats

DoD-38	Diagnostic Antigens of Leishmania tropica
DoD-39	A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces
DoD-40	Psychological and Neurobiological Consequences of the Gulf War Experience
DoD-41	Evaluation of Muscle Function in Persian Gulf Veterans
DoD-42	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment
DoD-44	Investigation of Seminal Plasma Hypersensitivity Reactions
DoD-45	Air Force Women's Health Surveillance Study
DoD-46	Exploratory Data Analysis with the CCEP Database
DoD-47	Study of Mycoplasmal Infections in Gulf War Veterans
DoD-48	Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs Selected Control Groups
DoD-49	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts
DoD-50	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways
DoD-51	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses
DoD-52	Female Gender and Other Potential Predictors of Functional Health Status Among Persian Gulf War Veterans
DoD-53	Long-Term Effects of Subclinical Exposures to Sarin
DoD-54	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure
DoD-55	Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects
DoD-56	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine
DoD-57	Physiologic Effects of Stress in Gulf War Veterans

DoD-58	Illness Among Persian Gulf War Veterans: Case Validation Studies
DoD-59	Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis
DoD-60	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness
DoD-61	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid
DoD-62	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice
DoD-63	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity
DoD-64	Individual Differences in Neurobehavioral Effects of Pyridostigmine
DoD-65	Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment
DoD-66	Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction
DoD-67	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria
DoD-69	Five-Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents
DoD-70	War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes
DoD-71	A Comparison of Post Deployment Hospitalization Between Vietnam and Gulf War Veterans
DoD-72	Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals
DoD-73	Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes
DoD-74	Relationship of Stress Exposures to Health in Gulf War Veterans
DoD-75	Toxic Interactions of Prophylactic Drugs and Pesticides
DoD-76	Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel
DoD-77	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War

DoD-78	Experimental Models of Gulf War Syndrome
DoD-79	Time Course of Stress-induced Impairment of Blood Brain Barrier
DoD-80	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells
DoD-81	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress
DoD-82	Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs
DoD-83	Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism
DoD-84	Psychobiologic Alterations in Persian Gulf War Veterans with and without PTSD
DoD-85	CNS Cytokines and CRH in Gulf War Veterans with Multiple Unexplained Symptoms
DoD-86	Effects of Combat Stress on Structure and Function of the Hippocampus
DoD-87	Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related Quality of Life among PGWVs
DoD-88	Clinical Relevance of Novel Immunological Markers in PTSD
DoD-89	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder
DoD-90	SPECT Benzodiazepine Receptor and MR Imaging in PTSD
DoD-91	Neurological and Circadian Substrates of PTSD-like Behaviors
DoD-92	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder
DoD-93	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up
DoD-94	Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. Gulf War Veterans
DoD-95	Development of Diagnostic tools and alternative treatment drugs for Leishmania
DoD-96	Deployment Health Center

DoD-97	Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis
DoD-98	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans
DoD-99	DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: Hospitalizations
DoD-100	Antibodies to Squalene
DoD-101	Mechanisms in Chronic Multisymptom Illnesses
DoD-102	Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans
DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals
DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome
DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala
DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War-related illness
DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity
DoD-108	Health Status of Current National Guard Members
DoD-109	Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms
DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy
DoD-111	Autonomic Dysfunction in Gulf War Veterans
DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?
DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects
DoD-114	A Re-examination of Neuropsychological Functioning in Persian Gulf War Veterans

DoD-115 A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D)

DoD-116 VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V)

DoD-116 A Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA)

DoD-116 B Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly VA/DoD- 2DB)

DoD-117 Patterns of Pre-Persian Gulf War Illness and Health Care Seeking

DoD-118 An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also VA-61)

DoD-119 Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also VA-55)

DoD-120 Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents

DoD-121 Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development

DoD-122 Carcinogenic Potential of Depleted Uranium and Tungsten Alloys

DoD-123 Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys

DoD-124 Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin

DoD-125 A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74)

DoD-126 Blood-Brain Barrier Transport of Uranium

DoD-127 Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man

DoD-128 Multifactorial Assessment of Depleted Uranium Neurotoxicity

DoD-129 Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness

DoD-130 Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents

DoD-131 Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses

DoD-132 Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness

DoD-133 Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome

DoD-134 Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin

DoD-135 Biochemical Markers for Exposure to Low Doses of Organophosphorous Exposure

DoD-136 A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure

DoD-137 Low Level Exposure to Sulfur Mustard: Development of a SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin

DoD-138 Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents

DoD-139 Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses

DoD-140 US Department of Defense Surveillance for Neoplasms in Infancy

DoD-141 Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans

DoD-142 Illnesses Among Persian Gulf War Veterans: Case Validation Studies (Iowa / Great Britain)

DoD-143 Millennium Cohort Study (See also VA-78)

DoD-144 Psychological Health Screening: Methods and Metrics for Deployed Forces

DoD-145 Early Intervention Research Program to Enhance Soldier Resilience

DoD-146 Assessment of Toxicology Assays Methods & Chemical Exposures Among a Cohort of US Marines

DoD-147 Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications

DoD-148 Predicting operational readiness for deployed Army National Guard and Army Reserve soldiers and families

DoD-149 Longitudinal Health Study of Gulf War Veterans

DoD-150 Validation Study of Gulf War Deployment Files

DoD-151 Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in Gulf War Veterans

DoD-152 Characterization of Intracellular Signaling Pathways Activated by Nerve Agents

DoD-153 Gulf War Illness Research

DoD-154 Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-88)

DoD-154 Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-88)

DoD-155 Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide

DoD-156 The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant

DEPARTMENT OF HEALTH AND HUMAN SERVICES PROJECTS

HHS-1	Health Assessment of Persian Gulf War Veterans from Iowa
HHS-2	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18
HHS-3	Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires
HHS-4	Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian Gulf War Veterans In Mississippi
HHS-5	Cognitive Function and Symptom Patterns in Persian Gulf Veterans
HHS-6	Defining Gulf War Illness
HHS-7	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid
HHS-8	Strategy to Identify Non-Additive Response to Chemical Mixtures
HHS-9	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments
HHS-10	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline
HHS-11	Deployment to the Gulf War and the Subsequent Development of Cancer

DEPARTMENT OF VETERANS AFFAIRS PROJECTS

VA-1	Mortality Follow-up Study of Persian Gulf Veterans
VA-2	National Health Survey of Persian Gulf Veterans
VA-2 A	VA National Survey of Persian Gulf Veterans - Phase I
VA-2 B	VA National Survey of Persian Gulf Veterans - Phase II
VA-2 C	VA National Survey of Persian Gulf Veterans - Phase III
VA-3	Use of Roster of Veterans Who Served in Persian Gulf Area
VA-4	Boston Environmental Hazards Research Center Program
VA-4 A	Evaluation of Cognitive Functioning of Persian Gulf Veterans
VA-4 B	Evaluation of Neurological Functioning in Persian Gulf Veterans
VA-4 C	Gulf War And Vietnam Veterans Cancer Incidence Surveillance
VA-4 D	Evaluation of Respiratory Dysfunction Among Gulf War Veterans
VA-4 E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility
VA-4 F	Validity of Computerized Tests
VA-5	East Orange Environmental Hazards Research Center Program
VA-5 A	Health and Exposure Survey of Persian Gulf Veterans
VA-5 B	Physiological and Psychological Assessments of Persian Gulf Veterans
VA-5 C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans
VA-5 D	Effects of Genetics and Stress on Responses to Environmental Toxins

VA-6	Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research
VA-6 A	Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I)
VA-6 B	Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II)
VA-6 C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III)
VA-6 D	DNA Damage from Chemical Agents and Its Repair (Project IV)
VA-6 E	Clinical and Epidemiology Leishmania Research
VA-7	Desert Storm Reunion Survey
VA-8	Psychological Test Data of Gulf War Veterans Over Time
VA-9	Evaluation of Cognitive Functioning in Persian Gulf War Veterans Reporting War-related Health Problems
VA-10	Memory and Attention in PTSD
VA-11	Neuropsychological Functioning in Veterans
VA-12	Psychological Assessment of Operation Desert Storm Returnees
VA-13	Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot Study
VA-15	Vaccine-Mediated Immunity Against Leishmaniasis
VA-16	Protective Immunity in Experimental Visceral Leishmaniasis
VA-17	Immunological Evaluation of Persian Gulf Veterans
VA-18	Chronic Gastrointestinal Illness in Persian Gulf Veterans
VA-20	Psychological Adjustment in Operation Desert Shield/Storm Veterans
VA-21	A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in ODS

