Research Advisory Committee on Gulf War Veterans' Illnesses

June 17-18, 2013 Committee Meeting Minutes

Department of Veterans' Affairs
Washington, DC

Research Advisory Committee on Gulf War Veterans' Illnesses
Boston University School of Public Health
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I hereby certify the following minutes as being an accurate record of what transpired at the June 17-18, 2013 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

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Attendance Record

Members of the Committee
James Binns, Chairman
Roberta White, Scientific Director
Floyd Bloom
Joel Graves
Anthony Hardie
Marguerite Knox
William Meggs
James O'Callaghan
Lea Steele
Beatrice Golomb

Committee Staff
Kimberly Sullivan, Associate Scientific Director
Megan Yee

Designated Federal Officer
Victor Kalasinsky

Guest Speakers
Henry Heng
Dawn Provenzale
Fiona Crawford
Rakib Rayhan
Julia Golier

VA Office of Research and Development
Robert Jaeger
Victor Kalasinsky
Timothy O'Leary

VA Office of Public Health
Victoria Davey

VA Office of Public and Intergovernmental Affairs
Jose Riojas, VA Chief of Staff
Robert Jesse, Principal Deputy Under Secretary of Health

VA Office of General Counsel
Jonathan Gurland

Abbreviations

ACTH – Adrenocorticotropic Hormone
ALS – Amyotrophic Lateral Sclerosis
BOLD – Blood Oxygen Level Dependent
CAM – Complementary and Alternative Medicine
CDMRP – Congressionally Directed Medical Research Program
CFS – Chronic Fatigue Syndrome
CMI – Chronic Multisymptom Illness
CPAP – Continuous Positive Airway Pressure
CPT – Continuous Performance Test
DEET – N,N-Diethyl-meta-toluamide
DFP – Diisopropyl Fluorophosphate
DoD – Department of Defense
DTI – Diffusion Tensor Imaging
FACA – Federal Advisory Committee Act
FM – Fibromyalgia
GW – Gulf War
GWI – Gulf War Illness
IBS – Irritable Bowel Syndrome
IND – Investigational New Drug
IOM – Institute of Medicine
LDN – Low Dose Naltrexone
LOI – Letter of Inquiry
MS – Multiple Sclerosis
NCCA – Non Clonal Chromosome Abberations
NIEHS – National Institute of Environmental Health Sciences
OEF – Operation Enduring Freedom
OIF – Operation Iraqi Freedom
OND – Operation New Dawn
OPH – Veterans Affairs Office of Public Health
ORD – Veterans Affairs Office of Research and Development
OSTP – Office of Science and Technology Policy
PB – Pyridostigmine Bromide
PTSD – Post-Traumatic Stress Disorder
SSRI – Selective Serotonin Reuptake Inhibitor
RAC – Research Advisory Committee on Gulf War Veterans' Illnesses
RFA – Request for Application
TBI – Traumatic Brain Injury
VA – Veterans Affairs
VBM – Voxel Based Morphology
WRIISC – War Related Illness and Injury Study Center

Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
June 17-18, 2013

Department of Veteran Affairs, 810 Vermont Avenue, Room 230, Washington, DC

Agenda
Monday, June 17, 2013

8:00 – 8:25	**Informal gathering, coffee**	
8:25 – 8:30	**Welcome, introductory remarks**	**Mr. Jim Binns, Chairman** **Res Adv Cmte Gulf War Illnesses**
8:30 – 9:00	**Welcome and Remarks**	**Mr. Jose Riojas, VA Interim Chief of Staff**
9:00 – 9:45	**Genomic instability in Gulf War Illness**	**Dr. Henry Heng** **Wayne State University**
9:45 -10:30	**Gulf War Era Cohort and Biorepository Study (CSP #585) update**	**Dr. Dawn Provenzale** **Durham VA Medical Center**
10:30 – 10:45	**Break**	
10:45 – 11:30	**Lipidomic and proteomic profiles of GWI animal models and clinical translation**	**Dr. Fiona Crawford** **Tampa VA Medical Center**
11:30 – 12:15	**Neuroimaging biomarkers in Gulf War Illness**	**Mr. Rakib Rayhan** **Georgetown University**
12:15 - 1:15	**Lunch**	
1:15 – 2:00	**Mifepristone treatment trial of Gulf War multisymptom illness**	**Dr. Julia Golier** **Bronx VA Medical Center**
2:00 – 3:15	**Committee and Panel Discussion: Treatment development discussion**	**Mr. Jim Binns, Chairman** **Dr. Kimberly Sullivan, Assoc. Scientific Dir.** **Res. Adv Cmte Gulf War Illnesses**
3:15 – 3:30	**Break**	
3:30 – 5:00	**Committee Discussion: 2013 Committee Report**	**Mr. Jim Binns, Chairman** **Dr. Roberta White, Scientific Director** **Res. Adv Cmte Gulf War Illnesses**
5:00 – 5:30	**Public comment**	

Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
June 17-18, 2013

Department of Veteran Affairs, 810 Vermont Avenue, Room 230, Washington, DC

Agenda
Tuesday, June 18, 2013

8:00 – 8:30	**Informal gathering, coffee**	
8:30 – 9:00	**Update of VA ORD Gulf War research Portfolio**	**Dr. Victor Kalasinsky** **Dr. Robert Jaeger** **Dr. Timothy O'Leary** **VA Office of Research and development**
9:00 – 9:30	**Update of OPH Gulf War Research Program**	**Dr. Victoria Davey** **VA Office of Public Health**
9:30 – 10:30	**Discussion of Overarching VA Approach to Research**	**Dr. Robert Jesse** **Principal Deputy Under Secretary of Health**
10:30 – 10:45	**Break**	
10:45 - 11:30	**Federal Advisory Committee Ethics Training**	**Mr. Jonathan Gurland**
11:30 – 12:00	**Committee Discussion**	**Mr. Jim Binns, Chairman** **Dr. Roberta White, Scientific Director** **Dr. Kimberly Sullivan, Assoc. Scientific Dir.** **Res Adv Cmte Gulf War Illnesses**
12:00 – 12:30	**Public comment**	
12:30	**Adjourn**	

DAY 1

The June 17th, 2013 meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses (hereinafter referred to as the Committee) was held in the Sonny Montgomery Room (Room 230) at the U.S. Department of Veterans Affairs Central Office, 810 Vermont Avenue, NW Washington DC.

Welcome and Introductory Remarks

Mr. James Binns, Committee Chair

Chairman Binns called the meeting to order at 8:30 AM. He thanked Dr. White, Dr. Sullivan and the staff at Boston University for creating an excellent scientific program. He also thanked the outside speakers and VA staff for attending the meeting. Finally, he thanked the members of the public and the Gulf War (GW) veterans who traveled at their own expense to attend the meeting.

Chairman Binns stated that there were some issues that needed to be discussed before starting the scientific portion of the program. He said that he had received a letter from the Interim Chief of Staff Mr. Riojas informing Chairman Binns of changes ordered to the RAC charter and membership, which were already approved by Secretary Shinseki. These changes involved altering the oversight function of the committee and the provision that allows it to have its own independent staff. Chairman Binns met with Chief of Staff Riojas and other senior officials in Washington, DC on May 29th to discuss the changes. He composed a letter to Mr. Riojas, which he shared with the members of the committee. Chairman Binns explained that the veteran members of the committee had also composed a letter, that was subsequently shared with the committee and interested congressional offices.

Chairman Binns introduced and welcomed Mr. Riojas, who was there to address the Committee.

Welcome and Remarks

Mr. Jose Riojas, VA Interim Chief of Staff

Mr. Riojas greeted the Committee and thanked the GW veterans present for their service. He thanked Chairman Binns for making time on the agenda for him to speak to the Committee. Mr. Riojas noted that he is also a GW veteran and is proud of his service and thankful for coming back from his deployment in good health, but he understood that some of the men and women he served with are not in good health. He said that he takes seriously the responsibility of ensuring that ill GW veterans receive the benefits they deserve from the department. Mr. Riojas stated that Secretary Shinseki also agrees with this sentiment and that was why the Gulf War Task Force was established. He stated that the task force had re-energized the department's efforts and extended presumption of service connection for nine infectious diseases associated with GW service. Mr. Riojas said that the Secretary wants to change the culture at the VA so veterans are not left with similar unresolved issues from past wars.

Mr. Riojas stated that he and the Secretary take the allegations made in March by Dr. Steven Coughlin on the VA's mishandling of data on Gulf War Illness very seriously, but that he could not responsibly conclude that the allegations were true until the current investigation that had

begun was concluded. He said that the VA greatly values the Committee's input with regard to VA's research efforts and said that a majority of the Committee's recommendations were included in the VA's approved research topics. Mr. Riojas stated that senior VA staff were concerned that the Committee was involving itself in issues that go beyond its charter. He stated that the Committee's statutory charge is to advise the VA on research strategies aimed at improving the VA's ability to serve GW veterans. He then suggested that the Committee had become involved in matters beyond its research oversight charge, detracting from its important work on research.

