Research Advisory Committee on Gulf War Veterans' Illnesses

October 25-26, 2004 Committee Meeting Minutes

U.S. Department of Veterans Affairs
811 Vermont Ave, Room 819
Washington, D.C.

DEPARTMENT of VETERANS AFFAIRS

Research Advisory Committee on Gulf War Veterans' Illnesses
VA Eastern Kansas Healthcare System (T-GW)
2200 S.W. Gage Blvd. Topeka, KS 66622

I hereby certify the following minutes as being an accurate record of what transpired at the October 25-26, 2004, meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses.

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/signed/
James H. Binns,
Chairman
Research Advisory Committee on Gulf War Veterans' Illnesses

Table of Contents

Attendance Record

Members of the Committee
James H. Binns, Chairman
Nicola Cherry
Beatrice Golomb
Joel Graves
Robert W. Haley
Marguerite Knox
William J. Meggs
Pierre J. Pellier
Steve Robinson
Steve Smithson
Lea Steele

Consultant to the Committee
Jack Melling

Committee Staff
Laura Palmer
Christine Rasmussen

Guest Speakers
Jack M. Heller
Warren J. Wortman
Jeff Kirkpatrick
MAJ Christine Moser
CAPT R. Eugene Godwin
David Cowan
Charles Engel
Stephen Fihn
Quentin Deming
William Weiss

Abbreviations

AChE	Acetylcholinesterase
ACR	Armored Cavalry Regiment
ALS	Amyotrophic Lateral Sclerosis
CCEP	Comprehensive Clinical Evaluation Program
CRADO	Chief Research and Development Officer (VA)
DESP	Deployment Environmental Surveillance Program
DoD	Department of Defense
GWI	Gulf War illness
LOI	Letter of Intent
OSAGWI	U.S. Department of Defense Office of the Special Assistant on Gulf War Illnesses
NASA	National Aeronautics and Space Administration
NOAA	National Oceanic and Atmospheric Administration
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
ORD	Office of Research and Development (VA)
RAC-GWVI	Research Advisory Committee on Gulf War Veterans' Illnesses
RFA	Request for Applications
UIC	Unit ID Code
USACHPPM	U.S. Army Center for Health Promotion and Preventive Medicine
VA	U.S. Department of Veterans Affairs

Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
U.S. Department of Veterans Affairs
Lafayette Building, 811 Vermont Ave. N.W. (Room 819) Washington, D.C.

Agenda
Monday, October 25, 2004

8:30-8:45	Welcome, introductions, opening remarks	Mr. Jim Binns
8:45-10:15	Environmental Monitoring in the 1991 Gulf War: Overview, troop location data, and estimates of exposure to oil well fire smoke	Dr. Jack Heller, Mr. Warren Wortman, Mr. Jeff Kirkpatrick, U.S. Army Center for Health Promotion and Preventive Medicine
10:15-10:30	Break	
10:30-11:15	Environmental Monitoring in Current Deployments	MAJ Christine Moser, U.S. Army Center for Health Promotion and Preventive Medicine
11:15-12:00	Fuel Exposures During the Gulf War	CAPT Eugene Godwin, Occupational Safety and Health Branch, U.S. Navy Medical Service Corps
12:00-1:00	Lunch	
1:00-1:45	Exposure to Smoke from Oil Well Fires and Other Combustion Products: Overview of Epidemiologic Findings	Dr. Lea Steele, Dr. Chris Rasmussen
1:45-3:00	Did Exposure to Oil Well Fire Smoke in the Gulf War Increase the Risk of Asthma Among Veterans? A Review of Three Recent Studies	Dr. David Cowan, Walter Reed Army Institute of Research
3:00-3:15	Break	
3:15-3:30	Identifying and Evaluating Treatments for Gulf War Veterans' Illnesses	Dr. Lea Steele
3:30-5:00	Clinical Outcomes at the Walter Reed Deployment Health Clinical Center	Dr. Charles Engel, Walter Reed Army Medical Center
5:00-5:30	Public Comment Period	
5:30	Adjourn for the day	

Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
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Agenda
Tuesday, October 26, 2004

8:30-9:30	VA Office of Research and Development Update on Gulf War Illness-related Research Activities	Dr. Stephan Fihn, VA Chief Research and Development Officer
9:30-10:00	Committee discussion	
10:00-10:15	Break	
10:15-12:00	Louisiana Medical Foundation's Clinical Trial of Antibacterial Treatment for Gulf War Illnesses	Dr. Quentin Deming, Mr. Bill Weiss
12:00-1:00	Lunch	
1:00-1:45	Update on Published Research Related to Gulf War Veterans' Illnesses	Dr. Beatrice Golomb
1:45-2:30	Committee Business	Staff
2:30-3:00	Public Comment Period	
3:00	Adjourn	

Welcome, introductions, and opening remarks

Mr. James H. Binns, Jr., Chairman

Chairman James Binns called the meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses (RAC-GWVI) to order at 8:30 a.m.

Chairman Binns announced that a date had been set for the public release of the Committee's report. He stated that there would be a press conference on Friday, November 12, 2004, at 3:00 p.m. at the Department of Veterans Affairs (VA) Central Office, Room 230. He noted that the release had been delayed twice due to scheduling conflicts, which would not allow all key players, notably Secretary Principi, to be present. As the report had not been released yet, he asked Committee members to refrain from discussing it either during or outside the meeting, and to refer any questions to Dr. Lea Steele, the Committee's Scientific Director.

Chairman Binns thanked Dr. Steele for organizing the meeting, and turned the proceedings over to her. Dr. Steele introduced the Committee's newest staff member, Dr. Christine Rasmussen. Dr. Rasmussen has a PhD in Physiology, with a background in neurophysiology and reproductive immunology.

Overview of the Assessment of U.S. Forces Exposure to Oil Well Fire Emissions in the Persian Gulf in 1991.

Dr. Jack Heller, PhD
Director, Health Risk Management Directorate
U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM)

Dr. Steele introduced Dr. Jack Heller.

Dr. Heller presented an overview of the assessment of U.S. forces exposure to oil well fire emissions in the Persian Gulf in 1991. (See Appendix A – Presentation 1.) He stated that their research unit entered the area in early May 1991, when 585 fires were burning. He noted that the maximum number of oil well fires burning at any one time was 605. He stated that the research-sampling units continued collecting samples until the fires were extinguished, with some sites having background data collected for an additional month. He stated that a total of 10 sampling sites were established, which were maintained for various durations of time.

Mr. Steve Robinson asked whether sampling had occurred within the smoke plume, outside the smoke plume, or both. Dr. Heller stated that the research-sampling stations were established where the troops were located. He stated that the objective was to characterize the plume only if it impacted U.S. forces. He noted that the troops' exposure varied because the smoke plume would change direction daily.

Mr. Robinson asked why the 11th Armored Cavalry Regiment (ACR) had been chosen as the research study group. Dr. Heller stated that the researchers were in Kuwait, waiting for an invitation to enter the theater, and had heard that the 11th ACR was the next group going into theater. He stated it was a random decision, and from a scientific standpoint, it seemed fortuitous that they were stationed at Camp Doha, which was one of the closest camps (about 15 km) from the oil well fires.

Mr. Joel Graves asked if any research had be conducted in the areas where the oil well smoke was the most concentrated, e.g. thickest and darkest. Dr. Heller stated that the National Oceanic and Atmospheric Administration (NOAA) and National Aeronautics and Space Administration (NASA) at Langley had conducted a number of flights through the plume, determining the concentrations of various pollutants at

various air levels. Mr. Jeff Kirkpatrick, speaking from the audience, said that they could provide the concentration data from the "grab" samples, but didn't recall whether a risk assessment had been performed.

Mr. Graves stated that he had been stationed at Kuwait City, an area where the smoke was quite thick. Mr. Graves stated, in early March 1991, it was so dark at 12 p.m. (noon) that a soldier was not able to read a paperback book in front of his or her face. He stated the oil permeated everything, e.g. food, clothes, etc. He stated it hadn't been possible to wash it out of the clothes. He noted that there were thousands of troops living in this "toxic fishbowl."

Dr. Heller stated that, unfortunately, sampling had not been possible at that time, as they had to wait for an invitation to enter the theater. He noted that they had modeled what the exposure might have been, but there weren't actual measured data.