VA-36	Stress Symptoms and Their Causal Attribution in Desert Storm Veterans
VA-40	Musculoskeletal Symptoms in Gulf War Syndrome
VA-46	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder
VA-47	Retrospective Verification of Mustard Gas Exposure
VA-48	Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance
VA-49	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction
VA-50	Neuropsychological findings in a sample of Operation Desert Storm veterans
VA-51	Psychobiological Assessment of Desert Storm Veterans
VA-53	Spouses and Children Program
VA-54	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress
VA-55	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also DoD-119)
VA-56	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13)
VA-57	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13)
VA-58	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13)
VA-59	Demonstration Treatment Program for Gulf War Veterans With Unexplained Physical Symptoms (13)
VA-60	Identification and Management of Sleep Disorders in Gulf War Veterans
VA-61	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also DoD-118)
VA-62	A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V)
VA-63	VA/DoD Core funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D)

VA-63 A	Follow-Up Investigation of troops exposed to nerve agents at Aberdeen Proving Ground (Pilot Study) (See also DoD-116A; formerly VA/DoD-2VA/2DA)
VA-63 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB)
VA-64	Boston Environmental Hazards Research Center
VA-64 A	Functional Neuroimaging in Lead Exposed Adults
VA-64 B	Quantification and Validation of Structure-Function relationships through visuospatial test performance
VA-64 C	Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in veteran populations
VA-65	San Antonio Environmental Hazards Research Center
VA-65 A	Does a variant of the human SOD2 gene increase sensitivity to hazards?
VA-65 B	The contribution of FEN-1 to genetic integrity subsequent to oxidative stress
VA-65 C	The importance of hydrogen peroxide detoxification in cellular protection
VA-65 D	Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental hazards?
VA-66	Physiological Responding in Posttraumatic Stress Disorder
VA-67	Olfactory Functioning in Gulf War Veterans
VA-68	Family Study of Fibromyalgia
VA-69	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans
VA-70	A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8
VA-71	Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome
VA-72	Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses
VA-73	Pain Sensitivity in Gulf War Veterans with Medically Unexplained Musculoskeletal Pain

VA-74	A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125)
VA-75	ALS and Veterans: Are Veterans at Increased Risk?
VA-76	Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD
VA-77	HPA Axis Reactivity in Men and Women with Chronic PTSD
VA-78	Millennium Cohort Study (See also DoD-143)
VA-80	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress
VA-81	Stress, Pro-Inflammatory Cytokines and Coping Behavior
VA-82	Pituitary Adrenal Function in People with Fatiguing Illness
VA-83	Neuropsychological Assessment of a Population-Based Sample of Persian Gulf War Veterans and Controls
VA-84	Neurobiology of Severe Psychological Trauma in Women
VA-85	Associative Learning in Veterans with and without Combat Experience
VA-86	A Clinical Trial of Magnetic Stimulation in Depression
VA-87	Improving Outcomes of Depression in Primary Care
VA-88	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also DoD-154)
VA-89	National Registry of Veterans with Amyotrophic Lateral Sclerosis
VA-90	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness
VA-90A	Neuronal Hyperexcitability and Motor Neuron Regeneration
VA-90B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders
VA-90C	Developmental Differences in Alcohol Withdrawal Sensitivity
VA-90D	Seizures and Neuroplasticity: Physiology and Biochemistry

VA-91 The Role of Dietary Choline in Neuroprotection

VA-92 Acetylcholinesterase Activity In Gulf War Veterans

VA-93 HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans

Appendix A 2

Project List by Research Focus Area

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Brain & Nervous System				
Clinical			DoD-101	Mechanisms in Chronic Multisymptom Illnesses
Clinical			DoD-111	Autonomic Dysfunction in Gulf War Veterans
Clinical			DoD-131	Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses
Clinical			DoD-132	Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat
Clinical			DoD-86	Effects of Combat Stress on Structure and Function of the Hippocampus
Clinical			VA-12	Psychological Assessment of Operation Desert Storm Returnees
Clinical			VA-13	Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot
Clinical			VA-20	Psychological Adjustment in Operation Desert Shield/Storm Veterans
Clinical			VA-21	A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in Operation Desert Storm
Clinical			VA-50	Neuropsychological findings in a Sample of Operation Desert Storm Veterans
Clinical			VA-64 B	Quantification and Validation of Structure-Function relationships through visuospatial test performance
Clinical			VA-66	Physiological Responding in Posttraumatic Stress Disorder
Clinical			VA-67	Olfactory Functioning in Gulf War Veterans
Clinical			VA-69	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans

Major Focus Area / Primary Focus Area *Research Type*	Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Brain & Nervous System				
Clinical			VA-71	Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome
Clinical			VA-73	Pain Sensitivity in Gulf War Veterans with Medically Unexplained Musculoskeletal Pain
Clinical			VA-76	Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD
Clinical			VA-77	HPA Axis Reactivity in Men and Women with Chronic PTSD
Clinical			VA-83	Neuropsychological Assessment of a Population-Based Sample of Persian Gulf War Veterans and Controls
Clinical			VA-84	Neurobiology of Severe Psychological Trauma in Women
Clinical			VA-85	Associative Learning in Veterans with and without Combat
Clinical	Chemical Weapons		DoD-63	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity
Clinical	Diagnosis		DoD-147	Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications
Clinical	Diagnosis		DoD-32	Neuropsychological Functioning in Persian Gulf Era Veterans
Clinical	Diagnosis		VA-4 F	Validity of Computerized Tests
Clinical	Environmental Toxicology		VA-64 A	Functional Neuroimaging in Lead Exposed Adults
Clinical	Prevention	History of Alcoholism	DoD-83	Risk for Stress-related Substance Abuse: the Effects of Family
Clinical	Symptoms & General Health		DoD-36	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms

Major Focus Area / Research Type	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Brain & Nervous System				
Clinical	Symptoms & General Health		DoD-40	Psychological and Neurobiological Consequences of the Gulf War Experience
Clinical	Symptoms & General Health		DoD-41	Evaluation of Muscle Function in Persian Gulf Veterans
Clinical	Symptoms & General Health		DoD-84	Psychobiologic Alterations in Persian Gulf War Veterans with and without PTSD
Clinical	Symptoms & General Health		DoD-89	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder
Clinical	Symptoms & General Health		HHS-5	Cognitive Function and Symptom Patterns in Persian Gulf Veterans
Clinical	Symptoms & General Health		VA-10	Memory and Attention in PTSD
Clinical	Symptoms & General Health		VA-11	Neuropsychological Functioning in Veterans
Clinical	Symptoms & General Health		VA-4 A	Evaluation of Cognitive Functioning of Persian Gulf Veterans
Clinical	Symptoms & General Health		VA-4 B	Evaluation of Neurological Functioning in Persian Gulf
Clinical	Symptoms & General Health		VA-51	Psychobiological Assessment of Desert Storm Veterans
Clinical	Symptoms & General Health		VA-54	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress
Clinical	Symptoms & General Health		VA-6 A	Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I)
Clinical	Symptoms & General Health		VA-7	Desert Storm Reunion Survey
Clinical	Symptoms & General Health		VA-9	Evaluation of Cognitive Functioning in Persian Gulf War Veterans Reporting War-related Health Problems

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Brain & Nervous System				
Clinical	Symptoms & General Health	Diagnosis	DoD-31	Dysregulation of the Stress Response in the Persian Gulf Syndrome
Clinical	Symptoms & General Health	Diagnosis	DoD-67	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria
Clinical	Symptoms & General Health	Environmental Toxicology	VA-5 C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans
Clinical	Symptoms and General Health		DoD-133	Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome
Clinical	Symptoms and General Health		DoD-153	Gulf War Illness Research
Clinical	Treatment		DoD-90	SPECT Benzodiazepine Receptor and MR Imaging in PTSD
Clinical	Treatment		VA-89	National Registry of Veterans with Amyotrophic Lateral Sclerosis
Clinical	Treatment	Symptoms & General Health	DoD-85	CNS Cytokines and CRH in Gulf War Veterans with Multiple Unexplained Symptoms
Clinical	Symptoms and General Health		VA-90	Differential Gene Expression in Pathologies associated with Neuronal Hyperexcitability: Links to Gulf War Illness
Clinical	Symptoms and General Health		VA-90A	Neuronal Hyperexcitability and Motor Neuron Regeneration
Clinical	Symptoms and General Health		VA-90B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders
Clinical	Symptoms and General Health		VA-90C	Developmental Differences in Alcohol Withdrawal Sensitivity
Clinical	Symptoms and General Health		VA-90D	Seizures and Neuroplasticity: Physiology and Biochemistry
Clinical	Prevention		VA-91	The Role of Dietary Choline in Neuroprotection
Epidemiology			DoD-114	A Re-examination of Neuropsychological Functioning in Persian Gulf War Veterans
Epidemiology			DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Brain & Nervous System				
Epidemiology			DoD-82	Feasibility of Developing a Registry of PTSD Affected Veteran
Epidemiology			VA-36	Stress Symptoms and Their Causal Attribution in Desert Storm
Epidemiology			VA-61	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also
Epidemiology			VA-64	Boston Environmental Hazards Research Center
Epidemiology			VA-72	Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses
Epidemiology			VA-75	ALS and Veterans: Are Veterans at Increased Risk?
Epidemiology	Prevention		DoD-144	Psychological Health Screening: Methods and Metrics for Deployed Forces
Epidemiology	Prevention		DoD-87	Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related Quality of Life
Epidemiology	Symptoms & General Health		DoD-23	Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families
Epidemiology	Symptoms & General Health		DoD-52	Female Gender and Other Potential Predictors of Functional Health Status Among Persian Gulf War Veterans
Epidemiology	Symptoms & General Health		VA-68	Family Study of Fibromyalgia
Epidemiology	Symptoms and General Health		DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military

