Overview of the Gulf War Illness Research Program (GWIRP)

Presented to
Research Advisory Committee on Gulf War Veterans’ Illnesses
Department of Veterans Affairs

E. Melissa Kaime, MD, FACP
Captain, Medical Corps, USN
Director, CDMRP

29 June 2010
Introduction

- Overview of the CDMRP
- GWIRP Funding History
- FY06-FY10 CDMRP Management Summary

**Partnerships**

**Advocates**
- Demonstrate need
- Participate at all levels
- Passion and perspective
- GWIRP Consumers are ill Gulf War veterans
- In touch with a network of other GW veterans

**Researchers**
- Innovation and gaps
- Risk/Benefit
- Product-oriented

**Congress**
- Add funds to budget
- Targeted guidance
- Opportunity to leverage

**DOD**
- Program management
- Regulatory and budget requirements
- Institute of Medicine (IOM) model
CDMRP Unique Features

- Funds added to the Department of Defense budget by Congress – not part of the POM*
- Two-tier formal review of proposals – IOM model
- Consumer advocates involved throughout process
- Vision is adapted yearly: Facilitates rapid change to address research gaps, develop new award mechanisms, and devise investment strategy
- Fund highly innovative research
- Funding flexibility
  - No “pay line”
  - Second level review based on impact, relevance, and portfolio balance
  - No out-year budget commitments

*Program Objectives Memorandum

Scope of CDMRP Funds and Awards

- Proposals Received since 1992: 71,168
- Proposals Funded since 1992: 9,895
CDMRP-Funded Awards Rate

Data as of end of FY09

Program Cycle
Pre-Award Management
DOD Gulf War Illness (GWIRP) Funding History

- **Military Operational Medicine Research Program** (MOMP) - USAMRMC
- Gulf War Illness Research Program (GWIRP)
- Gulf War Illness Research Program (CDMRP)
- Amyotrophic Lateral Sclerosis Therapy Development for Gulf War Illness Research Program (MOMP & CDMRP)
- Peer Reviewed Medical Research Program (CDMRP)

Funding History:

- **FY06 & FY08**: $15M
  - 5 Program Announcements Released
  - 193 Preproposals Received
  - 79 Full Submissions
  - 21 Awards

- **FY09**: $8M
  - 4 Program Announcements Released
  - 48 Preproposals Received
  - 36 Full Submissions
  - 8 Awards (in negotiations)

- **FY10**: $8M
  - 4 Program Announcements Released
  - 8 Awards Anticipated

CDMRP GWIRP Synopsis

US Army Medical Research and Materiel Command
FY08 National Defense Authorization Act

HR 1585 Conferees directed the Secretary of the Army to utilize the authorized funding... to undertake research on Gulf War Illnesses. Conferees also directed that activities under the Gulf War Illnesses program include:

♦ Studies of treatments for the complex of symptoms known as “Gulf War Illness”
♦ No studies based on psychiatric illness and psychological stress as the central cause
♦ Competitive selection and peer review to identify research with the highest technical merit and military value

Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I
Dr. Kimberly Sullivan, Boston University School of Medicine

♦ Examined brain volumetrics and cognitive functioning of high- and low-exposed pesticide control personnel from the Gulf War
♦ Results suggest decreased white matter volumes are significantly correlated with increased health symptom reports and decreased executive domain functioning
♦ Results suggest that DEET and pyridostigmine bromide (PB) exposures are associated with significantly lower hippocampal volumes and lower performance on visual memory testing
Coenzyme Q10 for Gulf War Veterans with Chronic Symptoms
Dr. Beatrice Golomb, University of California, San Diego

- Dr. Golomb is conducting a clinical trial of the efficacy of coenzyme Q10 (Q10) to improve chronic GWI symptoms such as muscle pain and fatigue, as well as overall quality of life for ill Gulf War veterans.
- Q10 has anti-oxidant properties, boosts cell energy, and protects against apoptotic cell death.
- Dr. Golomb’s study has enrolled 46 Gulf War veterans to participate in this cross-over, multi-dose study. Participants are in various stages of progress through the study, with 33 having completed the dosing regimen.
- Outcome measures will include responses to quality-of-life surveys by the participants.

