

VA-ORD GULF WAR RESEARCH : Research Program Overview

Presented to:

Research Advisory Committee on Gulf War Veterans' Illnesses

VHA OFFICE OF RESEARCH AND DEVELOPMENT / Victor Kalasinsky and Robert Jaeger

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VA Office of Research and Development Strategic Plan (2010-2015)

MISSION:

To discover knowledge and create innovations that advance health care for our Veterans and our Nation

VISION:

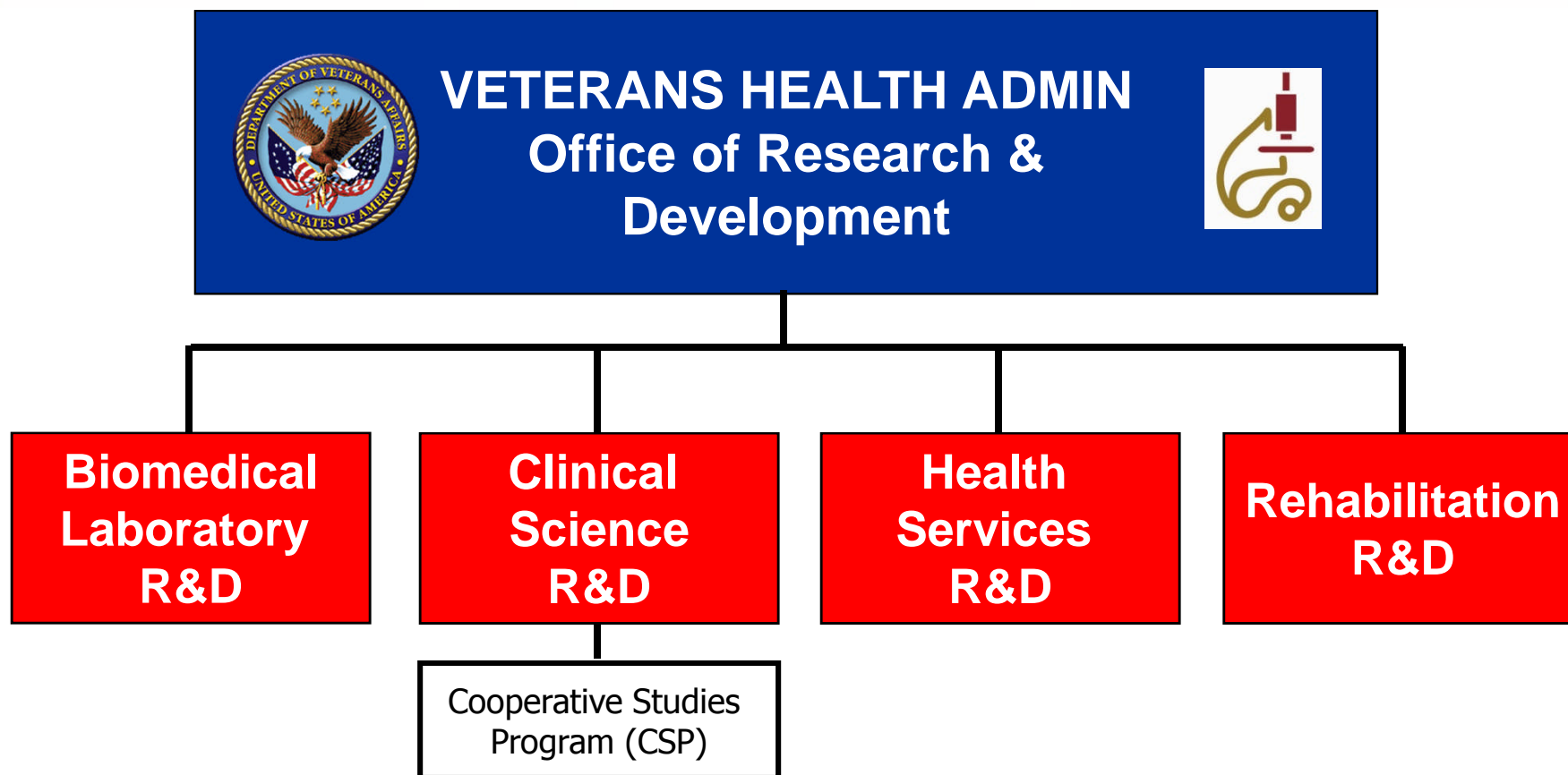
To be the premier research organization leading our Nation's efforts to enhance the health and well-being of Veterans by developing evidence-based clinical care and delivery systems improvements

http://vaww.va.gov/VHAOPP/POPlans/ORD_StrategicPlan2012.pdf

Nationwide VA Intramural Research Program Office of Research and Development

- **116 VAMCs have capacity for research**
 - **More than 90 are funded by VA at any time**
- **More than 2,100 Office of Research and Development (ORD) -funded projects**
- **Community of more than 3,000 VA researchers with a long history of significant research**
 - **Published at least 65,158 articles in last 9 years**
 - **Many appeared in high quality peer-reviewed journals, e.g., *New Engl J Med*, *J Amer Med Assoc*, and others**
- **Broad, extensive research portfolio that balances the needs of all Veterans**