Major Focus Area / Research Type	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Brain & Nervous System				
Epidemiology	Symptoms and General Health		VA-88	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military
Epidemiology	Symptoms and General Health		VA-92	Acetylcholinesterase Activity In Gulf War Veterans
Epidemiology	Symptoms and General Health		VA-93	HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans
Mechanistic			DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala
Mechanistic			DoD-80	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells
Mechanistic			DoD-91	Neurological and Circadian Substrates of PTSD-like Behaviors
Mechanistic			DoD-92	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder
Mechanistic			VA-81	Stress, Pro-Inflammatory Cytokines and Coping Behavior
Chemical Weapons				
Clinical	Diagnosis		VA-47	Retrospective Verification of Mustard Gas Exposure
Clinical	Pyridostigmine Bromide	Prevention	DoD-60	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness
Development	Diagnosis		DoD-49	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein
Epidemiology			DoD-116 A	Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA)
Epidemiology			VA-63 A	Follow-Up Investigation of troops exposed to nerve agents at Aberdeen Proving Ground (Pilot Study) (See also DoD-116A; formerly VA/DoD-2VA/2DA)

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Chemical Weapons				
Epidemiology	Symptoms & General Health		DoD-69	Five-Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents
Epidemiology	Symptoms & General Health		DoD-93	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up
Mechanistic			DoD-137	Low Level Exposure to Sulfur Mustard: Development of a SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin
Mechanistic			DoD-50	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways
Mechanistic	Brain & Nervous System		DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents
Mechanistic	Brain & Nervous System		DoD-53	Long-Term Effects of Subclinical Exposures to Sarin
Mechanistic	Diagnosis		VA-6 D	DNA Damage from Chemical Agents and Its Repair (Project IV)
Mechanistic	Environmental Toxicology		DoD-135	Biochemical Markers for Exposure to Low Doses of Organophosphorous Exposure
Mechanistic	Environmental Toxicology		DoD-136	A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure
Mechanistic	Environmental Toxicology		DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents
Mechanistic	Prevention		DoD-51	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses
Mechanistic	Pyridostigmine Bromide	Brain & Nervous System	DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects

Major Focus Area / Research Type	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Depleted Uranium				
Mechanistic			DoD-126	Blood-Brain Barrier Transport of Uranium
Mechanistic			DoD-127	Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man
Mechanistic			DoD-128	Multifactorial Assessment of Depleted Uranium Neurotoxicity
Mechanistic			DoD-129	Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness
Mechanistic			DoD-130	Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents
Mechanistic	Environmental Toxicology		DoD-7 A	Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling
Mechanistic	Environmental Toxicology		DoD-7 B	Carcinogenicity of Depleted Uranium Fragments
Mechanistic	Immune Function		DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metals
Mechanistic	Reproductive Health		DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development
Mechanistic	Symptoms & General Health		DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys
Diagnosis				
Clinical			DoD-47	Study of Mycoplasmal Infections in Gulf War Veterans
Development			DoD-100	Antibodies to Squalene
Development			DoD-66	Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction
Development			DoD-97	Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis

Major Focus Area / Research Type	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Environmental Toxicology				
Clinical	Brain & Nervous System	Interactions	VA-48	Cross-Sensitization as a CNS Model for Gulf War Chemical
Clinical	Diagnosis		VA-64 C	Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in veteran populations
Clinical	Symptoms & General Health		VA-4 D	Evaluation of Respiratory Dysfunction Among Gulf War Veterans
Development			DoD-16	Kuwait Oil Fire Health Risk Assessment
Development			DoD-18	Kuwait Oil Fires Troop Exposure Assessment Model (TEAM)
Development			DoD-19	Persian Gulf Veterans Health Tracking System
Development	Interactions		DoD-34	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents
Epidemiology			DoD-13	Effects of Persian Gulf War Service on Military Working Dogs
Mechanistic			DoD-134	Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin
Mechanistic			VA-65	San Antonio Environmental Hazards Research Center
Mechanistic			VA-65 A	Does a variant of the human SOD2 gene increase sensitivity to
Mechanistic			VA-65 B	The contribution of FEN-1 to genetic integrity subsequent to oxidative stress
Mechanistic			VA-65 C	The importance of hydrogen peroxide detoxification in cellular protection
Mechanistic			VA-65 D	Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental hazards?

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Environmental Toxicology				
Mechanistic	Brain & Nervous System	Chemical Weapons	DoD-22	Chronic Organophosphorus Exposure and Cognition
Mechanistic	Prevention		HHS-3	Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires
Mechanistic	Prevention		VA-4 E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility
Immune Function				
Clinical			DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War-related illness
Clinical			DoD-48	Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs Selected Control Groups
Clinical	Brain & Nervous System		DoD-88	Clinical Relevance of Novel Immunological Markers in PTSD
Clinical	Symptoms & General Health		VA-17	Immunological Evaluation of Persian Gulf Veterans
Clinical	Symptoms & General Health		VA-6 B	Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II)
Mechanistic			DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in Gulf War Veterans
Mechanistic	Interactions	Environmental Toxicology	HHS-7	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid
Mechanistic	Pyridostigmine Bromide	Interactions	DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Interactions				
Development	Environmental Toxicology		HHS-8	Strategy to Identify Non-Additive Response to Chemical Mixtures
Mechanistic	Brain & Nervous System	Chemical Weapons	DoD-54	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure
Mechanistic	Chemical Weapons	Brain & Nervous System	DoD-72	Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals
Mechanistic	Chemical Weapons	Brain & Nervous System	DoD-78	Experimental Models of Gulf War Syndrome
Mechanistic	Chemical Weapons	Pyridostigmine Bromide	DoD-55	Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects
Mechanistic	Chemical Weapons	Pyridostigmine Bromide	DoD-56	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine
Mechanistic	Chemical Weapons	Pyridostigmine Bromide	DoD-61	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid
Mechanistic	Chemical Weapons	Pyridostigmine Bromide	DoD-62	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice
Mechanistic	Environmental Toxicology		DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals
Mechanistic	Immune Function	Pyridostigmine Bromide	DoD-81	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and
Mechanistic	Pyridostigmine Bromide		DoD-77	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War
Mechanistic	Pyridostigmine Bromide	Brain & Nervous System	DoD-2	Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET
Mechanistic	Pyridostigmine Bromide	Brain & Nervous System	DoD-37	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Interactions				
Mechanistic	Pyridostigmine Bromide	Brain & Nervous System	DoD-75	Toxic Interactions of Prophylactic Drugs and Pesticides
Mechanistic	Pyridostigmine Bromide	Immune Function	DoD-76	Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel
Clinical	Pyridostigmine Bromide		DoD-124	Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin
Mechanistic	Pyridostigmine Bromide	Brain & Nervous System	DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide
Mechanistic	Environmental Toxicology		DoD-156	The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant
Leishmaniasis				
Clinical	Diagnosis	Treatment	VA-6 E	Clinical and Epidemiology Leishmania Research
Development	Diagnosis		DoD-38	Diagnostic Antigens of Leishmania tropica
Development	Diagnosis		DoD-8 A	Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL)
Development	Diagnosis		DoD-8 B	Development of a Leishmania Skin Test Antigen (LSTA)
Development	Diagnosis	Treatment	DoD-95	Development of Diagnostic tools and alternative treatment drugs for Leishmania
Mechanistic	Prevention		VA-15	Vaccine-Mediated Immunity Against Leishmaniasis
Mechanistic	Prevention		VA-16	Protective Immunity in Experimental Visceral
Mechanistic	Treatment		DoD-9	Identification of the Genetic Factors Which Control Tropism in Leishmania
Mortality				
Epidemiology			DoD-15	Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm
Epidemiology			VA-1	Mortality Follow-up Study of Persian Gulf Veterans

