



**VA-ORD GULF WAR RESEARCH : Research Program Overview**

Presented to:  
Research Advisory Committee on Gulf War Veterans' Illnesses

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April 20-21, 2015  
Washington, DC



**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:**

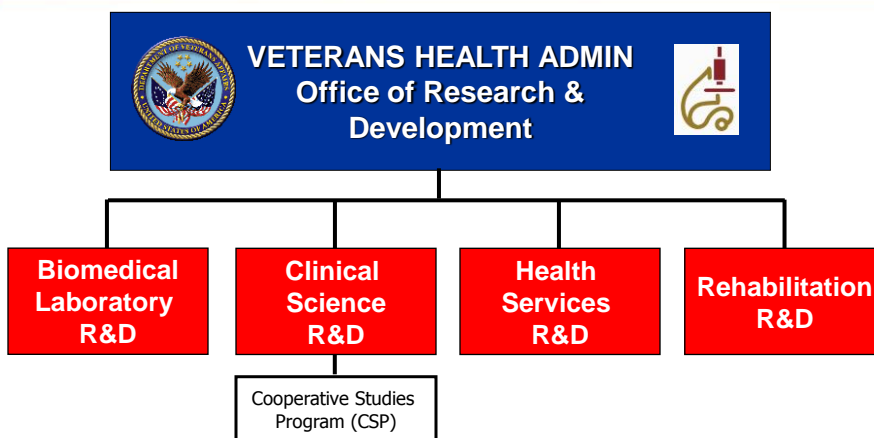
**To be the premier research organization leading our Nation's efforts to enhance the health and well-being of Veterans by developing evidence-based clinical care and delivery systems improvements**

[http://vaww.va.gov/VHAOPP/POPlans/ORD\\_StrategicPlan2012.pdf](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



## 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

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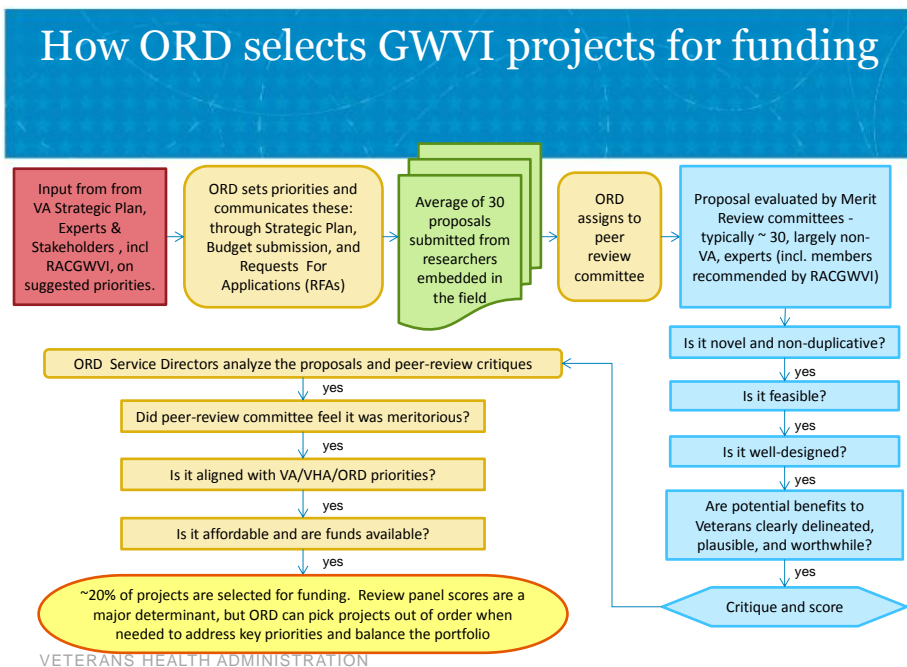
5

## VA Office of Research and Development Application Process

- 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 the research that might be most beneficial to ill Gulf War Veterans.
- ORD invites VA intramural researchers to submit proposals for Gulf War research using the mechanism of “Requests for Applications” (RFAs).
- Since 2011, these RFAs have been issued by ORD twice per year on a consistent basis.
- VA/ORD has a specific Merit Review Panel, with expertise in Gulf War issues, to insure high quality, independent, and unbiased reviews of Gulf War research proposals submitted to ORD.

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6



## Gulf War Research – Requests for Applications (RFAs)

**Biomedical Laboratory Research & Development (BLR&D):**

- BX-15-011  
Award for Research on Gulf War Veterans' Illnesses (GWVI)
- BX-15-012  
Pilot Projects for Research on Gulf War Veterans' Illnesses (GWVI)

**Clinical Science Research & Development (CSR&D):**

- CX-15-011  
Award for Research on Gulf War Veterans' Illnesses (GWVI)
- CX-15-012  
Pilot Projects for Research on Gulf War Veterans' Illnesses (GWVI)
- CX-15-013  
Award for Research on Treatments for Gulf War Veterans' Illnesses (GWVI) – (clinical trial)

**Health Services Research & Development (HSR&D):**

- HX-15-017  
Targeted Solicitation for Service-Directed Research Award on Health Services Research on the Care of Gulf War Veterans

## 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.

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9

## 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**
- **Subject to future updates as needed (2015 Update)**
- **Plan is comprehensive, with particular emphasis on Treatments and Diagnosis**
- <http://www.research.va.gov/resources/pubs/docs/GWResearch-StrategicPlan.pdf>

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10

**Gulf War Research Strategic Plan (2013-2017)**  
**Eight Focus Areas**  
 (<http://www.research.va.gov/pubs/docs/GWResearch-StrategicPlan.pdf>)

- **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 Genetics, Genomics, 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 – 2014)**