Office of Research and Development Organizational Chart



How does the VA Office of Research and Development determine what Gulf War research projects will be funded?

- The clinicians and researchers who treat and interact with ill Gulf War Veterans seeking care in VA Hospitals and Medical Centers are the best and most qualified individuals to propose what research might be most beneficial to ill Gulf War Veterans.
- Gulf War Research “Requests for Applications” (RFAs) are developed by VA/ORD staff, based on advice from FACA advisory committees (NRAC and RACGWVI), senior VA leadership, Veterans Service Organizations, research recommendations in reports from the Institute of Medicine (IOM), consultation with other federal agencies supporting Gulf War Research (for example DoD/CDMRP), and the results of past and currently funded ORD research projects and programs.
- VA/ORD also consults on a regular basis with other entities within VA (such as Office of Public Health and Patient Care Services)
- VA/ORD invites VA intramural researchers to submit proposals for Gulf War research twice per year, using the mechanism of “Requests for Applications” (RFAs)

Gulf War Research – Requests for Applications (RFAs)

How does the RFA process work?

- RFAs are directed to VA intramural research investigators, inviting them to submit proposals for Gulf War research projects they are convinced have the potential to help advance knowledge to help ill Gulf War Veterans.
- The RFAs listed on the next slide are highly specific to Gulf War Veterans.
- Since 2011, these RFAs have been issued by ORD twice per year on a consistent basis. This is essential for the successful conduct of a growing research program.
- VA/ORD staff actively encourage VA/ORD investigators to respond to these RFAs, and are available to provide advice as needed to potential applicants.
- VA/ORD has a specific Merit Review Panel, with expertise in Gulf War issues, to insure a high quality, independent, and unbiased reviews of Gulf War research proposals submitted to VA/ORD. This panel also has members that were suggested by the RAC.
- Based, on the evaluation and summary statements of the Merit Review panel, and programmatic considerations, VA/ORD selects proposals to receive funding.
- VA/ORD staff work with applicants who were not successful of their initial submission to improve their proposal, based on comments from the scientific review.

Gulf War Research – Requests for Applications (RFAs)

Biomedical Laboratory Research & Development (BLR&D):

BX-14-011

Award for Research on Gulf War Veterans' Illnesses (GWVI)

BX-14-012

Pilot Projects for Research on Gulf War Veterans' Illnesses (GWVI)

Clinical Science Research & Development (CSR&D):

CX-14-011

Award for Research on Gulf War Veterans' Illnesses (GWVI)

CX-14-012

Pilot Projects for Research on Gulf War Veterans' Illnesses (GWVI)