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Mortality				
Epidemiology	Prevention		DoD-102	Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans
Prevention				
Epidemiology			DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy
Epidemiology			HHS-9	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments
Epidemiology	Symptoms and General Health		DoD-140	US Department of Defense Surveillance for Neoplasms in Infancy
Epidemiology	Treatment		HHS-10	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline
Epidemiology	Treatment	Brain & Nervous System	DoD-145	Early Intervention Research Program to Enhance Soldier Resilience
Pyridostigmine Bromide				
Clinical			DoD-11	Male/Female Differential Tolerances to Pyridostigmine
Clinical	Brain & Nervous System	Prevention	DoD-64	Individual Differences in Neurobehavioral Effects of Pyridostigmine
Epidemiology			DoD-17	Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning
Epidemiology	Prevention		DoD-21	Study of Variability In Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals With Symptoms Following Participation in Operation Desert Storm
Mechanistic	Brain & Nervous System		DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity
Mechanistic	Brain & Nervous System		DoD-59	Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Pyridostigmine Bromide				
Mechanistic	Brain & Nervous System		DoD-79	Time Course of Stress-induced Impairment of Blood Brain Barrier
Mechanistic	Brain & Nervous System		VA-49	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction
Mechanistic	Brain & Nervous System	Interactions	VA-80	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment
Mechanistic	Environmental Toxicology		VA-6 C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III)
Mechanistic	Interactions		DoD-10	Pyridostigmine Synergistic Toxicity Study
Mechanistic	Interactions		DoD-139	Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses
Mechanistic	Interactions		VA-5 D	Effects of Genetics and Stress on Responses to Environmental
Mechanistic	Prevention		DoD-33	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity
Reproductive Health				
Clinical			VA-53	Spouses and Children Program
Clinical	Symptoms & General Health	Immune Function	DoD-44	Investigation of Seminal Plasma Hypersensitivity Reactions
Epidemiology			DoD-1 C	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among Gulf War veterans and other active-duty
Epidemiology			DoD-1 D	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in Gulf War

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Reproductive Health				
Epidemiology			DoD-1G	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian Gulf War Veterans
Epidemiology			DoD-35	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War.
Epidemiology			HHS-4	Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian Gulf War Veterans In Mississippi
Symptoms & General Health				
Clinical			DoD-1 A	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees
Clinical			DoD-65	Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment
Clinical			VA-18	Chronic Gastrointestinal Illness in Persian Gulf Veterans
Clinical			VA-40	Musculoskeletal Symptoms in Gulf War Syndrome
Clinical	Brain & Nervous System		DoD-57	Physiologic Effects of Stress in Gulf War Veterans
Clinical	Brain & Nervous System		DoD-58	Illness Among Persian Gulf War Veterans: Case Validation Studies
Clinical	Brain & Nervous System		VA-4Core	Boston Environmental Hazards Research Center Program
Clinical	Brain & Nervous System		VA-5 B	Physiological and Psychological Assessments of Persian Gulf Veterans
Clinical	Brain & Nervous System		VA-5 Core	East Orange Environmental Hazards Research Center Program

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Symptoms & General Health				
Clinical	Brain & Nervous System		VA-8	Psychological Test Data of Gulf War Veterans Over Time
Clinical	Brain & Nervous System	Reproductive Health	DoD-45	Air Force Women's Health Surveillance Study
Clinical	Brain and Nervous System		VA-82	Pituitary Adrenal Function in People with Fatiguing Illness
Clinical	Diagnosis		DoD-109	Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms
Clinical	Immune Function	Brain & Nervous System	DoD-42	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment
Epidemiology			DoD-1 B	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not.
Epidemiology			DoD-1 E	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study
Epidemiology			DoD-1 F	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: GWV vs. NDV
Epidemiology			DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome
Epidemiology			DoD-116 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly VA/DoD- 2DB)

Major Focus Area / Primary Focus Area *Research Type*	Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Symptoms & General Health				
Epidemiology			DoD-120	Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents
Epidemiology			DoD-14	Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry
Epidemiology			DoD-39	A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces
Epidemiology			DoD-4	The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey
Epidemiology			DoD-46	Exploratory Data Analysis with the CCEP Database
Epidemiology			DoD-70	War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes
Epidemiology			DoD-71	A Comparison of Post Deployment Hospitalization Between Vietnam and Gulf War Veterans
Epidemiology			DoD-73	Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes
Epidemiology			DoD-74	Relationship of Stress Exposures to Health in Gulf War Veterans
Epidemiology			DoD-94	Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. Gulf War Veterans
Epidemiology			DoD-98	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Symptoms & General Health				
Epidemiology			DoD-99	DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: Hospitalizations
Epidemiology			HHS-1	Health Assessment of Persian Gulf War Veterans from Iowa
Epidemiology			HHS-11	Deployment to the Gulf War and the Subsequent Development of Cancer
Epidemiology			HHS-6	Defining Gulf War Illness
Epidemiology			VA-2	National Health Survey of Persian Gulf Veterans
Epidemiology			VA-2 A	VA National Survey of Persian Gulf Veterans - Phase I
Epidemiology			VA-2 B	VA National Survey of Persian Gulf Veterans - Phase II
Epidemiology			VA-3	Use of Roster of Veterans Who Served in Persian Gulf Area
Epidemiology			VA-4 C	Gulf War And Vietnam Veterans Cancer Incidence Surveillance
Epidemiology			VA-46	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder
Epidemiology			VA-5 A	Health and Exposure Survey of Persian Gulf Veterans
Epidemiology			VA-6 Core	Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research
Epidemiology			VA-63 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB)
Epidemiology			VA-70	A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8

Major Focus Area / *Research Type*	Primary Focus Area: Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Symptoms & General Health				
Epidemiology	Brain & Nervous System		DoD-141	Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans
Epidemiology	Brain & Nervous System		DoD-142	Illnesses Among Persian Gulf War Veterans: Case Validation Studies (Iowa / Great Britain)
Epidemiology	Brain & Nervous System		DoD-143	Millennium Cohort Study
Epidemiology	Brain & Nervous System		VA-78	Millennium Cohort Study
Epidemiology	Brain & Nervous System	Diagnosis	VA-2 C	VA National Survey of Persian Gulf Veterans - Phase III
Epidemiology	Chemical Weapons		DoD-116	VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly
Epidemiology	Chemical Weapons		VA-63	VA/DoD Core funding of the Medical Follow-Up Agency (See also DoD-116; formerly
Epidemiology	Diagnosis		HHS-2	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18
Epidemiology	Prevention		DoD-108	Health Status of Current National Guard Members
Epidemiology	Prevention		DoD-117	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking
Epidemiology	Reproductive Health		DoD-30	Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study
Epidemiology	Reproductive Health	Treatment	DoD-96	Deployment Health Center
Epidemiology	Brain and Nervous System		DoD-149	Longitudinal Health Study of Gulf War Veterans
Epidemiology	Symptoms and		DoD-150	Validation Study of Gulf War General Health Deployment Files

Major Focus Area / *Research Type*	Primary Focus Area / Secondary Focus Area	Tertiary Focus Area	Project Number	Project Title
Treatment				
Clinical			VA-56	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13)
Clinical			VA-57	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13)
Clinical			VA-60	Identification and Management of Sleep Disorders in Gulf War Veterans
Clinical	Brain & Nervous System		DoD-125	A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74)
Clinical	Brain & Nervous System		VA-59	Demonstration Treatment Program for Gulf War Veterans With Unexplained Physical Symptoms (13)
Clinical	Brain & Nervous System		VA-74	A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125)
Clinical	Brain & Nervous System		VA-86	A Clinical Trial of Magnetic Stimulation in Depression
Clinical	Brain & Nervous System		VA-87	Improving Outcomes of Depression in Primary Care
Clinical	Symptoms & General Health		DoD-115	A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D)
Clinical	Symptoms & General Health		DoD-119	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also VA-55)
Clinical	Symptoms & General Health		VA-55	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also DoD-119)
Clinical	Symptoms & General Health		VA-62	A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V)
Clinical			VA-58	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13)

Appendix A 3

Project Funding

(As of September 30, 2003)

NOTES ON REVISED TABLE OF SPENDING FOR GULF WAR VETERANS' ILLNESSES RESEARCH

General

1. All entries for research funding reflect money centrally committed to researchers (both intramural and extramural) to carry out the specific projects. These funds do not cover operational costs for administration, infrastructure, etc. Each department allocates these costs in slightly different ways, making it difficult to accurately account for these funds. For example, in VA the research appropriation does not pay for clinician/investigator salaries. By law those funds must come from the patient care appropriation.
2. A "blank" funding entry generally reflects years in which a project was not active (e.g. it had not started or it had come to an end).
3. Some multiyear projects receive all of their funding in the fiscal year of the authorization and appropriation. For those, the dollars authorized and appropriated are shown for that fiscal year. The remaining funding entries show $0 for the years that the project is active.
4. Some intramural projects/programs are supported out of operational costs. For those projects, $0 is entered for the funds in the fiscal years that the project is active.
5. Programs consisting of multiple projects are represented in one of two ways depending on how funds are centrally allocated:
   a**. Funds centrally allocated to the program**: These programs are shown in the table as a main program indicated by project designation such as DoD-1, and projects in the program as DoD-1A, DoD-1B, etc. All funds are shown under the main program. Blank funding entries are shown for the individual projects.
   b. **Funds centrally allocated to projects within a program**: The funds for these programs are only indicated by their projects without a main program identifier, for example, VA-2A and VA-2B.