CNDP1 Polymorphisms and Carnosine Therapy in GWI
Dr. James Baraniuk, Georgetown University

- This study uses a two-pronged approach of investigating CNDP1 status as a biomarker for GWI and testing carnosine as a potential treatment.
- 100 GWI and healthy veterans will be evaluated for CNDP1 status (cheek swab) as well as pain sensitivity and muscle strength to further identify GWI parameters.
- Pharmacologically replacing depleted carnosine in the brain of GWI veterans could improve sleep problems, pain, and other symptoms; functional MRI will be used to measure the impact of carnosine treatment.
- Enrollment in the study is progressing; Dr. Baraniuk also reports finding a high rate of migraine headaches in GWI participants and proposes to investigate the finding further in future grant applications.
Other FY06 GWIRP Awards

- Investigating a new use for mifepristone in a clinical trial to determine if its properties can improve the health of Gulf War veterans with chronic multisymptom illness
- Using an animal model of sarin-induced GWI to examine heart rate variability and autonomic nervous system activity to identify potential biomarkers for Gulf War Illness
- A study of the pathophysiology underlying depleted uranium (DU) toxicity that examines glutamate concentration; this project will also examine the effectiveness of memantine and riluzole in an animal model

FY08 GWIRP Awards Highlights

- A cross-over clinical trial of Naltrexone and Dextromethorphan in ill Gulf War veterans to treat neuroinflammation and relieve GWI symptoms
- Investigating reduced blood flow and coagulation as an underlying cause of GWI and an avenue for therapeutic development
- Investigating small intestinal bacterial overgrowth (SIBO) as an underlying cause of GWI
- Extensive molecular profiling of GWI patients’ gene expression and cytokine concentration before and after an exercise challenge to inform potential therapeutic options
- A clinical trial investigating the effectiveness of acupuncture in the treatment of GWI
- An investigation of the antioxidant analgesic drug Flupirtine in an animal model of GWI exposures
DOD Congressionally Directed Medical Research Programs

GWIRP FY09 Awards

<table>
<thead>
<tr>
<th>Award Mechanism</th>
<th>Preproposals Received</th>
<th>Proposals Received</th>
<th>Recommended for Funding</th>
<th>Funds Allocated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Trial Award</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Innovative Treatment Evaluation Award</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>$1.1M</td>
</tr>
<tr>
<td>Evaluation Award (ITEA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Investigator-Initiated Research Award</td>
<td>40</td>
<td>31</td>
<td>6</td>
<td>$5.2M</td>
</tr>
<tr>
<td>Research Award (IIRA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>48</strong></td>
<td><strong>36</strong></td>
<td><strong>8</strong></td>
<td><strong>$6.3M</strong></td>
</tr>
</tbody>
</table>

FY09 GWIRP Awardees

**Dr. David Carpenter (ITEA)**  
*State University of New York, Albany*  
*Gulf War Illness: Evaluation of an Innovative Detoxification Program*

**Dr. Ashok Tuteja (ITEA)**  
*Western Institute for Biomedical Research*  
*Probiotic (Bifidobacterium infantis) for Gulf War Illness*

**Dr. Henry Heng (IIRA)**  
*Wayne State University*  
*Genome Instability: A Common Link in Gulf War Illness Patients*

**Dr. Anne Louise Oaklander (IIRA)**  
*Massachusetts General Hospital*  
*Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness?*
FY09 GWIRP Awardees (cont.)