CX-14-013

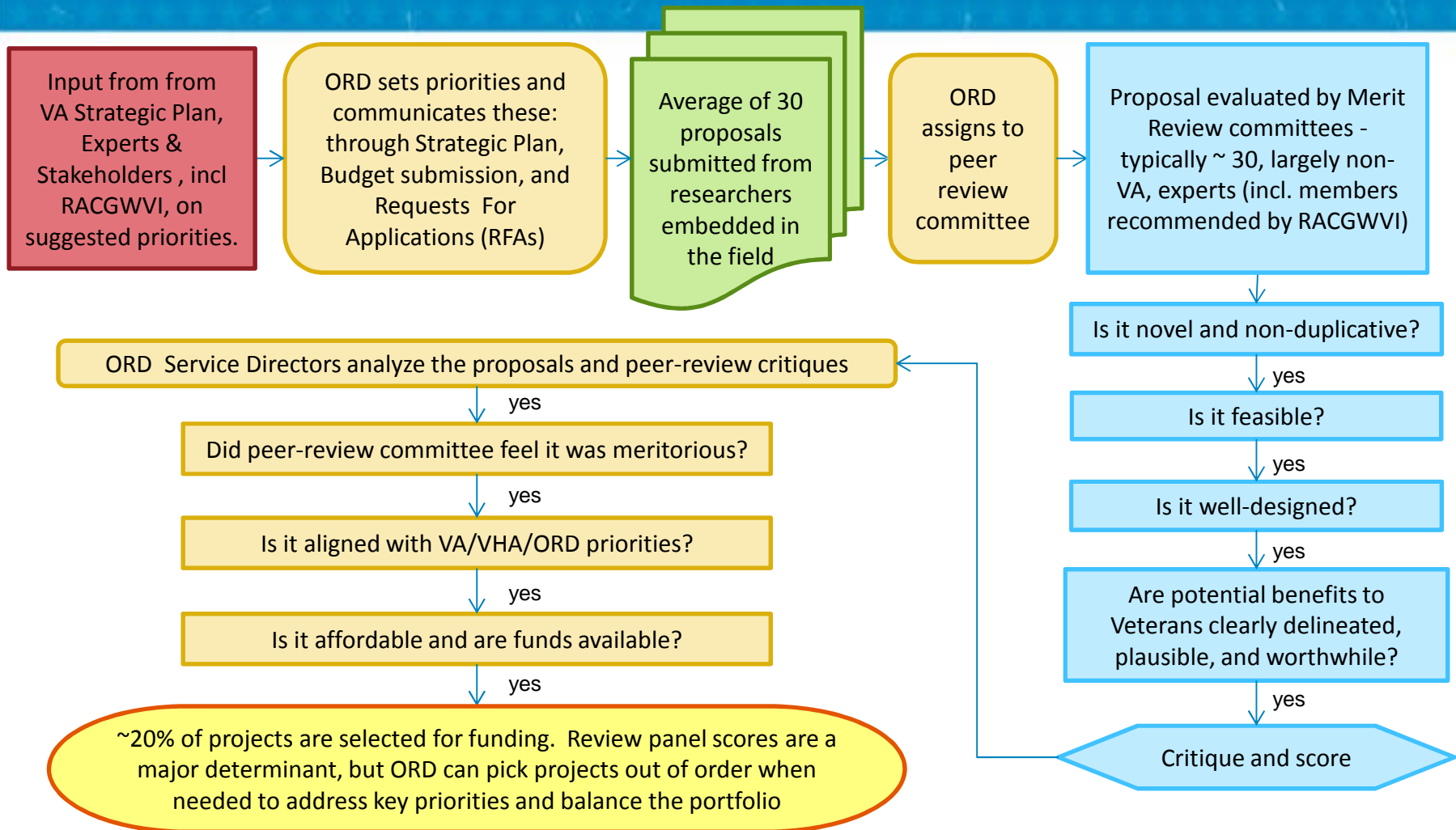
Award for Research on Treatments for Gulf War Veterans' Illnesses (GWVI) – (clinical trial)

Health Services Research & Development (HSR&D):

HX-14-011

Targeted Solicitation for Service-Directed Research Award on Health Services Research on the Care of Gulf War Veterans

How ORD selects GWVI projects for funding



VA Office of Research and Development

- **VA research is driven by improving health care for all Veterans**
 - **Investigator-initiated research (Clinician Researchers)**
 - Pilot projects
 - Merit review
 - Clinical Trials
 - Career Development Awards
 - **Service-directed research**
 - **Cooperative Studies Program (CSP)**
- **Public Access to Information about VA/ORD funded research**
 - <http://clinicaltrials.gov> Information on current and past clinical trials
 - <http://projectreporter.nih.gov/> Information on current and previously funded research projects
 - <http://www.ncbi.nlm.nih.gov/pubmed> Published results of research studies
 - <http://www.rehab.research.va.gov/jour/jourindx.html> Official Journal of ORD

VA/ORD-Based FACA Committees (Federal Advisory Committee Act)

- **National Research Advisory Council (NRAC)**
 - To provide advice to the Under Secretary for Health and the Secretary of Veterans Affairs on research and development sponsored and/or conducted by the Veterans Health Administration, to include policies and programs of the Research and Development Office
- **Research Advisory Committee on Gulf War Veterans' Illnesses (RACGWVI)**
 - To provide advice and make recommendations to the Secretary of Veterans Affairs on proposed research plans and strategies related to understanding and treating the health consequences of military service in the Southwest Asia theater of operations during the 1990 - 1991 Gulf War
 - Mandated by Congress in 1998; first chartered in January, 2002
- **Genomic Medicine Program Advisory Committee (GMPAC)**
 - To provide advice to the Secretary on the scientific and ethical issues related to the establishment, development, and operation of the Program in order to further VA's medical research in providing Veterans with Medical care and treatment.