Specific

1. DoD-4 is part of a larger US Army study conducted at Walter Reed Army Institute of Research. Funding for this project has been combined into project DoD-23. In addition, projects DoD-8A and 8B are part of a larger US Army study in which all funding has been combined and is shown under program DoD-8.
2. HHS-3 was funded from the FY'91 appropriation, which is not included in this accounting.
3. HHS-4 was funded from the FY'93 appropriation, which is not included in this accounting.
4. Funds for VA-1 for FY'94 through FY'97 represent an aggregate of funds for both the VA Mortality Study and the VA National Survey of Persian Gulf Veterans. Beginning in FY'98, VA-1 reflects continuation of the VA Mortality Study. Beginning in FY'98, VA–2A, 2B, and 2C reflect funding for separate components of the VA National Survey of Persian Gulf Veterans.
5. In seven instances (DoD-115 & VA-62, DoD-116 & VA-63, DoD-118 & VA-61, DoD-119 &VA-55, DoD-125 & VA-74, DoD-143 & VA-78 ,and DoD154 & VA-88), two different designations represent the same project because both DoD and VA funded them jointly. The total funding appropriated for each of these five projects is broken down and reported separately by funding agency.

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-1	Naval Health Study Program	C	$725,000	$1,010,000	$2,250,000	$2,000,000	$2,654,000						$8,639,000
DoD-1A	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 1: A Study of Symptoms among 1500 Seabees.	C											$0
DoD-1B	Epidemiologic Studies of Morbidity among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not.	C											$0
DoD-1C	Epidemiologic Studies of Morbidity among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among Gulf War veterans and other active-duty personnel.	C											$0
DoD-1D	Epidemiologic Studies of Morbidity among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in Gulf War Veterans.	C											$0
DoD-1E	Epidemiologic Studies of Morbidity among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study.	C											$0

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-1F	Epidemiologic Studies of Morbidity among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: PGW vs. NDV.	C											$0
DoD-1G	Epidemiologic Studies of Morbidity among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian Gulf War Veterans.	C											$0
DoD-2	Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET.	C	$90,000	$0	$0	$0							$90,000
DoD-4	The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey.	C	$0										$0
DoD-7A	Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling.	C	$897,000	$0	$0	$0	$0						$897,000
DoD-7B	Carcinogenicity of Depleted Uranium Fragments.	C	$897,814	$0	$0	$0	$0	$121,400	$0				$1,019,214
DoD-8	Program DoD-8.	C	$773,000	$895,000	$652,000	$695,000	$694,000	$0					$3,709,000
DoD-8A	Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL).	C	$0	$0	$0								$0

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-8B	Development of a Leishmania Skin Test Antigen (LSTA).	C	$0	$0	$0	$0	$0	$0	$0	$0	0	$0	$0
DoD-9	Identification of the Genetic Factors Which Control Tropism in Leishmania.	C	$0	$150,000	$0	$0	$0						$150,000
DoD-10	Pyridostigmine Synergistic Toxicity Study.	C	$42,000	$44,000									$86,000
DoD-11	Male/Female Differential Tolerances to Pyridostigmine Bromide.	C	$549,000	$359,000	$0	$0	$0						$908,000
DoD-13	Effects of Persian Gulf War Service on Military Working Dogs.	O	$0	$0	$97,000	$200,000	$120,000	$200,000	$0	$0	$0	$0	$617,000
DoD-14	Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry.	C	$120,000	$0	$0	$0							$120,000
DoD-15	Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm.	C	$20,000	$0									$20,000
DoD-16	Kuwait Oil Fire Health Risk Assessment.	C	$345,000	$137,000	$50,000	$127,000							$659,000
DoD-17	Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning.	C	$21,000										$21,000
DoD-18	Kuwait Oil Fires Troop Exposure Assessment Model (TEAM).	C	$68,000	$151,000	$770,000	$193,000	$290,000	$295,000	$295,000	$306,000	$195,000	$225,000	$2,788,000
DoD-19	Persian Gulf Veterans Health Tracking System.	C		$25,000	$0	$0	$450,000	$450,000	$0	$0	$100,000	$50,000	$1,075,000

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-21	Study of Variability In Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals With Symptoms Following Participation in Operation Desert Storm.	C	$38,000	$100,000	$0	$0							$138,000
DoD-22	Chronic Organophosphorus Exposure and Cognition.	C	$375,000	$0	$0	$0	$0						$375,000
DoD-23	Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families.	C	$621,000	$688,000	$764,000	$985,000							$3,058,000
DoD-30	Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study.	C		$779,000	$0	$0	$0	$0	$0	$0			$779,000
DoD-31	Dysregulation of the Stress Response in the Persian Gulf Syndrome.	C		$971,000	$0	$0	$0	$0	$0				$971,000
DoD-32	Neuropsychological Functioning in Persian Gulf Era Veterans.	C		$353,000	$0	$0	$0	$0					$353,000
DoD-33	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity.	C		$354,000	$0	$0	$0	$0					$354,000
DoD-34	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents.	C		$283,000	$0	$0	$0	$0					$283,000

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-35	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War.	C		$427,000	$10,000	$63,000	$0	$10,500	$0	$0			$510,500
DoD-36	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms.	C		$416,000	$138,000	$0	$0	$0					$554,000
DoD-37	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats.	C		$934,000	$5,000	$0	$0	$0					$939,000
DoD-38	Diagnostic Antigens of Leishmania tropica.	C		$612,000	$0	$0	$0						$612,000
DoD-39	A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces.	C		$865,000	$0	$28,400	$155,000	$0	$124,868	$0			$1,173,268
DoD-40	Psychological and Neurobiological Consequences of the Gulf War Experience.	C		$264,000	$0	$0	$0	$0	$0	$0			$264,000
DoD-41	Evaluation of Muscle Function in Persian Gulf Veterans.	C		$906,000	$0	$0	$0	$0	$0				$906,000
DoD-42	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment.	C			$700,000	$0	$0	$0	$0	$0			$700,000

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-44	Investigation of Seminal Plasma Hypersensitivity Reactions.	C			$634,000	$0	$5,000	$14,200					$653,200
DoD-45	Physical and Emotional Health of Gulf War Veterans Women.	C	$247,068	$0	$299,274	$0	$456,732	$20,505	$0	$99,628	$0		$1,123,207
DoD-46	Exploratory Data Analysis with the CCEP Database.	C			$60,000	$100,000							$160,000
DoD-47	Study of Mycoplasmal Infections in Gulf War Veterans.	C			$112,000	$0	$0						$112,000
DoD-48	Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf War Syndrome Cohort vs. Selected Control Groups.	C			$74,000	$0	$0						$74,000
DoD-49	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts.	C			$927,000	$0	$0	$0	$0				$927,000
DoD-50	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways.	C			$699,000	$0	$0	$0					$699,000
DoD-51	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses.	C			$864,000	$0	$0	$0	$0				$864,000

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-52	Female Gender and Other Potential Predictors of Functional Health Status Among Persian Gulf War Veterans.	C	$414,000	$0	$0	$0	$0	$0					$414,000
DoD-53	Long-Term Effects of Subclinical Exposures to Sarin.	C			$1,000,000	$400,000	$0	$0	$217,137	$0			$1,617,137
DoD-54	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure.	C			$315,000	$100,000	$0	$0	$0				$415,000
DoD-55	Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects.	C			$500,000	$136,000	$0	$0	$0	$0			$636,000
DoD-56	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine.	C			$685,000	$100,000	$0	$0	$0	$0			$785,000
DoD-57	Physiologic Effects of Stress in Gulf War Veterans.	C				$909,000	$0	$0	$0	$0	$0		$909,000
DoD-58	Illness Among Persian Gulf War Veterans: Case Validation Studies.	O				$2,208,000	$0	$0	$4,264	$267,337	$0	$0	$2,479,601
DoD-59	Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis.	C				$625,000	$0	$0	$0	$0			$625,000
DoD-60	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness.	C				$125,000	$0	$0					$125,000