Ms. Marguerite Knox asked if the research-sampling unit had been invited earlier into the current theater. Dr. Heller stated that they had been prepositioned with trained staff to do the monitoring. He stated that only nine oil well fires had been ignited in the current conflict.

Dr. Robert Haley asked if troops had been exposed to PCBs and dioxins from the oil well/transformer fires. Dr. Heller stated that they had found extremely low levels of these pollutants in their samples.

Dr. William Meggs asked for clarification about the time delay between the start of the 1991 oil well fires and the monitoring of these fires. Dr. Heller stated that the fires had been started at the end of February 1991. He stated that the research sampling units began monitoring on May 1, 1991. Dr. Meggs noted that seasonal changes might have varied the activity of the oil well fire smoke plumes. Dr. Heller agreed this was certainly possible.

Dr. Nicola Cherry noted that silica was a carcinogen, and was present in large quantities in this sandy region. She noted that, with tremendous heat, potentially more toxic forms of silica could be produced. Dr. Heller stated they had only looked at silica, which was generally found to be in particulate shapes that were weathered, with no sharp edges. Dr. Cherry asked if the silica had been heated. Dr. Heller stated that most of the fires were above the desert level, which limited the amount of silica/sand in the mix.

Chairman Binns asked if there were other exposures, from an industrial chemical point-of-view, which Dr. Heller might consider relevant. Dr. Heller stated that the collected samples and resulting analyses would have picked up all the components from industrial sources.

Chairman Binns asked about the progress of the Harvard study regarding the oil well fire effects on Kuwaiti and Saudi citizens. Dr. Heller stated that their unit had provided the researchers with the data, but were not involved in the project. He stated that he had not heard back from the researchers, so he wasn't sure of their progress.

Chairman Binns thanked Dr. Heller.

Troop Location Information and Database

Mr. Warren Wortman
Research Environmental Geographer, Kadix Systems
Deployment Data Archiving & Policy Integration, USACHPPM

Dr. Steele introduced Mr. Wortman.

Mr. Wortman gave an overview of USACHPPM's oil well fire registry database and website. (See Appendix A – Presentation 2.) Using troop location information, he stated that they were able to provide a veteran with information as to whether he or she had been exposed to oil well fires, and if so, a health risk assessment chart. The website is located at: https://usachppm.apgea.army.mil/gwf/entry.asp

Mr. Wortman explained that they had worked with the Department of Defense's Office of the Special Assistant on Gulf War Illnesses (OSAGWI) to come up with the best approach for determining UICs (Unit ID Codes) for each veteran. He stated that they had used the most conservative approaches, e.g. assumed that an individual was located in the area identified with their UIC the entire time. Discussion occurred as to which data sources were used and the limitations of this data.

Mr. Graves asked how many veterans were considered in the high cancer risk category. Mr. Wortman stated that none were in the "high" group, because oil well fires, alone, would not cause a dramatic increase in cancer risk. He noted that these determinations were based on both sampled and modeled data.

Ms. Knox asked if they had a better handle on where troops and individuals are located in the current conflict. Mr. Wortman stated they did, noting that they were receiving electronic data now and beginning to analyze it.

Dr. Steele asked about the promotion of the oil well fire registry website. Mr. Steve Smithson stated that an article about it had been in the October edition of the American Legion's magazine. He stated that they had received some feedback from veterans about wanting to correct their information. Mr. Wortman stated that was good because it helped improve the registry's information.

Exposure to Smoke from the Kuwait Oil Well Fires

Mr. Jeffrey Kirkpatrick
Acting Program Manager, Global Threat Assessment Program, USACHPPM

Dr. Steele introduced Mr. Kirkpatrick.

Mr. Kirkpatrick gave an overview of USACHPPM's dispersion modeling of U.S. troop exposure to oil well fires in early 1991. (See Appendix A – Presentation 3.)

Mr. Graves noted that the winds were from the East in February-March 1991, and that the exposure to oil was much worse during the rains. Mr. Kirkpatrick stated that precipitation had been a factor included in the exposure model.

Dr. Cherry inquired as to how the components of the crude oil were determined. Discussion occurred. Dr. Heller acknowledged that there might have been a few unknowns, but that they had looked for everything that was known to be present in the crude oil. He noted that they had performed mass spectrometry on the collected samples.

Dr. Steele asked whether the researchers had taken into account acute, high exposures experienced by certain troops. Mr. Kirkpatrick stated they would have to run a query through the database to identify these troops. He did note that they had seen the highest levels of contaminants from samples taken at the Ahamdi Hospital, which was 1 – 1 ½ km from the oil well fires.

Dr. Meggs commented that while studies of this sort have their place, they have no bearing on causation of illness in given individuals who are sick.

Chairman Binns thanked Mr. Kirkpatrick.

The meeting adjourned at 10:15 a.m. for a break.

The meeting reconvened at 10:30 p.m.

Environmental Monitoring in Current Deployments

MAJ Christine Moser, MPH, RS, DAAS
Program Manager, Deployment Environmental Surveillance, USACHPPM

Dr. Steele introduced Major Christine Moser.

Major Moser gave an overview of the environmental monitoring conducted by the Deployment Environmental Surveillance Program (DESP) for military deployments since 1996, including Iraq, Afghanistan, the Balkans, and Somalia. (See Appendix A – Presentation 4.)

She stated that samples were sent to either USACHPPM main analytic facilities at Aberdeen Proving Ground or USACHPPM Europe at Landstuhl, Germany. She stated that shortest turn-around time was 7 days, but was typically 14 days.

Dr. Cherry inquired about the technical guidelines issued for chemical exposures, and the amount of information contained within it. Major Moser stated that the guidelines contained a multitude of information, much more than a list of chemicals, and was consistently being revised when new data were available. She stated that the last revision was in January 2004.

Dr. Pellier inquired about the awareness of these guidelines within the chain of command. Major Moser stated that the environmental scientist within the unit was charged with knowing this information. The Commanding Officer was typically not aware of these standards, relying on their environmental staff for expertise in this arena. She noted that there were more environmental science officers/environmental engineers due to the Army's new structure for brigade combat teams. She stated that use of the environmental staff, however, depends on the operation, and the command and branch structure. If it is a smaller operation, the commanding officer may choose not to take environmental personnel out in the advance party. There was discussion about the differences in environmental surveillance among the various military branches.

Dr. Cherry asked how conservative the guidelines were. Dr. Heller stated that the guidelines were developed from civilian toxicity values and guidelines, but modified for specific military exposures.

Dr. Steele inquired as to the different environmental contaminants identified in Operation Iraq Freedom/Operation Enduring Freedom (OIF/OEF). Major Moser stated that there was high particulate matter, i.e. respirable matter such as sand, sulphur, sodium dichromate, etc., which was requiring constant

education about proper protection methods. She stated that they were able to measure 2.5 micron particulates, but have been looking mostly at 10 micron and larger.

Dr. Heller noted that their goal was to get this information quickly and make it available to VA for treatment of returning veterans. He noted that Department of Defense's (DoD's) operational risk management differed from EPA risk management.

Dr. Golomb noted that there was a theory known as "Al-Eskan disease", which centered on exposure to sand. She stated it had been theorized that sand particulates were small enough to make it into the alveoli of the lungs. She wondered if other environmental contaminants piggyback on the sand, and whether they were looking at this issue. Major Moser stated that they were, analyzing the filters for several different contaminants to make sure they weren't missing something. Mr. Kirkpatrick stated that, in 1991, a significant number of air and soil samples were sent for particle sizing/electron microscopy. He stated that the historical sample data showed minimal 2.5-micron particles, with most being in the 3-8 micron range. He stated that they were in the process of collecting additional samples, which would be sent to another lab, for particle size analysis for the current operation. He noted that all air filters were weighed before being sent to labs for analysis. It was also noted that bandanas would filter out the larger particles, but that it was not known how much protection would be provided for smaller sized particles.

Chairman Binns mentioned last year's DoD report on pesticides, which noted that 41,000 troops in the first Gulf War were overexposed to pesticides. He stated that he had been told informally that adjustments had been made in the amount of pesticide use during the current deployment. He asked if they would comment on this. Major Moser discussed the emerging Leishmaniasis problem, having over 700 troops being afflicted so far. She commented that adjustments resulting in a decrease of pesticide use would seem to hurt the troops because these troops weren't being adequately protected. She discussed the problems with making sure that the troops were protected from sand flies. Dr. Golomb noted that permethrin has been shown to cause, in animal studies, widespread brain and acetylcholinesterase inhibiting properties. Dr. Heller stated that they were tracking pesticide use in the current deployment.