VA/ORD Gulf War Research Strategic Plan (2013-2107)

- **Process to develop Plan began in January, 2011**
- **Submitted for concurrence within VA in August, 2012**
- **Internal VA approval in February, 2013**
- **Public release by VA in May, 2013**
- **“Living Document” subject to future updates as needed**
- **Plan is comprehensive, with particular emphasis on Treatments and Diagnosis**
- <http://www.research.va.gov/resources/pubs/docs/GWResearch-StrategicPlan.pdf>

Gulf War Research Strategic Plan (2013-2107)

Eight Focus Areas

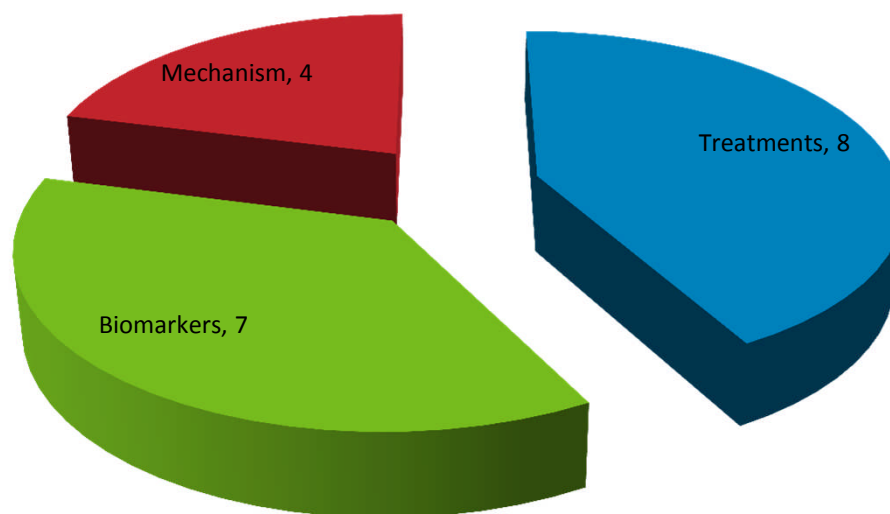
- **5.1 Symptomatic and Specific Treatments**
- **5.2 Databases and Continued Surveillance**
- **5.3 Establish an Evidence-Based Case Definition of Chronic Multisymptom Illness in Gulf War Veterans**
- **5.4 Genetic, Genomic, and Systems Biology**
- **5.5 Biomarkers**
- **5.6 Animal Models**
- **5.7 Improve Coordination and Communication**
- **5.8 Translate Research Findings into Practice**

VA-ORD Gulf War Research Funding (2004 – 2013)

Fiscal Year (FY)	VA Merit Review	UTSW Contract	FY Total
2004	\$ 7.64 M		\$ 7.64 M
2005	\$ 9.48 M		\$ 9.48 M
2006	\$ 13.01 M		\$ 13.01 M
2007	\$ 7.06 M	\$ 15.00 M	\$ 22.06 M
2008	\$ 6.93 M	\$ 15.00 M	\$ 21.93 M
2009	\$ 9.63 M	\$ 6.97 M	\$ 16.60 M
2010	\$ 11.57 M	\$ 2.29 M	\$ 13.86 M
2011	\$ 5.54 M	\$ 0.03M	\$ 5.57 M
2012	\$ 6.72 M		\$ 6.72 M
2013	\$ 7.94 M		\$ 7.94 M
Total 2004-2013	\$ 85.52 M	\$39.29 M	\$ 124.81 M

VA-ORD Gulf War Research Recently Funded Projects

New Gulf War Research Projects 2010-2013 (n = 19)



Gulf War Research Projects Active in 2014 (slide 1 of 2)

- Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex (5.1)
- Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis (5.5, 5.6)
- Somatic hypersensitivity in Veterans with IBS (5.1)
- Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease (5.4, 5.6)
- Immunoregulation of Myelin Specific T Lymphocytes (5.4, 5.6)
- Central Mechanisms Modulating Visceral Sensitivity (5.4, 5.6)
- Neuroprotection and Myelin Repair Mechanisms in Multiple Sclerosis (5.4, 5.6)
- Sleep Neurobiology and Circuitry (5.4, 5.6)
- Prevention of Hippocampal Neurodegeneration Due to Age and Apnea (5.6)
- Epigenetic Mechanisms Relevant to the Pathogenesis of ALS (5.4, 5.6)
- Nanoparticle Coupled Antioxidants for Respiratory Illness in Veterans (5.1, 5.6)
- Impact of exercise training on pain and brain function in Gulf War Veterans (5.1)
- Memory and Mood Enhancing Therapies for Gulf War Illness (5.1, 5.6)
- rTMS for the Treatment of Chronic Pain in GW1 Veterans (5.1)