Mr. Riojas stated that the recent changes to the Committee's charter were intended to make sure the Committee's work remains focused on research consistent with the Federal Advisory Committee Act (FACA), which requires advisory committees to limit their work to the purposes for which they were established. He said the purpose of the Committee is to advise the Secretary on research and that members can raise any other concerns outside of the context of the Committee. Mr. Riojas said that VA leadership would be interested in hearing the concerns, but said that he could not allow the non-research concerns to be the focus.

He noted that the Committee's charter, which has to be followed by law, limits membership to two or three year terms with reappointments for just one or two years. He stated that in recent years those rules were not enforced, allowing members to stay on indefinitely, which denies other qualified people the opportunity to advise the Secretary. He said that at present everyone's term had expired so the Secretary had decided to appoint new members, while keeping roughly half of the current members. Mr. Riojas said the Committee still had several things that need to be finished such as the updated Scientific Report, which will require several Committee members to stay on the Committee until completed. He stated that the Secretary has asked Chairman Binns to remain as Committee Chairman for another year for the sake of continuity and to recommend which Committee members should be retained.

Finally, Mr. Riojas stated that the VA had not cut the Committee budget. He said that the VA had changed the estimate in the Committee charter for how much the Committee spends each year into a limit. He noted that the Committee had not exceeded that limit in the last four years, so this should not be a concern. Mr. Riojas stated that the VA values the Committee's work and appreciates the value that each member has brought to the Committee. Mr. Riojas said that they are committed to allowing the Committee to maintain its independence and advise the Secretary, but that the Secretary would like more senior VA staff members to become more involved with the Committee. He noted that Dr. Robert Jesse, the Principal Under Secretary for Health, and Dr. Madhulika Agarwal, the Deputy Under Secretary for Health for Policy and Services, would be personally responsible to the Secretary and ensuring the VA is moving forward appropriately. Mr. Riojas then thanked Chairman Binns for the opportunity to address the committee.

Chairman Binns thanked Mr. Riojas and then asked the Committee members if they had statements or questions for Mr. Riojas. Dr. William Meggs, a medical doctor specializing in medical toxicology and emergency medicine, is currently treating 40-50 GW veterans in his practice. He stated that GWI is no longer a mysterious disease and that the cause and nature have been documented, but said there is still no cure or definitive treatment for the illness. Dr. Meggs stated that science has now made it clear that there can be long-term effects from toxic exposures

without the presence of an acute poisoning event. He mentioned human studies including those of Iranian citizens exposed to sarin/cyclosarin during the Iran-Iraq war who have similar chronic symptoms as GWI. He also cited animal model studies demonstrating permanent alterations in brain functioning with manifestations such as fatigue, concentration difficulties, mood, neuropathic pain, and autonomic dysfunction after exposure.

Dr. Jim O'Callaghan, a basic neuroscientist, who has served on the Committee for several years, stated that he felt that the work the Committee has done has reflected their efforts to come up with good science and nothing else. He agreed that the current request for applications (RFAs) coming from the VA include the recommendations from the Committee. However, he said that he has never seen anything from the Committee demonstrating that it had overstepped its bounds out of the research area into a more political or otherwise inappropriate area. Dr. O'Callaghan noted that the reports that have come from the Committee are all steeped in science and a focus on determining what constitutes GWI and recommendations for potential treatments or avenues of research. He again emphasized that in his experience nothing has gone beyond the basis of science with regard to the Committee activities.

Dr. Kimberly Sullivan, the associate scientific director and a research scientist at Boston University School of Public Health, stated that she has done many studies with GW veterans primarily assessing cognitive functioning and corresponding brain imaging patterns. She said that she has come in contact with many hundreds of veterans both as a researcher and as part of her Committee duties. Dr. Sullivan reported that many GW veterans feel that they are not being taken seriously by VA and they have noted to her that the Secretary has never attended one of the Committee meetings since he took office and they would like to see this change.

Dr. Roberta White, a neuroscientist and environmental health specialist who chairs the department of environmental health at Boston University and is also the Associate Dean of Research, stated that she has been a Committee member for 6 years and has served as the scientific director for the past few years. She stated that she has been doing GW research since 1993 when initially requested by the VA. Dr. White said that the major contribution of the Committee has been to bring new scientific approaches to GWI to the table, encouraging research directly on GWI and sponsoring presentations on mechanisms that explain the relationship of exposures from the chemicals which result in illnesses and intoxications seen in GW veterans. She also commented that the strategic plan and other initiatives the Committee has recently participated in was at VA invitation. She stated that it is difficult to separate science from how science is instituted, supported, and initiated but she feels that the Committee has acted in an appropriate manner given the charge that was given by Congress for this Committee.