Chairman Binns thanked Major Moser.

Summary of Potential Fuel Exposures During the Persian Gulf War: U.S. Navy & U.S. Marine Corps

CAPT R.E. Godwin, MSC, USN
Head, Occupational Safety and Health Branch, U.S. Navy Bureau of Medicine & Surgery

Dr. Steele introduced Captain Godwin.

Captain Godwin gave a summary of the U.S. Navy and Marine Corps potential fuel exposures during the Desert Shield/Desert Storm. (See Appendix A – Presentation 5.)

Mr. Smithson noted that there were reports, following the 1991 Gulf War, that tanker trucks were used for both fuel and water transport. He asked if they had investigated these reports, and if so, could Captain Godwin confirm or deny this occurrence. Captain Godwin stated he, personally, was unaware of this happening. He stated that while it was possible that it had occurred, the Navy and Marines were trained not to do something this "stupid." He stated that sampling, mainly for biological concerns, was conducted on water tankers. Dr. Golomb stated that such occurrence had happened stateside, noting a situation in which a tanker was used to carry fuel, followed by orange juice concentrate.

Mr. Smithson and Dr. Steele stated that they had heard numerous reports of this cross-contamination happening, but wanted to know if it had been confirmed. Major Moser did confirm that the Army had aggressively investigated this in the first Gulf War, and had found some local contractors who did do this. She stated that, once known, the contractors were no longer used. Mr. Ed Bryan, an audience member, stated that he had witnessed a similar situation in a military tank near Savannah, GA.

Chairman Binns asked if there any questions for the morning's speakers. Mr. Steve Robinson asked if the Committee might be able to request USACHPPM to model the maximum exposure to oil well fire, over a particular time period, e.g. eight-day period, to assess the potential risks of exposures reported by Gulf War veterans in and around oil well fires. Chairman Binns asked how difficult/easy this type of modeling would be. Mr. Kirkpatrick stated that they had a partial answer from sample data for the Ahmadi hospital, but would need to do additional assessments.

Mr. Graves noted that none of the data presented that morning showed anything like what the troops were exposed to while living in the plume for a week. Dr. Heller acknowledged that this was model data, and noted that there had been plume transits/inversions. Mr. Graves suggested that a plume re-creation study be conducted in an isolated area, with sampling equipment directly within the plume. Dr. Golomb suggested taking a subset of veterans who experienced heavy oil well fire smoke and evaluate their health outcomes.

Chairman Binns asked when the British and French environmental monitors were able to begin sampling in the first Gulf War. Mr. Kirkpatrick stated it was March 1991, and that this data was in the Arabian Gulf Report.

Dr. Christine Rasmussen asked if they had estimated how many soldiers were heavily exposed to these oil well fires. Mr. Graves stated that in the area he served, it would be the 1st Tiger Brigade, and 1st and 2nd Marine Divisions. This was estimated to be about 10,000-20,000 troops.

Chairman Binns thanked the morning speakers again. He stated that the Committee had often wondered what was taking place, in the category of "lessons learned." He stated it was impressive that there had been changes, and was appreciative of those trying to make sure whatever had happened in the first Gulf War didn't happen again. He noted that there was a public comment period at the end of the afternoon session, and asked attendees to sign up.

The meeting adjourned at 11:45 p.m. for lunch.

The meeting reconvened at 1:00 p.m.

Health Outcomes in Relation to Petroleum Combustion Exposures During the Gulf War

Dr. Lea Steele, PhD, Scientific Director, RAC-GWVI
Dr. Christine Rasmussen, PhD, Research Health Scientist, RAC-GWVI

Dr. Steele and Dr. Rasmussen presented a summary of the general health effects of components of oil well smoke and jet fuel, along with epidemiologic findings in Gulf War veterans relating to exposure to oil well fires and tent heaters. (See Appendix A - Presentation 6.) Dr. Cherry noted that all UK troops were exposed on some level to oil well fires, as they had to drive through the affected area when they left theater. She noted, however, that her study had found no significant correlations of symptoms with these shorter-term exposures in adjusted analyses.

Dr. Haley noted that it was hard to determine the magnitude of associations with exposures in the Iowa study, since they had only reported prevalence differences. Dr. Heller noted that Dr. Etzell had done a study on oil well firefighters. He stated occupational health records had been kept on these firefighters.

Dr. Haley commented that some of the reported studies may have controlled for factors that shouldn't have been controlled for, which might have wiped out some significant findings. He stated that it was important to put estimates of relative risk for different exposures of concern into context, to determine the range of risks found to be associated with different types of exposures. Dr. Steele agreed and stated this would be addressed in summary fashion, at a future meeting, to allow a more informed analysis of the relative importance of different possible contributors to GWI.

Did Exposure to Oil Well Fire Smoke During the Gulf War Increase the Risk of Asthma among Veterans? A Review of Three Studies

Dr. David N. Cowan, PhD, MPH
Division of Preventative Medicine, Walter Reed Army Institute of Research
EPICON Associates, L.L.C.

Dr. Steele introduced Dr. Cowan.

Dr Cowan presented a review and comparison of three epidemiological studies that examined the risk of asthma among Gulf War veterans exposed to oil well fire smoke. (See Appendix A – Presentation 7.)

With respect to Table 3, Dr. Cowan made the following speculations as to why there did not appear to be a significant association between oil fire smoke and asthma among veterans who were smokers:

a) Healthy smoker effect: The oil well fires didn't affect those individuals who weren't affected by cigarette smoking either. Those individuals who were highly sensitive to cigarette smoke became non-smokers and were then similar to never-smokers;
b) No additional response available: Current smokers simply had reached an overload, and no further response was possible; and
c) Clinician diagnostic bias: If a smoker came in with a cough, the clinician makes the diagnosis of "smoker's cough" rather than asthma.

Dr. Cherry inquired if smokers had been categorized by the duration that they had smoked. Dr. Cowan indicated this hadn't been done.

Dr. Steele noted that the possibility of error might be less in Dr. Cowan's study than in the other two he described, and that his study had found a possible dose-response effect – higher modeled exposure was

associated with a higher rate of respiratory illness. She noted that Dr. Cowan's study also had sources of error that would have probably caused his estimates of increased risk to be "watered down." She stated that, if researchers were able to prepare a better model for exposure and acquire better diagnoses, the odds ratio would likely have been even higher. Dr. Cowan agreed.

Dr. Haley and Dr. Cowan discussed the control issues surrounding the three studies. Dr. Haley stated that Dr. Cowan's study had the "right" controls, and agreed about the possible misclassification errors with the other two studies.

Dr. Pellier complimented Dr. Cowan on his presentation. Dr. Pellier noted that there were studies that showed an association between respiratory and some acute digestive symptoms. He asked if Dr. Cowan had considered analyzing digestive symptoms, e.g. chronic diarrhea, in his own study. Dr. Cowan stated that the original database was still in existence, so, while it would take some effort, it was possible to do.

In response to a question from Dr. Cherry, Dr. Cowan indicated that retrieval of DOD's Comprehensive Clinical Evaluation Program (CCEP) paper files would be necessary to address the issue as to whether these were new onset asthma cases or exacerbation of a pre-existing condition. He indicated this would be time and resource intensive. He noted that asthma was an exclusion determinate for the military, but acknowledged that some may lie about their condition. He was not sure if asthma would preclude deployment.

Dr. Steele commented that Dr. Cowan's study may be the only study with a specific physician-diagnosed condition shown to be significantly elevated in association with a specific Gulf War exposure. She stated that this may have long-range implications in terms of disability benefits.

Dr. Cherry speculated that many veterans with asthma may not have participated in the CCEP. If those who did come forward were more likely to be the subpopulation whose asthma got worse after going to the Gulf, it would be difficult to determine from study data whether oil fire exposure was associated with new cases of asthma or exacerbation of pre-existing conditions. Dr. Cherry noted that her group had done a study, which wasn't published yet, of young adolescent males who, at age 5-6 years old, had been exposed in the Gulf War oil well fires. She stated that they had found no increase in new onset cases, but had seen a worsened condition in those with pre-existing asthma.