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-61	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid.	C				$1,586,000	$0	$0	$0				$1,586,000
DoD-62	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice.	C				$201,000	$0	$0					$201,000
DoD-63	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity.	C				$1,626,000	$0	$0	$0				$1,626,000
DoD-64	Individual Differences in Neurobehavioral Effects of Pyridostigmine.	C				$1,900,000	$18,516	$0	$190,595	$0			$2,109,111
DoD-65	Multi-Disciplinary Pathophysiologic Studies of Neurotoxic Gulf War-Related Neurologic Syndromes Leading to Diagnosis and Treatment.	C				$3,000,000	$0	$0	$0	$0			$3,000,000
DoD-66	Testing for Mycoplasmal Infection Replicability of Nucleoprotein Gene Tracking and Forensic Polymerase Chain Reaction.	C			$49,940	$100,000	$40,000	$403,000	$140,319	$0			$733,259
DoD-67	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria.	C				$3,400,000	$0	$0					$3,400,000

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-69	Five-Year Follow-Up of Army Personnel Potentially Exposed to Chemical Warfare Agents.	C				$946,160	$0	$0	$110,000	$0	$245,910	$0	$1,302,070
DoD-70	War Syndromes from 1900 to the Present: Symptom Patterns and Long Term Health Outcomes.	C				$734,687	$0	$115,000	$0	$0			$849,687
DoD-71	A Comparison of Post-Deployment Hospitalization Incidence between Vietnam and Gulf War Veterans.	C				$566,000	$0	$0	$0				$566,000
DoD-72	Long-Term Effects of Subchronic Exposure to Sarin, Alone and with Stress and Other Chemicals.	C				$996,000	$0	$0	$0	$0	$0		$996,000
DoD-73	Post-Deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes.	C				$500,000	$0	$0	$0	$0			$500,000
DoD-74	Relationship of Stress Exposures to Health in Gulf War Veterans.	C				$161,489	$1,991,330	$0	$0	$0	$0		$2,152,819
DoD-75	Toxic Interactions of Prophylactic Drugs and Pesticides.	C					$1,380,157	$0	$0	$0	$0	$0	$1,380,157
DoD-76	Evaluation of Immunotoxicity Due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel.	C					$448,369	$0	$0	$0	$0	$0	$448,369

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-77	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War.	C					$760,031	$0	$0	$0	$0		$760,031
DoD-78	Experimental Models of Gulf War Syndrome.	C					$2,179,097	$444,800	$0	$0	$0		$2,623,897
DoD-79	Time-course of Stress-Induced Impairment of the Blood Brain Barrier.	C				$100,200	$0	$0	$0				$100,200
DoD-80	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells.	C				$297,400	$0	$0	$0	$0	$0		$297,400
DoD-81	Immunotoxicity Due to Coexposure of DEET, Pyridostigmine, and Stress.	C				$300,000	$0	$0	$0	$0	$0		$300,000
DoD-82	Feasibility of Developing a Registry of PTSD-Affected Veteran Sib Pairs.	C				$172,000	$0	$0	$0	$0	$0		$172,000
DoD-83	Risk for Stress-Related Substance Abuse: Effects of Family History of Alcoholism.	C				$299,700	$0	$0	$0	$0	$0		$299,700
DoD-84	Psychobiological Alterations Of Persian Gulf War Veterans with and without PTSD.	C				$300,000	$0	$0	$0	$0	$0		$300,000
DoD-85	Central Nervous System Cytokines and CRH in Gulf War Veterans with Multiple Unexplained Symptoms.	C				$149,900	$149,200	$0	$0	$0	$0		$299,100
DoD-86	Effects of Combat Stress on the Structure and Function of the Hippocampus.	C				$300,000	$297,800	$0	$0	$0	$0	$0	$597,800

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	Project Title	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-87	Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related Quality of Life among PGWVs.	C				$289,100	$0	$0	$0	$68,044	$0	$0	$357,144
DoD-88	Clinical Relevance of Novel Immunological Markers in PTSD.	C				$242,300	$0	$0	$0	$0	$0		$242,300
DoD-89	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder.	C				$288,500	$0	$0	$0	$0	$0		$288,500
DoD-90	SPECT Benzodiazepine Receptor and MR Imaging in PTSD.	C				$200,000	$100,000	$0	$0	$0	$0		$300,000
DoD-91	Neurological and Circadian Substrates of PTSD-Like Behaviors.	C				$300,000	$299,000	$0	$0	$0			$599,000
DoD-92	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward and Animal Model of Chronic Stress and Posttraumatic Stress Disorder.	C				$249,700	$0	$0	$0	$0	$0		$249,700
DoD-93	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up.	C						$970,700	$0	$0			$970,700

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	Project Title	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-94	Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. Gulf War Veterans.	C						$557,173	$206,727	$0	$0		$763,900
DoD-95	Development of Diagnostic tools and alternative treatment drugs for Leishmania.	C						$1,500,000	$1,500,000	$1,500,000	$1,500,000		$6,000,000
DoD-96	Deployment Health Center.	O						$1,500,000	$1,500,000	$2,250,000	$1,750,000	$1,750,000	$8,750,000
DoD-97	Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis.	C						$177,300	$146,742	$151,202	$151,000		$626,244
DoD-98	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans.	O						$332,500	$188,000	$364,182	$0	$0	$884,682
DoD-99	DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: Hospitalizations.	C						$207,876	$204,205	$224,265	$0	$0	$636,346
DoD-100	Antibodies to Squalene.	C						$582,756	$0	$50,000	$487,333	$0	$1,120,089
DoD-101	Mechanisms in Chronic Multisymptom Illnesses.	O						$2,903,408	$5,542,189	$0	$4,786,192	$644,870	$13,876,659

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-102	Case-control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-deployed Veterans.	C						$249,908	$0	$253,793	$0	$281,950	$785,651
DoD-103	Human Metabolism & Interactions of Deployment-related Chemicals.	O						$583,319	$46,315	$0	$0	$349,994	$979,628
DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome.	C						$1,003,937	$9,311	$0	$0	$40,844	$1,054,092
DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala.	O						$950,490	$0	$0	$0	$0	$950,490
DoD-106	The role of Th1/Th2 cytokine balance in Gulf War-related Illness.	C						$292,411	$0	$0	$0		$292,411
DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity.	O						$875,373	$10,825	$0	$0	$0	$886,198
DoD-108	Health Status of Current National Guard Members.	C						$578,970	$0	$264,375	$174,651	$0	$1,017,996
DoD-109	Disordered responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms.	C						$917,762	$147,523	$397,243	$0	$0	$1,462,528
DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy.	C						$127,920	$63,705	$0	$0		$191,625
DoD-111	Autonomic Dysfunction in Gulf War Veterans.	O						$999,144	$0	$0	$0	$189,609	$1,188,753

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?	C						$256,916	$0	$0	$0		$256,916
DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine-Neurochemical, Behavioral, and Physiological Effects.	O						$802,140	$0	$0	$0	$0	$802,140
DoD-114	A Re-Examination of Neuropsychological Functioning in Persian Gulf War Veterans.	C						$593,712	$0	$0	$0		$593,712
DoD-115	A Randomized Multi-Center Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (see also VA-62; formerly VA/DoD-1D).	C						$1,000,000	$2,000,000	$0	$0		$3,000,000
DoD-116	VA/DoD Core Funding of the Medical Follow-up Agency (See also VA-63; formerly VA/DoD-2D).	O	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$2,500,000
DoD-116A	Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground, (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA).	C				$0	$0						$0

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-116B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly listed as VA/DoD-2DB).	C				$0	$0	$0					$0
DoD-117	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking.	C							$1,232,050	$0	$0		$1,232,050
DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) among GWVs (See also VA-61).	C							$430.824	$832,272	$0		$1,263,096
DoD-119	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT). (See also VA-55.)	C						$500,000	$1,000,000	$0	$0		$1,500,000
DoD-120	Assessing Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents.	C						$239,000	$316,000	$0	$0		$555,000
DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel on Pregnancy and Offspring Development.	C				$300,000	$250,000	$25,000	$15,000	$15,000			$605,000
DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys.	C				$25,000	$25,000	$25,000	$30,000	$35,000			$140,000
DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys.	C						$15,000	$20,000	$15,000			$50,000