Dr. Lea Steele, an epidemiologist, has been on the Committee since its inception and previously served as the scientific director. She asked Mr. Riojas how the Committee had exceeded its statutory mandate. Mr. Riojas stated that he did not have the personal experience or an example to answer this question because he had just been in the job as Chief of Staff since the first of April and that he was referring to the charter and the work of the VA staff when he made his comments regarding the Committee. Dr. Steele commented that from the Committee's perspective that they have not in any way exceeded the charter or Committee mandate. She stated that the Committee has reviewed all federal programs that review the health of GW

veterans, advised the Secretary on a consistent basis, commented at Congress when asked to by Congress, and that all of these tasks are within the Committee charter. She also stated that there had been a general perception at VA and within the Committee that there was often tension between VA research officials and the Committee. She said that the Committee was charged with reviewing all federal programs. Early on the Committee did not praise very highly either the DoD or the VA research programs, but said that the DoD had changed their research practices over the past years, but the VA had not. Dr. Steele stated that the Committee has no political agenda, except to advise VA on the best research to finally help veterans who have been sick for the past 22 years. Mr. Riojas said that her concerns were shared and that Dr. Jesse and Dr. Agarwal will be heavily involved in the VA's efforts to work with the Committee. Dr. Steele stated that VA officials may not be aware that the VA is the outlier on this issue. She said the scientific community, the DoD, and other institutions have come together to understand GWI and determine what needs to be done, but the VA has continued to maintain an approach that has not been supported by the Committee and even by some VA investigators.

Dr. Floyd Bloom, a neuroscientist at the Scripps Institute in San Diego, a member of the National Academy of Sciences (NAS), the Institute of Medicine (IOM), and a member of the committee that will help develop a case definition of GWI, stated that when he joined the Committee six years ago, the scientific base of GWI was murky. He said there is now a growing body of literature that documents that those veterans serving in the GW have a particular syndrome of multi-symptom illness which can be traced to specific chemical factors. Dr. Bloom stated that the science of brain imaging over the last five years has revealed specific brain deficiencies that account for a large part of symptoms seen. He said that unless the research is done soon, treatments will never be developed for the long-lasting symptoms observed in these veterans. He noted that robbing the Committee of any of the members would impair the future course of the ability to treat the illness. Dr. Bloom encouraged the Secretary and Mr. Riojas to consider what has been accomplished and to help the Committee achieve more knowledge to help the veterans in the future.

Rev. Dr. Joel Graves, a GW veteran with GWI, said that his discussions with several individuals within VA indicate they don't believe there is a GWI. He stated that they believe it is PTSD, and exposures including the Khamisiyah detonations and Scuds being shot down were all instances of veterans stretching and trying to find something that could cause their problems. He said that another GW veteran committee member was in a unit that was in a bunker during the war, which caused them to be exposed to nerve agents that smelled of geraniums. Rev. Graves reported that his unit was also hit with nerve agents and that the chemical alarms around them went off during his deployment. Rev. Graves said that he gets very upset when he hears that all of his problems are from PTSD. He noted that when he returned home from deployment, his hair started falling out in clumps and then he began to have serious problems with his short term memory. Rev. Graves stated that the Committee's charter was designed so science could be explored without people being able to manipulate the committee. He said the charter itself mandated by Congress allows the Committee to dig deeper and go longer to discover what is happening to the veterans. He questioned whether the VA had the authority to change a congressional charter and attempt to turn the Committee into a typical VA research committee. He stated that the Committee was designed to be independent and to be above the influence of the people within the VA.

LTC Marguerite Knox, a GW veteran, stated that all of the individuals on the Committee are kind and bright. She said that she feels blessed to have served with them on the Committee. LTC Knox agreed with Dr. Steele and stated that the VA is the only entity that is not on board with the rest of the scientific community with regard to GWI. She said that maybe Mr. Riojas never heard former DoD Under Secretary of Health, Steven Joseph, lie to the public and to the nation about chemical exposure at Khamisiyah as she had. She stated that he has never been told by Joyce Lashof, the chair of the Presidential Advisory Committee on Gulf War Veterans' Illnesses (for which she also served), that the synergist effects of PB and chemical exposure cannot be included in their report, and that she had been black balled. LTC Knox has sat in committee meetings for that last 15 years trying to help her fellow veterans. She noted that Mr. Riojas said he is not rushing to judgment with regard to the Committee, but he is advising the Secretary to alter the Committee charter even though he does not know himself how the Committee has over-stepped the bounds of the Charter. She asked Mr. Riojas how that could be possible.