Dr. Haley noted there was a second mortality analysis performed which looked, over a period of several years, at the relative risk in deployed versus non-deployed mortality rates from different conditions. He had reviewed this data, and had noted that there was a significant increase in respiratory fatalities one year after the first Gulf War. He stated that, after this period of time, the respiratory fatalities decreased. He stated that he had always wondered if this had been an acute exacerbation of asthma.

Dr. Cowen noted that asthma was the one of the leading causes of evacuation during the 1991 Gulf War.

Dr. Cherry noted it would be interesting to determine if the individual was experiencing allergic or irritant asthma.

Mr. Robinson asked what weight had been given to the differences in asthma rates in theater vs. the general stateside population. Dr. Cowan noted that the general air quality in the Gulf region was terrible, e.g. sand, wood/manure fires, industrial fumes, etc.

Dr. Steele asked whether Dr. Cowan had looked at any other self-reported exposures in conjunction with asthma. Dr. Cowan stated that they had looked at tent heaters. He stated there was a significant

association, but didn't remember the magnitude. When asked about controlling for the effects of oil well fire smoke, Dr. Cowan stated that this was an observation made while doing steps in other analyses.

Chairman Binns asked whether the prevalence of asthma in deployed Gulf War veterans could be determined. Dr. Steele stated that rough estimates, from epidemiologic studies, showed 4-5% of deployed veterans had asthma compared with 1-2% non-deployed veterans. She stated that the asthma rate might be twice as high (8-10%) among deployed veterans exposed to oil well fire smoke.

Chairman Binns thanked Dr. Cowan.

The meeting adjourned at 2:50 p.m. for a break.

The meeting reconvened at 3:12 p.m.

Research on Treatments for Gulf War Veterans' Illnesses: Background and Context

Dr. Lea Steele, PhD
Scientific Director, RAC-GWVI

Dr. Steele gave an overview, including background and context, of research on treatments for Gulf War veterans' illnesses and the many challenges involved in this area of study. (See Appendix A – Presentation 8.)

Dr. Pellier commented that the antibiotic trial study was difficult to interpret because SF36 findings are composed of multiple elements, which are averaged. He noted that these findings, for an individual patient, needed to be carefully interpreted.

Dr. Steele reported that Chairman Binns and she had attended a seminar on a detoxification therapy for rescue workers at Ground Zero in Manhattan. This treatment had also been used for about 6 ill Gulf War veterans, 3 of which had been reported on at an earlier conference by Dr. David Root. She indicated that they had asked Dr. Root and the sponsors of the treatment clinic to provide systematically-collected data on outcomes seen in their patients that could allow a clearer evaluation of the potential effectiveness of the treatment. Mr. Robinson stated that he had learned about a similar program in the Odessa, TX, area. He stated that several veterans were reporting benefits, but that long-term implications following detoxification were unknown.

Dr. Golomb stated that, when asked several years ago, veterans were not reporting success with any of the known treatments. While there are still many questions, she stated that this type of treatment should be closely evaluated.

"In Return for Their Sacrifice" – Conceptional Basis & Clinical Outcomes of the Specialized Care Program at DoD Deployment Health Center

LTC Charles Engel, Jr., MD, MPH
Director, Deployment Health Clinical Center, Walter Reed Army Hospital

Dr. Engel gave an overview of the approaches used to treat veterans at DOD's deployment health centers, along with their findings relating to these treatments. (See Appendix A – Presentation 9.)

Following the presentation, Dr. Meggs noted that as a clinician one sees people disabled by disease, while other are not. He stated the question then arises as to when a condition becomes disabling. He asked Dr. Engel about his thoughts on this. Dr. Engel stated that their efforts were focused on taking those treatments that could have meaningful impact on the veteran's capacity to function, and making sure the patient was ready for a meaningful change.

Dr. Golomb asked about the deployment health center's staff attitude about Gulf War illnesses. Dr. Engel stated that there was a process of change with the model he had described. He stated some staff found the new model refreshing, while others, while well meaning, didn't agree with the approach. Dr. Golomb stated that she believed the model was good to a certain extent, but thought some effort should be directed toward finding treatments for the actual physical ailments. Dr. Engel thought this was an important policy question, but as a clinician, his efforts are directed towards helping his patients focus on their individual health situation.

Dr. Pellier asked as to the percentage of patients who were identified with anxiety disorders upon entry into the program. Dr. Engel acknowledged there were high rates of co-existing mental illness, e.g. depression. Dr. Pellier asked, as a result of this diagnosis, whether these patients received anti-depressant treatment. Dr. Engel stated this was part of the program.

Dr. Steele noted that, while there may sometimes not be an impressive increase of mean scores in a clinical trial, there may be a particular subset of individuals that shows an impressive increase in function. She noted the data relating to differences in improvement based upon gender. Dr. Engel agreed, and stated that further study was needed with larger sample sizes to identify these subsets. Dr. Steele asked whether patients with concurrent psychiatric diagnosis benefited more from the program. Dr. Engel stated that these individuals were in a relatively good prognosis group, but this was all on a relative spectrum.

Mr. Robinson stated that, for most Gulf War veterans, the Walter Reed deployment health center was one of the first places they've gone where they weren't attacked for their concerns, and received an active response to these concerns. He stated that this acknowledgement, along with learning the center's coping skills and three-month follow-up, was meaningful and helpful to these veterans. However, he noted that the veterans still remained ill, waiting for science to catch up. He stated that he supported what Dr. Engel was doing, and while it may not answer why the veterans were ill, it did provide them benefits. Dr. Steele agreed, and stated she had heard positive testimonials from veterans treated in this program. She noted the differences between VA's WRIISC centers' and DOD's deployment health center's approaches.

Ms. Marguerite Knox asked whether a patient suffering from Amyotrophic Lateral Sclerosis (ALS) had gone through their program, and whether he would advocate they do so. Dr. Engel stated there were limits to what this program could do. He noted that one service member did have a progressive neurological disease, but this condition had not yet been identified when he went through the program. Ms. Knox stated that there existed a problem in medicine today in acknowledging certain illnesses may be undiagnosed. She stated that she embraced this program's model because mind and body are connected. Thus, the emotional state of an ALS patient should be addressed just as his or her physical state. She noted that, while mental and physical illnesses are connected, these processes were also distinct.

Dr. Golomb stated there was a distinction between the idea of "mind" and the physiology of nervous system function. She stated that the original problem wasn't that Gulf War illness wasn't embraced as an illness, but that it was maligned and denounced. Dr. Engel noted that this reaction was not any different than reactions to chronic fatigue syndrome, fibromyalgia or low back pain.

Dr. Melling stated that he saw parallels with his own work from the late 1970s and early 1980s involving vocal spasmodic dystonia. He stated that patient improvement was seen when their illness was recognized. He noted that the value of Dr. Engel's program's acknowledgment of the veterans' illnesses might explain the modest improvements in patient health. Dr. Engel acknowledged that hope was instilled through the program.

Mr. Smithson asked how many of the veterans seen were Gulf War veterans. Dr. Engel stated that, out of the first 600 veterans, there had been approximately 400 Gulf War veterans. He stated that 1/3 of the veterans being seen currently were Gulf War veterans.

Dr. Haley noted that there were many practitioners who made dramatic claims about cures/recoveries, and many veterans were going to these alternative care providers making these claims. He asked for Dr. Engel's thoughts on this phenomenon. Dr. Engel stated that many individuals love to capitalize on desperation. He noted that individuals might not be able to ask hard questions when in this situation, making them vulnerable. He stated that it was the center's obligation to evaluate therapies in controlled clinical trials, even when they might not think they will work. He stated that the veterans needed to know the answers about various treatments, whether it was positive or negative. Dr. Pellier commented that there were several clinical trials being conducted on drugs for other conditions that were based on very little, if any, pathophysiological rationale.

Chairman Binns thanked Dr. Engel.

Public Comment – Day 1

Chairman Binns opened the floor to public comment.

Mr. Edward Bryan spoke to the Committee. He also provided the Committee with a two-page written comment. (See Appendix B - Public Submission 1.) He stated his belief that there were more oil well fires, i.e. 850, than noted by the morning's speakers. He stated that the Committee should consider the "batch effect", i.e., dispersion of smoke over the enemy ground, and the "chimney effect", i.e. the dispersion of smoke into the air. He stated that he hoped the Committee's charter might be modified to better help veterans for years to come. He mentioned his treatment at Walter Reed, and indicated that it had helped to a certain extent. He noted that he still needed treatment, and that the Walter Reed program needed a more in-depth neurological component to its program.