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	\$ 0.03 M	\$ 5.57 M
2012	\$ 6.72 M		\$ 6.72 M
2013	\$ 7.94 M		\$ 7.94 M
2014	\$ 9.73 M		\$ 9.73 M
<b>Total 2004-2014</b>	<b>\$ 95.25 M</b>	<b>\$ 39.29 M</b>	<b>\$ 134.54 M</b>

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

	<b>Proposals Received</b>	<b>Projects Funded</b>	<b>Funds Approved</b>
<b>Spring 2011</b>	10	1	\$ 4.0 M
<b>Fall 2011</b>	16	2	
<b>Spring 2012</b>	15	4	\$ 11.4 M
<b>Fall 2012</b>	17	3	
<b>Spring 2013</b>	22	5	\$ 12.6 M
<b>Fall 2013</b>	13	2	
<b>Spring 2014</b>	18	2	\$ 7.5 M
<b>Fall 2014</b>	22	3	

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13

## Gulf War Research Projects Active in 2015 (slide 1 of 2)

- Impact of exercise training on pain and brain function in Gulf War Veterans (5.1)
- rTMS for the Treatment of Chronic Pain in GW1 Veterans (5.1)
- Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI (5.1)
- Complementary Neurosteroid Intervention in Gulf War Veterans' Illnesses (5.1)
- Cognitive Rehabilitation Therapy for Gulf War Veterans (5.1)
- Complementary and Alternative Medicine in Veterans with Gulf War Illnesses (5.1)
  
- Diagnostic Utility of mtDNA Content and Exercise Challenge in Vets with GWI (5.1, 5.4)
- 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)
- Somatic hypersensitivity in Veterans with IBS (5.1)
- Vascular and Skeletal Muscle Function in Gulf War Veterans Illness (5.1, 5.4)
- Women vs. Men with GWI: Differences in Computational Models and Therapeutic Targets (5.1, 5.4)

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14



## Gulf War Research Projects Active in 2015 (slide 2 of 2)

- Central Mechanisms Modulating Visceral Sensitivity (5.4, 5.6)
- Immunoregulation of Myelin Specific T Lymphocytes (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)
- Memory and Mood Enhancing Therapies for Gulf War Illness (5.1, 5.6)
- 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)
- 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

- Randomized-Controlled Trial of a Drug Treatment for ill Gulf War Veterans (5.1)
- Neuroimaging and Biomarkers in Gulf War Veterans (5.5)
- Hippocampal Changes in Pyridostigmine-treated Rats (5.6)
- Models of Care for Gulf War Veterans (5.1)
- Exercise and Autonomic Dysfunction (5.1, 5.5)
- Translational Approaches to Treating Gulf War Illness (5.1, 5.8)
- Healthcare Utilization Patterns for Gulf War Era Veterans (5.1)



## Recently Completed Gulf War Research Projects

- 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)
- Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex (5.1)
- Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease (5.4, 5.6)
- Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis (5.5, 5.6)
- Understanding Pain of Gastrointestinal Origin in Women that Serve in OEF/OIF (5.5, 5.6)
- MEG Synchronous Neural Interactions (SNI) in Gulf War Veterans (5.5)

## Gulf War Research Activities Institute of Medicine (IOM) Reports

### “Chronic Multisymptom Illness in Gulf War Veterans: Case Definitions Reexamined”

**IOM Recommendation 1:** “The Committee recommends that the Department of Veterans Affairs consider the use of the Centers for Disease Control and Prevention and Kansas definitions because they capture the most commonly reported symptoms.”

**VA Response:** Concur

**IOM Recommendation 2:** “The committee recommends that the Department of Veterans Affairs, to the extent possible, systematically assess existing data to identify additional features of chronic multisymptom illness, such as onset, duration, severity, frequency of symptoms, and exclusionary criteria to produce a more robust case definition.”

**VA Response:** Concur

**IOM Recommendation 3:** “The committee recommends that the Department of Veterans Affairs use the term *Gulf War illness* rather than *chronic multisymptom illness*.”

**VA Response:** Concur in principle (“Gulf War illness presenting as chronic multisymptom illness”)

## Gulf War Research Activities Institute of Medicine (IOM) Reports

### Ongoing IOM projects

- **Gulf War and Health, Volume 10: Update of Health Effects of Serving in the Gulf War**
  - Began in December 2014
  - Will update previous IOM studies (Volumes 4 and 8)
  - Emphasis on:
    - Neurological disorders
    - Cancer (especially brain cancer and lung cancer)
    - Chronic multisymptom illness
- **Design of an Epidemiologic Study for MS and Other Neurologic Disorders in Pre- and Post-9/11 Gulf War Veterans**
  - Began in March 2015
  - Epidemiologic study rather than literature review

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19

## Gulf War Research Biorepositories

- **CSP #585 Gulf War Era Cohort and Biorepository (5.2, 5.4, 5.5)**
  - Deployed and non-deployed Veterans
  - Users of VA health care and non-users
  - Surveys and blood collection
  - Began contacting Veterans September, 2014
- **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
  - Review of pilot project in November, 2014
- [http://www.research.va.gov/programs/tissue\\_banking/gwvib/default.cfm](http://www.research.va.gov/programs/tissue_banking/gwvib/default.cfm)

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20

## Gulf War Research – VA-DoD Coordination

- **Regular briefings/updates between Gulf War Program Managers in VA/ORD and DoD/CDMRP**
- **Periodic review of proposals submitted/funded between agencies**
- **Annual Report to Congress (jointly with DoD)**
  - <http://www.research.va.gov/pubs/docs/GulfWarRpt13.pdf>
- **Joint VA/DoD Working Groups (Deployment Health and Medical)**

## Gulf War Research Activities

**QUESTIONS ?**