Mr. Riojas stated that the VA staff took the original law as they understood it and balanced it last year against the FACA requirements to ensure that the Committee was in compliance with the law. He then referred to Rev. Graves and told him that he does not believe himself that GWI is psychosomatic or is PTSD. He said that he is not a researcher, but he believes that from his personal experience as a veteran who also has friends who were negatively affected by their GW experience. LTC Knox stated that she was happy to hear this from Mr. Riojas, but that she was tired of the bureaucracy that the VA has continually put in front of veterans. She said that the Committee members did not sign up for the VA to change the charter and noted that Secretary Shinseki has never attended a Committee meeting since taking office and that under his administration no one has even sent appointment letters to the Committee members or thanked them for serving on the Committee. She felt that was incompatible with VA now implying that the Committee members were trying to take advantage by staying on the Committee indefinitely. LTC Knox then thanked Chairman Binns for his hard work on behalf of GW veterans and resigned her seat on the Committee.

Dr. Meggs then stated that the Committee was being accused of something, but the Committee had recently seen a number of things happen such as the GW Strategic Plan being rewritten with no explanation. He said that an IOM Committee was formed to discuss GWI treatments, but it was only composed of psychiatrists. He said that he felt as though there was an intentional effort to negate the science, and the Committee would like to know why this would be done.

Mr. Riojas thanked Chairman Binns for the time to speak to the Committee members directly. He stated that he, Dr. Jesse, Dr. Davey and others at the VA would get more involved. He said that he appreciated the candid professional comments from the Committee and said that the Committee and the VA share the same goal of doing what is right for veterans.

Chairman Binns thanked Mr. Riojas for his comments and stated that he hopes that he will reconsider the charter change and focus on the real problems at the VA with regard to GWI research.

Public Comment

Chairman Binns invited the public on the phone to comment on the topic and also moved the public comment time on the agenda to this time period. David Lashell, a veteran on the phone, stated that the VA counts nine infectious diseases as being part of GWI, but said that those diseases are common to a worldwide community. He stated that they are not included as a presumptive when filing a claim, and said they will be denied if the diseases were not recorded while on active duty. Mr. Lashell said the same thing goes for the presumption for fibromyalgia, chronic fatigue and irritable bowel syndrome (IBS). He stated that he has proof of denial for these so called presumed illnesses because he did not show them within one year after service or while on active duty. He asked when the VA would abide by the presumptions that they have already approved.

Glenn Stewart, another veteran on the phone, stated that he was also denied for his service claim. He said that the VA said they could not find any service-related connections despite the fact that he sent the VA hundreds of documents. Mr. Stewart said that it is impossible and noted that his active duty records show him complaining of symptoms at age 32 including irregular bowel movements, diarrhea, gagging, memory loss, joint pains, muscle pains, and more. He asked what 32 year old has diarrhea all the time. He said that the VA stated that the symptoms were caused by his aging, despite the fact that he had the problems when he was 32 years old. He stated that if it is not GWI, than he wants to know what it is.

Ronald Brown, a 45 year old disabled GW veteran stated that he had been diagnosed with restrictive airway disease without a known corresponding diagnosis. He said that it took him 17 years of denials and repeals to finally receive the benefits he deserved and earned while in service for his country. Mr. Brown stated that he hears reports about how much the VA cares about GW veterans, which he hopes are true, but noted that the VA's actions do not reflect this. He said that a fellow GW veteran Edward Castillo, was at the Khamisiyah bunker and received a letter from the DoD detailing exposure to sarin/cyclosarin, which noted that those exposed were twice as likely to develop brain cancer. However, Mr. Brown said that Edward's claim was denied and he passed away in 2005 from brain cancer with his claims never being approved. He stated that Edward's wife and two kids never received his benefits and were left to fend for themselves. Mr. Brown said Edward is just one of many veterans and their families who have had this experience, and noted that it is unacceptable. He said that these veterans did what was asked when the Country called upon them and that GW veterans deserve better than what they currently have to go through with the VA. He stated that it is time for the VA to do what is right and noted that actions speak louder than words.

Dr. Sullivan thanked Mr. Brown for his comments and said that she had spoken with several other GW veterans dealing with brain cancer from the Khamisiyah exposures. She stated that she works with them to get them the correct information to send in with their benefits claims and that she was sorry to hear that Edward did not get any of the benefits that he could have been entitled to. Dr. Sullivan stated that she believes that there is enough now known regarding increased risk of brain cancer mortality that presumption for service should be granted for sarin exposed GW veterans who develop brain cancer. She thanked Mr. Brown for bringing up this topic and said it remains an important issue.