Ms. Alison Johnson spoke to the Committee. She commented that it was interesting that 25% of veterans who left theater in March 1991 had GWI, while 31% of those who left in April-May 1991 were classified with GWI. She suggested that pyridostigmine bromide (PB) pills and pesticides helped to induce multiple chemical sensitivity (MCS) in ill veterans. She suggested that those ill veterans who were then exposed to oil well fires were more sensitive. She also suggested that long-term antibiotic use might increase veterans' problems.

Ms. Denise Nichols spoke to the Committee. She thanked the Committee for its work. She asked that the Committee bring in primary field sources, i.e. field experts, to come and speak at the meetings. She stated her belief that their reports had been changed. She noted that few ill veterans were part of ongoing treatment trials. She stated that more veterans needed more MRI exams. She stated that the veterans wanted to see if there was a problem, and noted this acknowledgement could also be therapeutic. She encouraged more research into immune system problems, mentioning Dr. Vojdani's work in this area. She stated that more work needed to be done to get "hard" diagnostics or markers, while waiting for

treatments. She stated this would at least show progress being made directly on the lives of ill Gulf War veterans. She concluded with a story about an ill veteran, confined to an electric wheelchair, who was diagnosed as suffering from a psychosomatic disorder.

The meeting adjourned for the day at 5:33 p.m.

The meeting reconvened the following day, October 26, 2004, at 8:30 a.m.

Office of Research And Development – Gulf War Update

Dr. Stephen Fihn, MD, MPH
Acting Chief Research & Development Officer (CRADO)
U.S. Department of Veterans Affairs

Chairman Binns introduced Dr. Fihn.

Dr. Fihn presented an overview of research funding provided as a result of VA's 2004 Gulf War illnesses Request for Applications (RFA). (See Appendix A – Presentation 10)

Dr. Steele inquired if it would be possible to have more details about the individual funded studies. Dr. Fihn stated that study abstracts could be provided.

Mr. Robinson asked how many treatment trial proposals had been submitted in response to the last RFA. He noted that the one treatment study that had been funded was one that the Committee had heard about at its June meeting, and that he was surprised it had been funded. Dr. Fihn stated that he would find out the answer to this question.

Dr. Golomb noted the obstacle of requiring principal investigators (PIs) to be employed by the VA in a "5/8th"or greater position. She asked for Dr. Fihn's thoughts about liberalizing this policy. Dr. Fihn stated that the VA's research was an intramural program, and very small compared to the National Institutes of Health research program (385 million vs. 30 billion). He stated that the primary purpose of VA's research program was to conduct meritorious research, while retaining and supporting VA physicians and researchers. He indicated that ORD was reluctant to change this policy, and was reluctant to grant waivers to this requirement.

Mr. Roger Kaplan, Special Assistant to the CRADO, stated that the Office of Management and Budget (OMB) had indicated, several years earlier, that relaxation of this policy would result in elimination of VA research appropriations.

Dr. Golomb noted that GWI funding was almost exclusively within the VA now, and this limited having all of the "best minds" working on these issues. Dr. Fihn disagreed, noting that there were thousands of non-VA researchers collaborating as co-investigators in VA studies. He noted that there was no requirement that the research be performed at VA facilities.

Dr Melling asked whether it was possible to make it a condition that VA researchers use outside co-investigators. He noted this would help broaden the VA's scientific capabilities. Dr. Fihn stated that the Merit Review Panels did look at the investigative team and evaluated it as a whole. He stated that joint solicitations had been tried, but that bureaucratic problems between the organizations had arisen. He stated a combined RFA with the Agency for Healthcare Research and Quality for the last two years had not resulted in a single proposal. He did stress that the current process gives higher scores to highly

qualified research teams. He stated that there was broad collaboration between VA and non-VA researchers, noting that VA investigators, in collaboration with universities, had received over 700 million dollars in NIH funding.

Dr. Meggs asked if there was a requirement that the PI spend more time on the project than the non-VA co-investigator. Dr. Fihn stated that the PI needed to be legitimate, i.e., couldn't be a shadow PI. He stated that the PI needed to be active, but that the co-investigator could be equally active. Dr. Meggs stated that, about three or four years earlier, several researchers wanted to get involved in GWI research. He stated that NIH had directed them to the VA, but that VA had not provided help in directing these investigators to an appropriate VA PI. He noted that this continued to be a hurdle to getting all the best minds together on this problem. Dr. Fihn stated he understood this criticism, but noted that 50 merit proposals had been submitted from within VA on the latest RFA. He stated this indicated interest within VA to conduct this type of research.

Dr. Golomb noted that this was a unique opportunity to study a unique group (Gulf War veterans) with implications well beyond this group. She commented that it was different phenomena than more-straight forward conditions, without many opportunities for outside researchers to get involved. She stated it was a pity to see administrative considerations superseding the veterans' interests. She noted that even Dr. Paul Greengard had found the process difficult, and if they had known how difficult it would be, they might not have pursued their submission. Discussion followed concerning NIH funding vs. VA "Five-eighth's" requirement for funding Gulf War illness research.

Dr. Haley stated that, while the Committee understood the realities for VA, it was passionate about the fact that GWI was a real problem, and needed to be addressed. He noted that this area of study had been an emotional "rollercoaster ride" for the past ten years. He noted that the Committee had produced an interim report two years ago, which received a firm commitment by VA to fund 20 million dollars in the FY2004 budget for Gulf War veterans' illnesses research. He expressed his disappointment at seeing 8 million dollars of FY2004 funding going to a combination of deployment and GWI research. He stated that the funding announcement had been very firm and very clear, but it seemed that the stress theory was still holding out in the VA bureaucracy. He stated this bureaucracy seemed to be derailing the money towards other research concerns.

Dr. Fihn stated that he was disappointed to hear Dr. Haley say this. He stated that the Secretary had kept to his commitments, and that VA was the only agency demonstrating commitment in this area of research. He stated that the Secretary also had a strong commitment to the veterans returning from the current deployment. He also noted that ORD could only fund what proposals are being submitted by its scientists. He stated that ORD was passive, i.e., did not dictate, when it came to proposal content. He stated that ORD defined areas of research, but didn't dictate further than that. He stated that the submitted proposals did have to pass scientific peer review, with an eye towards creating a good mix. He acknowledged that one could argue that the peer review committees might not have done their job appropriately. He stated this was always a problem with peer review. He stated that sometimes the committees may be too specialized or narrow, and may miss new ideas and approaches, while other committees may be too broad and lack the expertise to judge highly technical and focused projects. He stated that he didn't understand how VA bureaucracy had interfered with this process, noting that no money had been held back, funding those studies received.

Dr. Melling commented that, from his experience, it was hard to get people to break out of established patterns unless someone steps in and gives guidance. Dr. Fihn stated that was the plan with the new RFA.

Dr. Fihn noted that the stress research would benefit veterans of the current deployment. Dr. Haley acknowledged that this was true and that PTSD would be a problem for those returning now, but stated that Gulf War I veterans have a unique problem that had never been adequately studied, and that this problem was only going to be addressed by VA. Dr Fihn stated he was not able to answer all these concerns fully because he couldn't speak as to FY2005 plans at the time.

Dr. Cherry expressed concern that there had been only one treatment proposal. She asked Dr. Fihn if this was because: (1) there was no hope for any treatment; or (2) "intellectual poverty" in this area existed among those qualified to submit proposals at VA. Dr. Fihn responded that it was a difficult area of study, because there were no great treatment candidates at this time and there were inherent difficulties, such as identifying the affected population needing treatment.

Chairman Binns encouraged other Committee members to express their thoughts.

Mr. Robinson stated that veterans were frustrated, and were tired of seeing some of the research being funded as GWI research, e.g. telemedicine. He stated his hope that the establishment of the merit review panel, with outside experts, would help fix this problem. He stated that there had been a historical barrier to the types of treatment trials or research being done. He noted that these individuals weren't "bad" people, but that there had been barriers that had thwarted good science. He stated that the Committee was making recommendations about the positive way forward, and didn't want to see backward steps in this process. He expressed his hope that there would be the opportunity to have individuals, identified by the Committee, on the merit review panel. Dr. Fihn stated that ORD would take the Committee's recommendations seriously, but the ultimate decision as to who sat on the panel would be made by ORD.