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-124	Randomized, Controlled Trial of Combination Treatment with Pyridostigmine, DEET, and Permethrin.	O						$1,283,218	$0	$0	$0	$0	$1,283,218
DoD-125	A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women. (See also VA-74.)	O							$445,078	$0	$0	$0	$445,078
DoD-126	Blood-Brain Barrier Transport of Uranium	O							$790,884	$0	$0	$0	$790,884
DoD-127	Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man	C								$399,582	$0	$0	$399,582
DoD-128	Multifactorial Assessment of Depleted Uranium Neurotoxicity	O							$661,156	$0	$0	$328,734	$989,890
DoD-129	Inhalation of Uranium Oxide Aerosols: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness	O								$1,276,220	$0	$0	$1,276,220
DoD-130	Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents	O								$983,164	$0	$0	$983,164
DoD-131	Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illness	O								$5,377,526	$0	$500,000	$5,877,526
DoD-132	Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness	O								$792,198	$0	$0	$792,198

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-133	Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome	O								$884,087	$0	$0	$884,087
DoD-134	Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin	O							$775,155	$0	$0	$0	$775,155
DoD-135	Biochemical Markers for Exposure to Low Doses of Organophosphorus Insecticides	O							$786,408	$0	$0	$0	$786,408
DoD-136	A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure	O								$748,858	$0	$0	$748,858
DoD-137	Low Level Exposure to Sulfur Mustard: Development of a SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin	O								$600,111	$0	$0	$600,111
DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents	O								$434,795	$0	$0	$434,795
DoD-139	Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses	C							$892,399	$500,885	$0		$1,393,284

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-140	US Department of Defense Surveillance for Neoplasms in Infancy	O								$764,879	$0	$0	$764,879
DoD-141	Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans	C								$149,993	$0	$0	$149,993
DoD-142	Illness Among Persian Gulf War Veterans: Case Validation Studies	O								$0	$0	$168,962	$168,962
DoD-143	Millennium Cohort Study (See also VA-78)	O							$3,000,000	$1,000,000	$1,250,000	$2,000,000	$7,250,000
DoD-144	Psychological Health Screening: Methods & Metrics for Deployed Forces	O						$109,000	$295,000	$250,000	$300,000	$0	$954,000
DoD-145	Early Intervention Research Program to Enhance Soldier Resilience	O								$250,000	$275,000	$275,000	$800,000
DoD 146	Assessment of Toxicology Assays Methods & Chemical Exposures Among a Cohort of US Marines	C								$100,000			$100,000
DoD-147	Development of Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications	O				$105,000	$200,000	$190,000	$260,000	$412,000	$696,111	$292,530	$2,155,641
DoD-148	Predicting operational readiness for deployed Army National Guard and Army Reserve soldiers and families	C								$100,000			$100,000
DoD-149	Longitudinal Health Study of Gulf War Veterans	O								$1,689,945	$0	$0	$1,689,945
DoD-150	Validation Study of Gulf War Deployment Files	C									$134,348	$0	$134,348

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in Gulf War	O									$482,274	$0	$482,274
DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents	O									$1,000,000	$1,019,440	$2,019,440
DoD-153	Gulf War Illness Research	O								$4,694,500	$4,950,000	$920,838	$10,565,338
DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-88)	O									$100,000	$566,542	$666,542
DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide	O										$1,021,862	$1,021,862
DoD-156	The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant	O										$1,519,951	$1,519,951
	DoD Total Funds		**$6,492,882**	**$10,973,000**	**$11,905,214**	**$28,880,536**	**$13,213,232**	**$22,674,338**	**$23,847,679**	**$28,752,084**	**$18,827,819**	**$12,396,126**	**$177,962,910**

Status: C=Complete; O=Ongoing

Department of Health and Human Services Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
HHS-1	Health Assessment of Persian Gulf War Veterans from Iowa	C		$1,764,762	$1,616,755	$0	$0	$162,000	$0	$0			$3,543,517
HHS-2	Disease Cluster in a PA Air National Guard Unit	C		$750,000	$0	$0	$16,055	$0	$0				$766,055
HHS-3	Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and Blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil	C	$0	$0	$0	$0	$0						$0
HHS-4	Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian Gulf War Veterans in Mississippi	C	$0	$0	$0								$0
HHS-5	Cognitive Function and Symptom Patterns in Gulf War Veterans	C					$600,000	$558,000	$660,000	$0	$0	$0	$1,818,000
HHS-6	Defining Gulf War Illnesses	C					$600,000	$480,000	$719,792	$200,000	$0	$0	$1,999,792

Status: C=Complete; O=Ongoing

Department of Health and Human Services Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
HHS-7	Immunotoxicity of Dermal Permethrin and Cis-Urcanic Acid	C					$175,706	$192,445	$187,647	$0			$555,798
HHS-8	Strategy to Identify Non-additive Response to Chemical Mixtures	C					$242,586	$247,933	$0	$0			$490,519
HHS-9	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments	O								$337,693	$339,814	$339,814	$1,017,321
HHS-10	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline	O								$461,177	$460,000	$460,000	$1,381,177
HHS-11	Deployment to the Gulf War and the Subsequent Development of Cancer	O										$164,291	$164,291
	Total HHS Funds		**$0**	**$2,514,762**	**$1,616,755**	**$0**	**$1,634,347**	**$1,640,378**	**$1,567,439**	**$998,870**	**$799,814**	**$964,105**	**$11,736,470**

Status: C=Complete; O=Ongoing

Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-1	Mortality Follow-up Study of Persian Gulf Veterans, Second Update.	O	$546,000	$340,000	$1,980,000	$440,032	$178,197	$166,848	$176,440	$171,154	$128,496	$0	$4,127,167
VA-2	National Health Survey of Persian Gulf Veterans.	C									$0		$0
VA-2A	National Health Survey of Persian Gulf Veterans - Phase I.	C	$0	$0	$0	$0	$18,111						$18,111
VA-2B	National Health Survey of Persian Gulf Veterans - Phase II.	C			$0	$0	$0	$0					$0
VA-2C	National Health Survey of Persian Gulf Veterans - Phase III.	C					$1,601,280	$3,571,932	$3,400,000	$2,344,427	$30,000		$10,947,639
VA-3	Use of Roster of Veterans Who Served In Persian Gulf Area.	C	$0	$0	$0	$0	$0	$0					$0
VA-4 TOTAL	Boston Environmental Hazards Research Center Program.	C	$98,300	$500,000	$500,000	$500,000	$500,000	$500,000	$229,500				$2,827,800
VA-4Core	Boston Environmental Hazards Research Center Program.	C											
VA-4A	Evaluation of Cognitive Functioning in Persian Gulf Veterans.	C											
VA-4B	Evaluation of Neurological Functioning in Persian Gulf Veterans.	C											

Status: C=Complete; O=Ongoing

Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-4C	Gulf War and Vietnam Veterans Cancer Incidence Surveillance.	C											
VA-4D	Evaluation of Respiratory Dysfunction among Gulf War Veterans.	C											
VA-4E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker for Susceptibility.	C											
VA-4F	Validity of Computerized Tests	C											
VA-5 TOTAL	East Orange Environmental Hazards Research Center Program	C	$100,000	$500,000	$500,000	$500,000	$500,000	$500,000	$326,900				$2,926,900
VA-5 Core	East Orange Environmental Hazards Research Center Program	C											
VA-5A	Health and Exposure Survey of Persian Gulf Veterans	C											
VA-5B	Physiological and Psychological Assessments of Persian Gulf Veterans.	C											
VA-5C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans.	C											
VA-5D	Effects of Genetics and Stress on Responses to Environmental Toxins.	C											

Status: C=Complete; O=Ongoing

Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-6 TOTAL	Portland Environmental Hazards Research Center: Environment, Veterans' Gulf War Syndrome. Core: Clinical and Epidemiology Research.	C	$99,279	$499,583	$498,695	$499,198	$499,926	$499,098	$233,290				$2,829,069
VA-6 Core	Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and Gulf War Syndrome. Core Project for Clinical and Epidemiology Research.	C											
VA-6A	Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I).	C											
VA-6B	Clinical and Neuroendrocrine Aspects of Fibromyalgia (Project II).	C											
VA-6C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III).	C											
VA-6D	DNA Damage from Chemical Agents and Its Repair (Project IV).	C											
VA-6E	Clinical and Epidemiology of Leishmania Research.	C											