MAJ Denise Nichols, a nurse officer who was deployed to care for the troops during the GW, said she would have never dreamed that GW veterans would be battling for benefits 22 years after the war. She stated that she is sick, Committee members are sick, and most every GW veteran that she talks to is having problems. MAJ Nichols said that she could not function in nursing and stopped working for the safety of the patients, the students she worked with and for herself several years ago. She stated that she involved herself in these meetings because she felt it was her sworn duty to help veterans. MAJ Nichols described getting phone calls from potentially suicidal veterans before a hotline existed, and that she felt that there were forgotten veterans helping each other on the internet but not being helped by the VA. She noted that she tracks the death records of GW veterans and noted that one veteran's wife had to fight with the VA for years before finally receiving the benefits for their children that her husband had earned. MAJ Nichols said it is a slap in the veterans face and a disgrace for the government that the veterans served to not provide the benefits that they deserve. She stated that she felt that the GW was becoming the forgotten war. She noted that the members of the Committee are the experts and to replace any of the members and change the charter will cause the VA to lose any trust that the veterans may still have in the VA.

Paul Sullivan, a GW veteran, noted his distress at the behavior of the VA staff to once again block objective, reasonable, scientific inquiry by the Committee. He stated that the Secretary of the VA himself has essentially removed Chairman Binns as chair and removed half of the Committee members' positions without consulting the Committee or understanding the law. He said the conclusion is that the VA is acting outside the law and that the VA is the outlier and the misbehaving body. Mr. Sullivan stated that the Chief of Staff and the Secretary are now blindly following the blunders, mistakes, manipulations of data, and other serious problems over the last 22 years. He said on the law, the VA has failed. He noted that the VA is also failing on the science, referencing many reports and studies that clearly show that GWI is real. He said that there are VA employees in the room who will do everything in their power to stop scientific inquiry, which is a serious problem. Mr. Sullivan reported that he was the executive director for the National Gulf War Resource Center in the 1990s, which worked with Congress to create a solution to stop the VA from blocking GW treatment and research. He stated that veterans have just spoken about the inability to receive benefits because a set of VA career staff have been intentionally blocking the scientific process.

Mr. Sullivan stated that the VA knows exactly what it is doing, noting the ramifications of what would have happened if the VA had not denied the veterans were exposed and sick. He said if research had started 20 years ago the science would be two decades further along in finding treatments. Mr. Sullivan stated that the veterans had to go around VA and work with Congress to create the Congressionally Directed Medical Research Program, noting that veterans would not be this far if they had not gone around the VA. He indicated that the net result of the VA's actions to stop the research that could lead to treatments and benefits for veterans is what caused the Committee to have a no confidence vote in the VA. Mr. Sullivan stated that the Chief of Staff admitted that the changes were initiated last fall, which was right after that vote. He noted that the VA finally decided to initiate the changes after a former VA researcher accused the VA of manipulating data.

Mr. Sullivan expressed his disappointment that the lack of leadership is coming from a General who served in the GW. He stated that the VA's actions are friendly fire and that veterans are being shot at from the rear. He said that he feels the VA is looking at hundreds and thousands of additional patients and claims at a time when the VA does not want them. He stated that they will not be the forgotten war and they will not be swept under the carpet. Mr. Sullivan pointed out that the VA leadership could not tell the Committee how they had gone outside their lane after stating that they had. He stated that GW veterans have reached out privately for weeks and the result was for the VA staff to lie and say it was simply an administrative act. He said some even said that GWI does not exist. Mr. Sullivan stated that the government is the outlier and the anomaly, which is preventing the veterans from getting their treatment and benefits.

Keith Nording, a retired staff sergeant, stated that he got interested in GWI years ago when no one knew what was going on and said he is interested in the research that is currently being done. He said that there needs to be more research, but noted that the government is not taking the research any further or publishing what they already have. Mr. Nording said that he has had four surgeries in the past 18 months due to GWI. He asked when veterans are going to get their compensations for presumptive conditions. He discussed a veteran that had IBS, a presumptive diagnosis, but did not get compensated because a compensation and pension (C&P) doctor said that he did not have IBS, despite 20 years of medical records documenting it. He expressed that he believes these actions are coming from the Secretary, the man who controls the VA. He noted that the Secretary needs to know what is going on and questioned whether the Secretary is fully informed. Mr. Nording asked why the Committee is being altered when it has been proven to work. He noted that he was taught as a private to not fix something that isn't broken. He said that the system does need to be fixed however, and re-emphasized the need for work to be published, indicating the VA has been preventing publications. Mr. Nording applauded the WRIISC center, but pointed out that there used to be 19 centers and now there are only 3 centers, which have long wait lists.