Chairman Binns offered his perspective on the history of the most recent (March 2004) RFA for GWI research. He stated that the former acting CRADO, Dr. Mindy Aisen, had spent a tremendous amount of time, in weekly ORD phone conversations to the VA research community, encouraging participation in this area of study. He stated that, at the letter of intent stage, there was an intention to review the proposals for relevancy to Gulf War illnesses and the RFA. He noted that there had been a suggestion that the Committee could serve in this capacity in an advisory capacity. He stated that legal issues arose, so no relevance review occurred at the time. He stated that the ultimate goal was to have a quality merit-review board with outside and government experts. However, due to time and regulation considerations, he stated that it was not possible to involve non-governmental employees in that particular review process. He acknowledged that ORD had been responsive to the Committee's suggestions regarding reviewers, but that many of the Committee's top picks were not able to serve on this particular review panel. He expressed a hope that: (1) future RFAs could be more specific; (2) proposals would be subject to a relevancy review process; and (3) the merit review panel would have more experts in the area of GWI research. He stated his impression that Dr. Fihn had judged the submitted proposals "by-the-numbers". He expressed his hope that these procedures would be improved to get better research outcomes.

Dr. Golomb made the point that there needed to be an effort to enhance the number of relevant proposals. She noted that the only GWI training for VA researchers had been several years earlier, and had focused on stress being the cause. In light of this direction by top VA officials, she commented it wasn't surprising that the majority of proposals submitted and funded through the March 2004 RFA were based upon the stress hypothesis. She stated that there was need to change the training of the merit review panel, along with a push to reeducate the VA research community as to the avenues that needed to be pursued in this research area. She also suggested that the Committee revisit the issue of encouraging alternative bodies, e.g. NIH, to open up to investigations related these areas.

Dr. Fihn stated that ORD had recently eliminated letters of intent (LOI) from the proposal process. He stated that these were viewed as an obstacle and red tape to investigators, so only notification of intent was being required. Mr. Kaplan stated that LOIs had been intended for notification, not as a form of triage. Discussion followed about issues related to the March 2004 RFA process.

Dr. Cherry asked whether the 2005 review panel would include non-governmental experts. Dr. Fihn stated that it would, using a standard of high-level scientific merit. Dr. Cherry asked if the Committee would be able to make recommendations as to non-government panelists. Dr. Fihn stated that they were interested in the Committee's advice, but that ORD would remain the ultimate decision-maker as to who is selected for the panel. He noted that scientific organizations needed to jealously guard the independence of its scientific review process.

Mr. Robinson stated that the Committee's recommendations should be part of the ORD process, and if ORD ignored these recommendations, it would be an equal injustice. Dr. Fihn expressed his belief and hopes to have a good working relationship with the Committee. Mr. Robinson asked that ORD not "guard the Committee out of the research" being conducted in this area. He acknowledged Dr. Fihn's need to protect the scientific process, but noted that the Committee was formed to make recommendations that would ultimately translate into treatments and research.

Mr. Graves stated that the Committee had recommended several times that stress research, like that proposed by the East Orange War-Related Injury and Illness Study Center (WRIISC), not be funded as GWI research. He expressed his disappointment as to the funding of some of the proposals under the March 2004 RFA. He stated that he was getting the feeling that ORD was not a real advocate of the Committee's concerns, and was trying to downplay the importance of its purpose and recommendations. He stated that ORD seemed to be focused on deployment health of the returning veterans, while older issues were relegated to a lower priority level. He stated his concern that ORD seemed ready to use money dedicated to GWI for deployment health research for the current conflict.

Dr. Fihn stated that he was sorry if he had conveyed this impression. He stated that he was simply trying to describe processes that he hadn't authored. He stated that he didn't think that the Committee recommendations had been dismissed. He acknowledged that some of the funded proposals did not fit with the scientific agenda set forward by the Committee, but noted that they were good and high-quality studies.

Ms. Knox commented that the Committee was emotional and passionate about this issue, and was disheartened because ORD wasn't "putting its money where its mouth was." She stated that the VA was combining deployment health issues with GWI, and even then, was not looking at two major problems of the current deployment, i.e. traumatic injury and leishmaniasis. Dr. Fihn stated that there were separate RFAs for traumatic amputation research. Ms. Knox expressed her disappointment that this wasn't the same for GWI. She stated that, while projects may have been good scientifically, much GWI funding had been wasted because it wasn't looking at treatment for GWI. She likened it to "sending your husband for a loaf of bread, and he brings back a gallon of milk." She emphasized that it had been fourteen years, and GW veterans still had not received needed treatments.

Dr. Fihn expressed his hope that, in the coming weeks, she would feel better about this conversation. He stated he was unable to discuss ORD's FY2005 plans at this time, but he believed the Committee would see constructive movement in this area. He noted that ORD did have a fiduciary duty to the research and legal processes. He acknowledged that there were areas of potential disagreement, e.g. the 5/8th requirement for PIs, but hoped that ORD's interactions with the Committee had been positive.

Mr. Graves stated that his impression wasn't based solely on the 5/8th requirement. He stated that his impression was based upon ORD's overall approach and attitude that GWI was not an important issue any more. He expressed his disappointment that other concerns were derailing important research. Dr. Fihn expressed his opposite view of the situation. He noted that this area of research was one of the largest funded areas in the VA's research portfolio, alongside cancer research. He acknowledged that VA was treating many veterans who had served in various conflicts, some recently and others not so recently. He expressed his commitment to the care and service of veterans, noting he had been a practicing VA physician and researcher since 1982.

Dr. Golomb explained that the Committee's impression of ORD's indifference to GWI research was due to ORD's focus on: (1) other deployments; and (2) legal requirements.

Chairman Binns stated that he understood, from a legal point view, that Dr. Fihn couldn't promise all Committee recommendations would be heeded. He noted, however, that during the last RFA process, ORD did seek out every qualified reviewer recommended by the Committee. He expressed concern about eliminating LOIs, noting that there needed to be a process to help shape the research being sought. In conclusion, he expressed his belief that Dr. Fihn had gone a long way in implementing some of the Committee's specific requests.

Chairman Binns thanked Dr. Fihn.

The meeting adjourned for a break at 10:05 a.m.

The meeting reconvened at 10:28 a.m.

Dr. Steele reported that the VA had been able to work out a new contract for the AChE-R research by Dr. Concanto and Dr. Soreq. She stated that lab and statistical analyzes should be available by the time of the Committee's next meeting.

Successful Antibiotic Treatment of the Gulf War Syndrome: A Pilot, Randomized, Placebo Controlled, Blinded Trial - Successful Trial of Urine Microscopy for Control of Antibiotic Treatment of Systemic Coccal Disease

Dr. Quentin B. Deming, MD, Professor Emeritus, Albert Einstein College of Medicine
Mr. William Weiss, retired Chief of the Office of Biometry and Field Studies, National Institute of Neurological Disorders and Stroke, National Institutes of Health

Dr. Steele introduced Dr. Deming and Mr. Weiss. She noted that the third investigator on this study, Dr. Edward S. Hyman, MD, FACP, had passed away in the spring of 2004. She stated that a collaborator on the study, Dr. Lauren Krupp would not be presenting at the meeting, but had conveyed to her a favorable impression of the results of this study.

Dr. Deming and Mr. Weiss gave an overview of their clinical trial of antibiotic treatment for ill Gulf War veterans. (See Appendix A – Presentation 11.) Dr. Deming noted that this study was distinct from large clinical trials, such as the one reported on by Dr. Sam Donta at the Committee's February 2004 meeting. He stated that this was a trial that tested a method, rather than a particular drug or dose. He provided background to the investigators' relationships, the evolution and methodology of this particular study, and Dr. Hyman's approach to treatment. He stated that the study was designed as a "black box" study, in which different individuals had received somewhat different administrations of the treatments used,

according to results of their specific tests and their responses to therapy. Mr. Weiss explained the study's design and results. Discussion followed about the results of the study.