Gulf War Research Projects Active in 2014 (slide 2 of 2)

- MEG Synchronous Neural Interactions (SNI) in Gulf War Veterans (5.5)
- Vascular and Skeletal Muscle Function in Gulf War Veterans Illness (5.1, 5.4)
- Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with GWI (5.1, 5.4)
- Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI (5.1)
- Examination of Cognitive Fatigue in Gulf War Illness Using fMRI (5.5)
- Longitudinal assessment of Gulf War veterans with suspected Sarin exposure (5.4, 5.5)
- Identification of Plasma Biomarkers of Gulf War Illness Using "omic" Technology (5.5, 5.6)
- Gulf War Exposures and the Molecular Mechanisms of Paternal Reproductive Risk (5.6)
- Complementary Neurosteroid Intervention in Gulf War Veterans' Illnesses (5.1)
- RCT of Duloxetine & Pregabalin for the treatment of Gulf War Illness in Veterans (5.1)
- Novel neurotrophic therapies in an optimized mouse model of GWVI (5.1, 5.6)
- Neuroinflammation, Oxidative Stress, and Hippocampal Defects in Gulf War Illness (5.5, 5.6)

Gulf War Research Projects Selected for funding

- Gulf War Exposures and Reproductive Risk (5.2, 5.4)
- Cognitive Rehabilitation Therapy for Gulf War Veterans (5.1)
- Neuroimaging and Biomarkers in Gulf War Veterans (5.5)
- Complementary and Alternative Medicine for Gulf War Veterans (5.1)

Response Statistics for VA-ORD Gulf War Research Requests for Applications (RFAs)

	Proposals Received	Projects Funded	Funds Approved
Spring 2011	10	1	} \$ 4.0 M
Fall 2011	16	2	
Spring 2012	15	4	} \$ 11.4 M
Fall 2012	17	3	
Spring 2013	22	5	} \$ 12.6 M
Fall 2013	13	2	
Spring 2014	18	June 2014	

Recently Completed Gulf War Research Projects (completed in FY 2013, publications will follow)

- Autonomic Functions of Gulf War Veterans with Unexplained Illnesses (5.1, 5.4)
- Motor Neuron Function of Gulf War Veterans with Excessive Fatigue (5.1, 5.4, 5.5)
- Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans (5.1)
- Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP (5.1)
- Behavior of Neural Stem Cells in a Rat Model of GWS (5.6)
- Multiple Sclerosis in Gulf War Veterans (5.3)
- A Randomized Controlled Trial of a Mindfulness-Based Intervention for Gulf War Syndrome (5.1)

Gulf War Research Biorepositories

- **CSP #585 Gulf War Era Cohort and Biorepository (5.2, 5.4, 5.5)**
 - Kick-Off meeting – August 29-30, 2013
 - Deployed and non-deployed Veterans
 - Users of VA health care and non-users
 - Surveys and blood collection
- **Gulf War Veterans' Illnesses Biorepository (5.2, 5.4, 5.5)**
 - Began operations – July, 2012
 - Enrolling Veterans to obtain medical records
 - Brain and spinal cord tissue to be collected post-mortem
- http://www.research.va.gov/programs/tissue_banking/gwvib/default.cfm

Gulf War Research Activities

- **Case Definition of Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans**
 - Institute of Medicine contract (May 1, 2013 – April 30, 2014)
- **Gulf War Veterans Outreach**
 - Briefings to VSOs
 - Brochures, publications, and web presence

<http://www.research.va.gov/resources/pubs/docs/state-of-va-research2012.pdf>

<http://www.research.va.gov/resources/pubs/docs/gwi-brochure.pdf>

Gulf War Research – VA-DoD Coordination

- **Annual briefings/updates between Gulf War Program Managers in VA/ORD and DoD/CDMRP**
- **Periodic review of proposals submitted/funded between agencies**
- **DoD/CDMRP briefings to RACGWVI**
- **Annual Report to Congress (jointly with DoD)**
 - <http://www.research.va.gov/resources/pubs/docs/GulfWarRpt12.pdf>
- **Special RFAs, coordinated between agencies**
- **Joint VA/DoD Working Groups (Deployment Health and Medical)**

Gulf War Research Activities

QUESTIONS ?