Angela McLamb, a veteran, stated that she became ill during the war and has been ill since. She said that the Committee charter needs to be taken back to the original charter and noted that the Committee is the main voice trying to do what is right and help the veterans. She expressed that veterans would most likely not get well if the Committee did not exist. Ms. McLamb noted that the Committee has a lot of experience with this complex illness, stating that she feels things will be missed if members are replaced because it is difficult to train someone with everything the Committee has learned over the years. She said that you cannot just read about it because GWI is so complex. Ms. McLamb also discussed that that unit locations and dates are incorrect in the records and that it needs to be fixed. She stated that the doctors need to be educated and their attitude toward GWI needs to be changed and this is something that has to come from the top.

David Lashell, a veteran attending by phone, stated that he attended the WRIISC center in East Orange County and noted that he could not speak more highly of them. He said that it does not mean that when the veterans return home that their local VA will accept the evaluation however. Mr. Lashell commended the Committee noting that it has been a long-standing very informative team. He stated to change the membership, would cause the research to go backwards in time instead of continuing to move forward.

Chairman Binns adjourned the committee for a brief break before reconvening and starting the scientific portion of the meeting.

After the break, Chairman Binns introduced Dr. Robert Jesse, the deputy under secretary for health. Chairman Binns stated that one of the clear problems is that there are people at the top of VA who are capable in their fields, but do not have the best preparation for medical research. He said that Dr. Jesse's presence was helpful in understanding the medical research because he is a trained cardiologist and a senior VA leader.

Dr. Jesse thanked Chairman Binns for the introduction and then explained that he preferred to be in listen mode and then speak and have more of a conversation on the second day of the meeting. He stated that he would be present for most of the two days and was looking forward to hearing about the research. He said that he does understand research as he got his PhD in biophysics before going to medical school. He indicated that he was anxious to hear the presentations and would engage in conversation on the second day.

Dr. Sullivan began the research portion of the program by thanking the speakers and stating that the Committee is grateful for their presence and happy to talk about the science of GWI. She introduced the first speaker Dr. Henry Heng.

Genomic Instability in Gulf War Illness

Dr. Henry Heng, Wayne State University

Dr. Heng began his presentation by noting how it is difficult to determine what causes an illness when there are a diverse number of possibilities, and discussed the role of genomic instability in GWI (Appendix A – Presentation 1). He said that even when a specific gene can be identified; it does not necessarily have clinical implications. Instead his work focuses on the genome, which is the combination of all sequences of genes combined with each individual's genomic topology, which is the network structure. He stated that genomic instability, which can occur due to a variety of physical stressors, can eventually cause a disease or illness. An unstable genome randomly impacts different pathways and biological systems resulting in the diverse symptoms displayed by patients. Genomic instability can lead to non-clonal chromosome aberrations (NCCA), or the mismatching of genes during replication. Dr. Heng reported a pilot study where he tested patients for a Discovery Channel Program and found that participants with GWI had a higher rate of NCCAs than both healthy controls and cancer patients. He showed slides demonstrating the amount and types of NCCAs found in the GW veteran participants, such as translocations, condensation, and fragmentation. His current DOD funded study is designed to compare whether these same results will be present in a larger group of GW veterans.

Rev. Graves asked Dr. Heng how this information could inform treatment and asked if he had any ideas for veterans exposed to organophosphate pesticides. Dr. Heng stated that he has not developed any treatments and suggested that monitoring of the system during treatment would be important because some treatments can make the genomic system more unstable (i.e. chemotherapy). He cautioned against pushing any treatment too hard for this reason.

Dr. Steele thanked Dr. Heng and asked him to describe his GW study further. Dr. Heng stated that the sample size was about 30 individuals. He said they used an age matched method with a military control group and a non-military control group. Dr. Steele asked if the GW veterans were ill or if they just had to have served in the war. Dr. Heng stated that the GW veterans included those who served in the GW and came to a clinic noting symptoms.

Dr. Meggs noted that the model states that a collection of physical stressors leads to the genomic instability which leads to illness. He stated that he feels the model indicates that each veteran group from different wars should be expressing the same symptoms, but he noted that veterans had unique exposures in different wars resulting in different symptoms. Dr. Heng agreed with Dr. Meggs and stated that his theory is that different exposures randomly (stochastically) alters different pathways, which causes different symptoms.