Dr. Golomb asked if any of the patients had suspected that they were being treated based upon adverse effects at the time. Dr. Deming stated that none of the patients had made assumptions like this, but that the evaluator had made the wrong assumption in two instances because the patient had diarrhea. He noted that there was a blinded nurse who evaluated each patient for adverse effects. He stated that two effects had been noted, but were not considered significant. The two effects were: (1) a significant increase in the creatine phosphokinase (CPK) level of one patient, which was determined to be due to the patient's starting an intense exercise regimen once he started feeling better; and (2) 10 Jarisch-Herxheimer reactions. These reactions are the body's response to an overrapid destruction of pathogens, leading to a faster release of immunologically active products than the body can handle. Dr. Deming stated that these reactions were considered a therapeutic reaction, and that Dr. Hyman's response to these symptoms was to slow the antibiotic infusion rate in the patient, along with the infusion rate of a placebo patient. He acknowledged that Dr. Hyman would immediately treat the patients for reported problems, e.g. candida, gastrointestinal problems, and thus might have eliminated other adverse effects.

Dr. Deming stated that they had treated the placebo patients with active therapy following the initial study, and thus the second part of the study constituted an open trial.

Dr. Golomb asked whether there had been follow-up work done with the patients. Dr. Deming stated that an attempt had been made to contact patients in 2000, and that 22 out of the 38 patients (60%) had been contacted. He stated that: (1) 8 patients felt perfectly well; (2) 4 patients were as bad as before the treatment; and (3) the other 10 had various levels of relapse but still felt better than before the trial. He stated that all of the urine samples at the end of IV treatment showed reduced bacterial counts.

Dr. Cherry asked for clarification about the circumstances or requirements for the discharge of a patient, i.e., when the patient felt better or when their urine was "clear." Dr. Deming stated that both were needed in adjusting therapy. He stated that Dr. Hyman's approach was guided by the urine results, but not exclusively so. He noted that a placebo patient was released at the same time as a treatment patient. He stated that neither patient (treated or placebo) was told the reason behind the discharge, just simply that the treatment period was over. Dr. Cherry expressed concern about using the patient's symptomatic declarations as a basis of discharge. Dr. Deming acknowledged this, but stated that none of the patients were discharged simply based upon personal declarations.

Dr. Golomb stated that she would agree that there could be a short-term response to the antibiotic treatment. She stated, however, that she was also disposed to believe that this would be the case in the general population. She stated she would be interested in the long-term effects after discontinuation of the antibiotics. Dr. Deming stated that, from their observations, continual treatment is necessary in some patients. He stated that the treatment formula was complicated, but that Dr. Hyman had been able to simplify it and develop a starting treatment package by the end of the study. Discussion occurred about the various antibiotics and dosages used in the study's treatment package.

Dr. Meggs asked about the study's published work. Dr. Deming stated that articles related to the methodology used in the study had been published, but not the treatment trial itself. Dr. Meggs asked if Dr. Deming could hypothesize how the cocci remnants were able to move from the blood to the urine. Dr. Deming stated that he couldn't say how it was transferred, but could give an example of a similar transfer. He referred to the work of a German physician named Kraus who published his candida research in the Lancet (1969). He stated that Dr. Kraus showed that, following ingestion of candida, it was found within an hour in both the blood and urine. He noted that the diameter of candida was three times bigger than

most bacteria. Dr. Meggs noted that it could have penetrated the tissues. Dr. Deming noted that tubercle bacilli appear in the urine of tuberculosis patients when the patient doesn't have tuberculosis in the kidney.

Dr. Deming stated that this study shows: (1) bacteria do play a role in the pathogenesis of this disease; and (2) it is possible to suppress these bacteria and effect a change in symptoms. He acknowledged that they hadn't: (1) shown where the infection was located or what the specific bacterium was; or (2) proven that the bacteria seen were causing the disease. He stated that not all the sediment cocci looked the same.

Dr. Deming stated that this study provided evidence that an antibiotic-responsive bacterium was related at some stage to the genesis of this disease. For corroboration, he noted: (1) Dr. Steele's study, which he stated showed a temporal and geographic focus of the high-incidence of this disease, characteristic of an infectious disease epidemic; and (2) that it was common for family members to be affected. He stated that it was hard to blame a toxic exposure when it appears to be transferred. He noted that the toxic exposure may have made the individual more vulnerable to infection.

Dr. Haley asked which paper provided the definitive bacteriologic method needed to continue this research. Dr. Deming stated that the method was in the Stain Tech paper and wasn't difficult to perform. He explained the technique.

Dr. Steele asked if the research could be done by following patient symptoms, rather than urine sampling. Dr. Deming indicated that it could, but offered to provide sample-processing training/consultation to any researcher who wished to pursue this research. Dr. Golomb noted that urine sampling would be easier to blind and be more objective. Dr. Deming noted that another way to control the study would be to set a finite length of time.

Dr. Pellier stated that he was intrigued by the presentation. He asked if the researchers had tried to characterize the cocci. Dr. Deming stated that Dr. Hyman would subdivide the urine sample. Dr. Hyman would send half to the routine hospital lab and evaluate the other half in his own anaerobic culture. Dr. Deming stated that the majority of the bacteria grown were streptococci, which were then sent to the hospital bacteriology lab and that the bacteria were morphologically different. He noted that this wasn't the first time this result had been found. He gave background information about research by Dr. Marcussen and Dr. Lowell Rantz of Stanford University.

Dr. Golomb noted that another hypothesis for this study's finding could be that there was an underlying factor that caused Gulf War veterans to be ill, and, in addition, they have a common bacterial colonization that is an energetic drain. Thus, she noted it might not be part of the etiology of GWI, but clearing the infection still helps the energy of the patient. Dr. Deming responded that the eight patients who remained asymptomatic after five years didn't fit this conclusion, but those who still required antibiotics might. Dr. Deming stated that he agreed that the other factors did make the patients more vulnerable, but it was unclear to what they were vulnerable.

Dr. Cherry asked why the study's results hadn't been published. Dr. Deming provided a background about the history and politics of the study and its' funding. He stated that they had submitted it to a number of journals, and was amazed by the disbelief and hostility of some of the reviews. He acknowledged that the study wasn't consistent with the methods taught in medical school. He went on to provide a Nobel Laureate's quote about peer review: "I have always felt that in the matter of Galileo, the Catholic Church got a bum rap. What Galileo suffered from was an excess of peer review."

Chairman Binns asked if Dr. Deming had used this technique in his hospital practice with chronic fatigue syndrome patients. Dr. Deming stated that he had used it to treat his rheumatoid arthritis patients, and acknowledged that the bacteria in the urine weren't diagnostic of GWI. He stated that some of these patients had gotten well, while others had not.

Chairman Binns thanked Dr. Deming.

The meeting adjourned for lunch at 12:32 p.m.

The meeting reconvened at 1:33 p.m.

Gulf War Research Update: October 2004

Dr. Beatrice Golomb, MD, PhD
Asst. Professor, University of California at San Diego School of Medicine

Dr. Golomb gave a brief review of recently-published Gulf War-related research in areas that included epidemiology, health effects, mechanisms and other related conditions. (See Appendix A – Presentation 12.)

General Committee Business

Chairman Binns noted that this was Dr. Cherry's final meeting as a Committee member. He thanked Dr. Cherry for her service on the Committee. He noted that she was serving, by request, a shortened term due to other professional demands. He expressed his hope that she would have changed her mind, and stated that he was sorry to see her go. He noted that her many contributions, which included demanding rigour and scientific accuracy in everything the Committee did, were a great benefit to the Committee. Dr. Cherry stated it had been a privilege to serve on the Committee, and hoped to help behind the scenes in the future.

Chairman Binns announced again that the Committee's 2004 report would be released on Friday, November 12, 2004, at 3:00 p.m. He stated that the press conference would be held in the main VA building, Room 230. Chairman Binns stated that he felt that Dr. Fihn had been at a disadvantage earlier in the day, because he was not able to address some concerns that would be answered at this press conference.

Dr. Pellier commented that he had been more disappointed with the news at the June 2004 Committee meeting than this meeting. He stated that, while there might be questions about how to spend the allocated research dollars specifically, he saw progress in the amount of funding. He also noted that the proposals presented to the Committee earlier in the morning had been very brief. He stated that he needed more information about the proposals before he could discount them. He noted that the Committee might not be happy with the outcome of the recent RFA, but that it should be looking at what it could do to make things better in the next funding cycle.

