

Research Advisory Committee on Gulf War Veterans' Illnesses
Annual Report 2015

1. Origin and Membership

The Research Advisory Committee on Gulf War Veterans' Illnesses was established pursuant to Public Law 105-368. Members are appointed by the Secretary of Veterans Affairs. Committee members who served during 2015 are listed in Appendix A.

2. Committee Activities

The Committee held three meetings in 2015: April 20 – 21, June 23 and September 29 in Washington, D.C. At the start of the year, the Secretary also appointed a new Committee Chairman, Stephen L. Hauser, MD. A fellow of the American Academy of Arts and Sciences and the American Academy of Physicians, and a member of the Institute of Medicine of the National Academy of Sciences, Dr. Hauser is the Robert A. Fishman Distinguished Professor and Chair of Neurology at the University of California, San Francisco. He was also appointed by President Obama to the Presidential Commission for the Study of Bioethical Issues and previously served as the Chair of the Institute of Medicine Committee on Gulf War and Health, and is committed to improving the health of ill Gulf War veterans.

The April meeting was Dr. Hauser's inaugural meeting as Chair of the Committee. After introductory comments Secretary McDonald presented an overview of VA health system and research enterprise, noting significant advances in healthcare contributed by the VA system. Additionally, he provided an overview of the "MyVA" effort and the VA research program. Dr. Carolyn Clancy, Interim Undersecretary for Health at the VA, emphasized the importance of the work of the Committee for the VA mission. After introductions of new Committee members, the agenda turned to a consideration of new analyses of gene exposure outcomes in Gulf War illness (GWI), and discussion of environmental exposures and their influence on axonal transport and memory formation in preclinical models. Next, the Committee heard presentations by the VA Office of Research and Development (ORD) summarizing the current Gulf War research portfolio, and by the Million Veteran Program. On the second day, the Committee underwent ethics and federal advisory committee training, heard a review of VA Office of Public Health Gulf War research, and closed with a broad discussion of the landscape and scientific trajectories

of current VA research programs related to service in the Gulf War and received public comment on these issues.

The June 23rd meeting continued an exploration and assessment of GWI related research across the VA ORD portfolio. At this meeting there was a particular focus on translation of basic research discoveries to the clinical research arena, and ultimately to care that is delivered at the bedside and clinic.

The third meeting focused on an assessment of biomarkers associated with GWI, including putative metabolomic and lipidomic biomarkers, mitochondrial function analyses, and functional imaging. The Committee also reviewed an update of a dietary polyphenol trial as well as an overview of the VA ORD portfolio. The meeting concluded with recognition of retiring committee members and solicitation of public comment.

Thus, the three meetings of the 2015 Committee focused, respectively, on basic preclinical research, translational clinical research programs, and biomarker research. The overall goal was to reassess current strategies and understand new developments as a prelude to proposing adjustments in this path forward.

Representatives from VA, DoD, and other federal agencies were invited to attend Committee meetings and participate in discussions with presenting scientists along with Committee members. All meetings were open to the public. Time was reserved to allow members of the public to provide comments on the Committee's work and on matters related to Gulf War research.

Committee members have been active participants in all aspects of the Committee's work. Meetings have been well-attended. The Committee has kept VA leadership and the Office of Research and Development (ORD) informed of its work and its findings on an ongoing basis. This task has been accomplished through attendance and participation of ORD officials at Committee meetings, and ongoing communications between the Committee chairman, scientific director and associate scientific director, and the Secretary's Office and ORD.

3. Support Activities

Responsibility for providing scientific and administrative support to the Committee has been provided by the Boston University School of Public Health, Department of Environmental Health, through a contract with the Bedford, Massachusetts VAMC. Committee member Dr.

Roberta White served as Scientific Director, and Dr. Kimberly Sullivan served as Associate Scientific Director. The contract with Bedford, Massachusetts VAMC came to an end in September, which also marked the completion of Drs. White's and Sullivan's eight years of dedicated service to the Committee.

Support activities for the Committee are transitioning from Boston, MA to San Francisco, CA to allow for better coordination with newly appointed Chairman, Dr. Stephen Hauser. Dr. Jon-Eric VanLeeuwen was hired at the end of 2015 to serve as Managing Director for the Committee and is overseeing the office relocation, which is expected to be complete in early 2016.