Dr. Mohan Sopori (IIRA)
*Lovelace Biomedical & Environmental Research Institute*
*Neuroimmune Interactions, Low-Dose Sarin Inhalation, and Gulf War Syndrome*

Dr. Gordon Broderick (IIRA)
*University of Alberta*
*Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness*

Dr. John Repine (IIRA)
*University of Colorado, Denver*
*Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome*

Dr. Timothy Juergens (IIRA)
*University of Wisconsin, Madison*
*Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome*

GWIRP FY10 Priority Areas

- Identification of effective treatments for GWI
- Improved diagnostic testing for GWI
- Improved understanding of GWI pathobiology
- Incorporation of case definitions for GWI
# FY10 GWIRP Investment Strategy (Proposed)

<table>
<thead>
<tr>
<th>Award Mechanism</th>
<th>Award Value (Direct Costs)</th>
<th>Award Duration</th>
<th>Anticipated Number of Awards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Trial Award</td>
<td>$1,500,000</td>
<td>4 years</td>
<td>1</td>
</tr>
<tr>
<td>Innovative Treatment Evaluation Award</td>
<td>$450,000</td>
<td>3 years</td>
<td>2</td>
</tr>
<tr>
<td>Investigator-Initiated Research Award</td>
<td>$600,000</td>
<td>3 years</td>
<td>3</td>
</tr>
<tr>
<td>Consortium Development Award</td>
<td>$200,000</td>
<td>1 year</td>
<td>2</td>
</tr>
</tbody>
</table>

---

## FY10 GWIRP Clinical Trial Award

### Intent:
Supports Phase II or III clinical trials focusing on treatments for GWI

### Key Features:
- Preliminary/preclinical data are required
- Open to investigators at all academic levels
- Maximum period of performance is 4 years
- Maximum allowable funding for the entire period of performance is $1.5M in direct costs

### Submission Deadlines:
- Preproposals due May 2010; 1 of 3 invited for full proposal
- Applications due 4 August 2010, by invitation only
FY10 GWIRP
Innovative Treatment Evaluation Award

Intent:
Supports exploratory or small-scale studies evaluating treatments not previously studied in GWI

Key Features:
♦ Preliminary data are not required
♦ Pilot Phase II or Phase I/II trial combinations are permitted
♦ Open to investigators at all academic levels
♦ Maximum period of performance is 3 years
♦ Maximum allowable funding for the entire period of performance is $450K in direct costs

Submission Deadlines:
♦ Preproposals due May 2010; 8 of 13 invited for full proposals
♦ Applications due 4 August 2010, by invitation only

FY10 GWIRP
Investigator-Initiated Research Award

Intent:
Supports new ideas in basic and clinical developmental research

Key Features:
♦ Preliminary data are not required
♦ Clinical trials are not allowed
♦ Open to investigators at all academic levels
♦ Maximum period of performance is 3 years
♦ Maximum allowable funding for the entire period of performance is $600K in direct costs

Submission Deadlines:
♦ Preproposals due May 2010; 32 of 68 invited for full proposals
♦ Applications due 4 August 2010, by invitation only
FY10 GWIRP
Consortium Development Award

Intent:
Supports initial development of infrastructure and collaborations for a multi-institutional consortium for GWI research

Key Features:
♦ Awardees expected to apply for FY11 Consortium Award
♦ Award funds consortium development, *not* research costs
♦ Open to investigators at all academic levels
♦ Maximum period of performance is 1 year
♦ Maximum allowable funding for the entire period of performance is $200K in direct costs

Submission Deadlines:
♦ Letter of Intent due May 2010; 5 letters received
♦ Applications due 4 August 2010

FY10 GWIRP Integration Panel Members

Roberta F. White, Ph.D. (Chair)
Boston University

Gudrun Lange, Ph.D.
VA New Jersey Health Care System

CAPT Braden Hale, M.D.
Naval Health Research Center

COL Cornelius Maher, M.D., Ph.D.
US Army Medical Command

Anthony Hardie
Veterans of Modern Warfare

Maj David Watson, Ph.D.
David Grant USAF Medical Center

Chris Kornkven
National Gulf War Resource Center