Chairman Binns acknowledged that there were some things that could have been done better. He noted that a list of potential reviewers for ORD consideration hadn't been pre-prepared. He stated, though, the Committee could be prepared for the next funding cycle. He agreed that the Committee didn't know the details of the rejected proposals. He stated that some of the proposals that the Committee liked had some

flaws, and there hadn't been time to correct them. He stated that there was room for opportunity, and greater success would be achieved with future research initiatives.

Dr. Steele raised the issue of having a relevancy panel review. She asked if Chairman Binns expected this idea to be implemented. Chairman Binns stated that he learned that morning that ORD would no longer be requiring LOIs be submitted. He noted that there needed to be a mechanism to shape the studies and ensure relevancy. He stated that, without LOIs, the RFA must be very specific. Dr. Haley stated that the specifications should be in the RFA. He stated that screening RFAs for relevancy might lead to censorship. He compared the RFA to an open contract, with the specifications spelled out clearly ahead of time so the product was responsive to the needs of the agency. Dr. Steele commented that this would be the ideal. However, she pointed out that the last RFA was specific to GWI, highlighting three areas of particular interest, and these weren't the areas particularly funded. Dr. Golomb agreed. Dr. Haley stated that the Committee might need to look at the entire RFA, not just specifications, including making sure the scoring criteria included relevancy.

Mr. Smithson asked if it would be within the Committee's purvue to go back and look at the March 2004 RFA, and comment on whether or not the proposals funded were in the direction favored by the Committee. Chairman Binns stated that the Committee's report might help in future RFAs, by providing researchers guidance and, perhaps, allowing them to cite specific Committee concerns in their proposals.

Mr. Robinson stated that he thought the morning's discussion was constructive. He stated that positive steps forward were being made. However, he noted that the Committee needed to be vigilant and do everything it could to make sure its recommendations were considered. He expressed his hope that Dr. Fihn understood that the morning's comments weren't an attack on him personally. He stated that it was simply an insistence that this Committee's recommendations be considered, especially since it had been over fourteen years with few answers for ill Gulf War veterans.

Dr. Golomb commented that Dr. Fihn didn't seem to embrace the Committee's concerns.

Dr Melling asked if it might be possible to include discriminators in the RFA, providing researchers guidance in their proposals. Dr. Haley stated that these could be built into the scoring criteria.

Mr. Robinson commented that GWI and deployment health RFAs needed to be separate. Dr. Golomb agreed, noting that it should be made clear that deployment research wasn't always related to the specific unique problems in Gulf War I veterans.

Chairman Binns stated that he had been trying to educate Dr. Fihn to some of this background history, but felt Dr. Fihn needed to hear the Committee's concerns. He asked that Committee members, in turn, give Dr. Fihn the benefit of the doubt, and withhold their judgment until the November 12th press conference. He expressed his belief that the "glass was half full", and there was progress.

With respect to intramural GWI research, Chairman Binns noted that the Committee's report did address the need for GWI research outside the VA. He stated that, based on comments before Congressman's Shays' committee in June 2004, Congress had provided a $5 million line item DOD appropriation for "extramural GWI research on chronic physiological brain effects." He stated that this money was in "the hands of the folks" at Fort Detrick. He acknowledged that, two or three years ago, this might not have been thought a great thing. However, he noted that these individuals were the ones who had found Drs. Greengard, Soreq, Henderson and Sastre, and brought them into the research area. He expressed a hope that a group of knowledgeable people, from each agency, could be assembled to plan a comprehensive government effort in GWI research. He commented that there were over 50 recommendations in the

Committee's report, some of which were prioritized. It was noted that the Committee needed to continue prioritizing its recommendations.

Mr. Robinson inquired about Chairman Binns' meetings regarding research monies available through the Department of Homeland Security. Chairman Binns stated they didn't have monies for research, rather for stockpiling supplies, etc. He noted that there was a White House Office of Science & Technology Policy task force, which included individuals from VA, DOD and Homeland Security, which was developing a strategy to address chemical threats.

RAC Committee Business

Dr. Lea Steele, PhD, Scientific Director, RAC-GWVI
Ms. Laura Palmer, Committee Manager, RAC-GWVI

Dr. Steele presented an outline for future Committee meetings and the issues to be addressed. (See Appendix A – Presentation 13.)

Mr. Robinson suggested that MS or similar neurological diseases be included on the consideration list. He stated that, while there might not be statistically significant number of veterans diagnosed with MS within the VA, it could be that these veterans aren't seeking treatment through the VA. Mr. Robinson noted that there was a MS conference in Sacramento, CA, on November 7, 2004.

Dr. Pellier suggested that dementias should be investigated as well. He also suggested that, within certain diagnosed conditions, e.g. ALS, with registries, the Committee investigate whether there was anything particular about the symptomlogy that would connect it with GWI. He would like to see a holistic view of neurodegenerative disorders in Gulf War veterans.

Dr. Cherry noted that GW veterans' symptoms may not be typical of those suffered by non-veterans who are affected by these neurodegenerative diseases.

Dr. Pellier noted that many of these neurodegenerative diseases had "pre" states, which, along with their presentations, should be investigated in GW veterans.

Dr. Pellier questioned why higher accident rates were found in Gulf War veterans. He noted neuro-cognitive disorders could increase one's chance of an accident. He wondered if there was a way to look into this. Discussion occurred.

Ms. Palmer provided an overview of the development and content of the Committee's website, including statistics about its usage by the public.

Chairman Binns thanked Dr. Steele and Ms. Palmer. He welcomed Dr. Rasmussen. He noted that, while considering its size, the staff had been very efficient and effective in its production of the Committee's 2004 report, along with organizing meetings and other work.

Public Comment – Day 2

Chairman Binns opened the floor to public comment.

Ms. Denise Nichols spoke to the Committee. She thanked the Committee for the work on the website. She suggested that there be a service to match outside researchers with VA researchers, allowing for more collaboration on GWI research. She suggested that the Committee produce a video narrative regarding GWI to show the merit review panel. She also suggested more attention to VA clinician/researcher education on current thought regarding GWI. She asked that everyone keep his or her spirits up and momentum going.

Ms. Alison Johnson spoke to the Committee. She expressed concern about Dr Hyman's antibiotic treatment. She read an excerpt from her book, "Gulf War Syndrome: Legacy of a Perfect War", regarding Mr. Bob Jones' treatment by Dr. Hyman. She stated that she had spoken with another veteran who wasn't cured. Dr. Steele stated she had spoken with the same veteran, and that he had told her that he had benefited from the treatment, but later relapsed. Ms. Johnson informed the Committee that she still wanted to provide her book and video, which had been recently updated and tightened, to the VA research community. She asked for the Committee's help in getting the money to do this. She stated that she would provide the materials at cost.

Ms. Venus-val Hammack spoke to the Committee. She also provided the Committee with a two-page written comment. (See Appendix B - Public Submission 2.) She stated that she had been frustrated following the February 2004 meeting, but felt better after this meeting. She hoped that the Committee would invite industrial hygienists to future meetings. She stated that industrial hygienists could provide a work place environment analysis of the Gulf War.

Mr. Harold Nelson spoke to the Committee. He thanked the Committee for inviting Dr. Deming and Mr. Weiss to speak about their treatment study. He thanked Dr. Deming for the treatment he received during the antibiotic treatment trial and indicated that the treatment had provided great benefit in his case. He stated that he would be willing to provide more information, from a patient's point-of-view, of Dr. Hyman and Deming's antibiotic treatment. Discussion about his symptoms and treatment followed.

Mr. Edward Bryan spoke to the Committee. He stated that the Committee needed to compare the batch vs. chimney effects of the oil well fires. He suggested that the Committee speak with Jim Tuite about oil well fires. He stated that the high incidence of accidents in Gulf War veterans should be investigated. He noted that there were several industrial pollutants during the Gulf War. He stated that there was one single-source sewer system, which might have created a bacterial problem. He stated that, by his own calculations, he would estimate 35,000, not 10,000, Gulf War I veterans have died. He stated that more needed to be done to calculate the death rate of Gulf War I veterans. He stated that more treatments needed to be sought, and that a letter should be sent to Congressman Shays' committee requesting more funding for this area of research.

Chairman Binns thanked the Committee members, speakers, and audience members.

Chairman Binns adjourned the meeting at 3:50 p.m.