Status: C=Complete; O=Ongoing

Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-7	Desert Storm Reunion Survey.	C	$0	$50,000									$50,000
VA-8	Psychological Test Data of Gulf War Veterans Over Time.	C	$0	$0	$0	$0	$0	$0	$0	$0	$0		$0
VA-9	Evaluation of Cognitive Functioning in Persian Gulf War Veterans Reporting War-related Health Problems.	C		$20,000									$20,000
VA-10	Memory and Attention in PTSD	C			$63,700	$57,000	$57,600	$0					$178,300
VA-11	Neuropsychological Functioning in Veterans	C	$0	$0									$0
VA-12	Psychological Assessment of Operation Desert Storm Returnees	C	$0	$0	$0	$0							$0
VA-13	Neurobehavioral Aspects of Persian Gulf Experiences : A Pilot Study	C	$0	$50,000									$50,000
VA-15	Vaccine-Mediated Immunity against Leishmaniasis	C	$64,300	$64,300	$0	$82,600	$80,000	$79,400	$41,540	$114,336	$119,600	$59,800	$705,876
VA-16	Protective Immunity in Experimental Leishmaniasis	C		$60,200	$60,700	$54,900							$175,800
VA-17	Immunological Evaluation of Persian Gulf Veterans	C	$0	$0									$0
VA-18	Chronic Gastrointestinal Illness in Persian Gulf Veterans	C		$0	$0								$0

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-20	Psychological Adjustment in Operation Desert Shield/ Storm Veterans	C	$0										$0
VA-21	A Comparison of PTSD Symptomology among Three Army Medical Units Involved in ODS	C	$0	$0									$0
VA-36	Stress Symptoms and their Casual Attribution in Desert Storm Veterans.	C		$0	$0	$0							$0
VA-40	Musculoskeletal Symptoms in Gulf War Syndrome.	C	$0	$0	$0	$0	$0	$0					$0
VA-46	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder.	C		$0	$0	$0	$0	$0	$0				$0
VA-47	Louisville Center for the Study of Environmental Hazards to Reproductive Health.	C				$349,700	$299,700	$299,700	$139,960				$1,089,060
VA-48	Cross-Sensitization as a CNS Model for Chemical Intolerance.	C					$99,900	$89,400	$92,840	$45,000			$327,140
VA-49	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction	C					$112,090	$147,950	$141,696	$144,024	$125,862		$671,622
VA-50	Neuropsychological findings in a sample of Desert Storm Veterans.	C		$0	$0								$0

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-51	Psychobiological Assessment of Desert Storm Veterans.	C	$0	$0	$0	$0	$0	$0	$0	$0			$0
VA-53	Spouses and Childrens Program.	C				$101,360	$98,651	$51,088	$33,655	$12,934	$25,000		$322,688
VA-54	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress	O						$53,400	$90,131	$86,895	$86,350	$72,700	$389,476
VA-55	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (see also DoD-115).	C						$447,742	$1,466,375	$1,981,963	$254,000		$4,150,080
VA-56	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13).	C					$54,100	$261,625	$161,175				$476,900
VA-57	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13).	C					$71,625	$253,625	$174,750				$500,000
VA-58	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13).	C					$84,714	$349,805	$262,496				$697,015
VA-59	Demonstration Treatment Program for Gulf War Veterans with Unexplained Physical Symptoms (13)	C					$45,750	$348,225	$259,500				$653,475
VA-60	Identification and Management of Sleep Disorders in Gulf War Veterans (13).	C					$121,125	$328,500	$246,375				$696,000

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-61	An Epidemiological Investigation into the Occurrences of Amyotrophic Lateral Sclerosis (ALS) among Gulf War Veterans.(See also DoD-118).	C							$0	$0	$110,600		$110,600
VA-62	A Randomized, Multi-Center Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (See also DoD 115; formerly VA/DoD 1V).	C						$788,000	3,756,826	$1,971,233	$44,250		$6,560,309
VA-63	VA/DoD Core funding of Medical Follow-Up Agency (See also DoD 116; formerly VA/DoD-2V/2D).	O	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$2,500,000
VA-63A	Follow-up Investigation of troops exposed to nerve agents at Aberdeen Proving Ground (Pilot Study) (See also DoD-116A;formerly VA/DoD-2VA/2DA).	C				$0	$0						$0
VA-63B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD 116B; previously VA/DoD-2VB).	C				$0	$0	$0					$0

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-64	Boston Environmental Hazards Research Center Program	O							$112,360	$299,700	$300,000	$297,000	$1,009,060
VA-64A	Functional Neuroimaging in Lead Exposed Adults.	O											
VA-64B	Quantification and Validation of Structure-Function relationships through visuospatial test performance.	O											
VA-64C	Development of a structural neurotoxicant assessment checklist (SNAC) for clinical use in veteran populations.	O											
VA-65	San Antonio Environmental Hazards Research Center	O							$116,750	$350,000	$300,000	$300,000	$1,066,750
VA-65A	Does a variant of human SOD2 gene increase Sensitivity to hazards?	O											
VA-65B	The contribution of FEN-1 to genetic integrity subsequent to oxidative stress.	O											
VA-65C	The importance of hydrogen peroxide detoxification in cellular protection.	O											
VA-65D	Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental exposure?	O											

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-66	Physiological Responding in Posttraumatic Stress Disorder	C						$0	$0	$0			$0
VA-67	Olfactory Functioning in Gulf War Veterans.	C							$7,500	$7,500			$15,000
VA-68	Family Study of Fibromyalgia	C							$46,700	$50,000	$50,000		$146,700
VA-69	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans	C							$122,243	$135,487	$141,815	$48,947	$448,492
VA-70	A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8	C					$50,051	$19,817	$6,204	$4,884	$4,900		$85,856
VA-71	Central Nervous System Modulation of Visceral Pain in Persian Gulf War Syndrome	C							$125,313	$181,692	$186,524	$47,975	$541,505
VA-72	Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illness	C									$50,000	$50,000	$100,000
VA-73	Pain Sensitivity in Gulf War Vets with Medically Unexplained Musculoskeletal Illness	C									$50,000	$50,000	$100,000
VA-74	A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (see also DoD-125)	O								$291,804	$896,550	$1,346,863	$2,535,217

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-75	ALS and Veterans: Are Veterans at Increased Risk?	O								$73,000	$139,600	$139,600	$352,200
VA-76	Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD	O									$145,100	$135,000	$280,100
VA-77	HPA Axis Reactivity in Men and Women with Chronic PTSD	O									$101,400	$101,300	$202,700
VA-78	Millennium Cohort Study (see also DoD-143)	O											$0
VA-80	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress	O										$203,400	$203,400
VA-81	Stress, Pro-Inflammatory Cytokines, and Coping Behavior	O										$193,800	$193,800
VA-82	Pituitary Adrenal Function in People with Fatiguing Illness	O									$88,000	$135,000	$223,000
VA-83	Neuropsychological Assessment of a Population-Based Sample of Persian Gulf War Veterans and Controls	O										$18,988	$18,988

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS*	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-84	Neurobiology of Severe Psychological Trauma in Women	O									$135,000	$135,000	$270,000
VA-85	Associative Learning in Veterans with and without Combat Experience	O									$60,400	$74,000	$134,400
VA-86	A Clinical Trial of Magnetic Stimulation in Depression	O									$131,400	$131,400	$262,800
VA-87	Improving Outcomes of Depression in Primary Care	O									$152,065	$201,926	$353,991
VA-88	Prospective Assessment of Neurocognition in Future Gulf-Deployed and Gulf-Nondeployed Military Personnel (see also DoD-154)	O										$24,057	$24,057
VA-89	National Registry of Veterans with ALS	O										$319,229	$319,229
VA-90	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness	O										$250,000	$250,000
VA-90A	Neuronal Hyperexcitability and Motor Neuron Regeneration	O											

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PROJECT NO	PROJECT TITLE	STATUS	FY 1994	FY 1995	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	TOTALS FY '94-'03
VA-90B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders	O											
VA-90C	Developmental Differences in Alcohol Withdrawal Sensitivity	O											
VA-90D	Seizures and Neuroplasticity: Physiology and Biochemistry	O											
VA-91	The Role of Dietary Choline in Neuroprotection	O										$0	$0
VA-92	Acetylcholinesterase Activity In Gulf War Veterans	O										$3,775	$3,775
VA-93	HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans	O										$56,750	$56,750
TOTALS			**$1,157,879**	**$2,334,083**	**$3,853,095**	**$2,834,790**	**$4,722,820**	**$9,006,155**	**$12,020,519**	**$8,516,033**	**$4,106,912**	**$4,646,510**	**$53,198,796**

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Department of Veterans Affairs
Veterans Health Administration
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Washington, DC 20420

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