In addition to ongoing activities relating to monitoring research relevant to the health consequences from the Gulf War, preparation of Committee reports, development of Committee meetings, and preparation of meeting minutes, the staff has primary responsibility for Committee administrative activities and management of the Committee's website.

4. Designated Federal Officer

The Designated Federal Officer for the Committee is Victor Kalasinsky, PhD, who also serves as manager for the Gulf War portfolio within the VA Office of Research and Development.

5. Accomplishments

The Committee concluded that VA research programs were making much needed and important progress towards the goal of understanding medical consequences of service in the Gulf Wars. As detailed below, the Committee also believes that three areas of science would benefit from additional development and focus. We respectfully present these in preliminary form, and plan to more fully develop and augment these recommendations as a primary goal for 2016. Our recommendations are:

Committee Recommendation Categories:

Integrating research outcomes into clinical care

- Recommend that the research and clinical sides of VA should collaborate more interactively.

- Recommend that VA physicians receive Gulf War illness (GWI) training to create some uniformity of care throughout the agency and uniformity of treatment for Gulf War Veterans.
- Recommend establishing or bolstering mechanisms for veterans to be able to easily contribute to research studies, such as biomarker studies (i.e. a simple and efficient system to obtain consent, blood collection, sample processing, and storage at VA hospitals).

Improving study methods and research follow-up

- VA should form a working group to assist in the development of a single case definition for GWI and to review the assessment variables and outcome variables for GWI research.
- Recommend that the categorization of deployed and non-deployed groups is corrected such that VA researchers and systems recognize that Gulf War Desert Storm ended April 11, 1991, not March 1, 1991. For example, this could be implemented in large VA survey and cohort studies for deployed vs non-deployed veterans.
- Recommend that the VA: (1) undertake an independent confirmation study of reported association of rare BChE variants associated with GWI in deployed veterans stratified based on their self-reported exposure histories; (2) examine the feasibility of sequencing the entire BCHE gene (both exons and introns), and extend this to other candidate genes (such as PON1, PON2, and PON3); (3) investigate the practicality of utilizing other repositories that can be used in this effort (i.e., including Million Veteran Program or coupled with DoD serum repository); (4) extend this strategy to ALS, another Gulf War-related disorder, in which rare PON variants are also associated with disease.
- Recommend that Gulf War Veterans within the closest proximity to Khamisiyah detonations (and highest risk of sarin exposure), as well as those that were nearest to oil wells, are followed as a surveillance group, since these groups may be at risk for brain cancer and possibly other disorders.

Translating research into therapy: treatment, prevention and repair

- Recommend that VA develop larger treatment trials from prior promising pilot treatment studies. This could include:
 - A follow-up study to the promising research outcomes of L-carnosine on IBS symptoms conducted by Baraniuk et al., (2013).
 - A follow-up study to the pilot continuous positive airway pressure (CPAP) treatment trial with GW veterans conducted by Amin et al., (2011).

Appendix A
Research Advisory Committee on Gulf War Veterans' Illnesses
2015 Committee Members

Chair

Stephen Hauser, MD, Robert A. Fishman Distinguished Professor and Chair, Department of Neurology, University of California, San Francisco.

Committee Members

Floyd E. Bloom, MD, Professor Emeritus, Molecular and Integrative Neuroscience Department, The Scripps Research Institute, La Jolla, California.

James A. Bunker, Executive Director, National Gulf War Resource Center (NGWRC).

Fiona Crawford, PhD, President, Roskamp Institute.

Beatrice A. Golomb, MD, PhD, Associate Professor of Medicine and of Family Preventative Medicine, University of California at San Diego, La Jolla, California.

Ronnie D. Horner, PhD, Professor, Department of Health Services and Management, Arnold School of Public Health, University of South Carolina.

Nancy G. Klimas, MD, Professor and Chair, Department of Clinical Immunology, Director, NSU COM Institute for Neuro-Immune Medicine, Nova Southeastern University.

Stephen L. Ondra, Chief Medical Officer and Senior Vice President, Health Care Service Corporation.

Frances E. Perez-Wilhite, North Carolina Military Business Center.

Martin Philbert, PhD, Professor and Dean, School of Public Health, University of Michigan.

Roberta F. White, PhD, Chair and Professor, Department of Environmental Health, Boston University School of Public Health; Scientific Director, Research Advisory Committee on Gulf War Veterans' Illnesses, Boston, Massachusetts.

Scott S. Young, MD, Executive Director and Senior Medical Director, Kaiser Permanente Care Management Institute.