Dr. Sullivan thanked Dr. Heng and asked him to clarify that when he used the term stressors he meant different environmental exposures and not psychological stressors. Dr. Heng agreed and said that he is not talking about psychological stressors. Dr. Sullivan then stated that she would be interested in seeing studies done on the specific exposures from the GW with regard to genomic instability testing. Dr. Heng agreed and said he would like to study subgroups of GW veterans. Dr. White commented that the term stress may not be well thought out in this context. She stated that a better term may be stressors or exposures, to make the model clearer. Rev. Graves agreed with Dr. White.

Dr. Sullivan thanked Dr. Heng and introduced Dr. Dawn Provenzale.

Gulf War Era Cohort and Biorepository Study (CSP #585) Update

Dr. Dawn Provenzale, Durham VA Medical Center

Dr. Provenzale discussed the Gulf War Era Cohort Biorepository Study (CSP #585) which aims to establish a research cohort of GW era veterans to be used for future studies (Appendix A – Presentation 2). The veterans who enroll in CSP #585 will complete a mail survey, give access to their medical/health records, records from any research projects they have participated in, and a blood specimen for blood banking and future analysis and research. The goal is to contact 10,000 veterans with the hope of having 3,000 or more veterans enroll in the cooperative study. Dr. Provenzale discussed the development of the survey and stated that it was currently in the process of cognitive testing, which she explained meant that in-person testing of survey items with veterans would be done with the goal of ensuring the survey was easily understandable to the participants and would be revised in accordance with the suggestions from the pilot participants. A kick-off meeting and training will occur in late August 2013, and she estimated the first mailings for the study would occur in September 2013. The coordinating center will be operational the day after the first mailing and the first blood draw is estimated to occur in October 2013. To conclude her presentation, Dr. Provenzale provided study information to the veterans in the audience explaining the enrollment and participation procedures, and she explained how other researchers could access and utilize the CSP data in the future.

Dr. Meggs asked why they are only getting a small amount of blood for so much work. He pointed out that it would be easy to quickly use the amount of blood being collected and discussed how other studies will require other specimens such as plasma, serum, and cells. Dr.

Provenzale stated that it is a point well taken and maybe they should collect more. She said that it is a pilot study to see what works and that it is important to understand that the veterans are willing to provide a blood sample and enroll in the project. She thanked Dr. Meggs and said it is something to consider.

Rev. Graves asked about the time frame of service for the participants and Dr. Provenzale responded that only veterans from the first Gulf War in 1991 will be included in the study.

Dr. Sullivan commented on the use of the term "cognitive testing", which means something different to neuropsychologists and is the specific testing of different cognitive domains with pencil and paper or computerized instruments. She suggested that it be called something else such as beta testing or pilot testing for comprehension of her survey. She then commended Dr. Provenzale for doing the beta testing and ensuring that veterans understand the questions and for ensuring the appropriate questions were included in the survey. Dr. Sullivan asked if the stored bloods would be available to VA and non-VA researchers. Dr. Provenzale said yes they would be available to VA and non-VA investigators. Dr. Sullivan's final question was whether Dr. Provenzale would work with the Boston brain and tissue bank for cross-recruitment because it would be ideal to have both bloods and brain tissue from the same participants. Dr. Provenzale stated that she has ongoing contact and discussions with that team to determine how to best align their projects.

Rev. Graves asked Dr. Provenzale about the cards she has for the study. She responded that there were information cards on the back table and that she was prepared to take names and contact information for any veterans interested in participating, which would allow for information to be mailed to them, but would not require their enrollment. Rev. Graves stated that he would like to be in the study and would be willing to give more blood. He asked if the five questions in the survey from Dr. Lea Steele were asked in regard to where people served in theater. Dr. Steele commented that the development of the survey was inclusive and she and Dr. Provenzale agreed that there were some questions included about location in theater. Dr. Steele stated that there are questions about specific exposures, but also asked Dr. Provenzale if the questions about country locations and time spent at sea were going to be asked. Dr. Provenzale stated that questions about time spent at sea were included, and also discussed that she believes veterans testing the survey will also write in questions that they feel are important to be included which could be addressed as the survey moves forward. Rev. Graves said those questions are important because location gives an indication as to what type of exposures that occurred and that results could be washed out if location and exposure are not specified for each veteran. Dr. Steele agreed with Rev. Graves.

Dr. Steele expressed that she was pleased that the data will be shared with other investigators. She reiterated that more blood should be collected in the study. She then asked if Dr. Provenzale was concerned about response rates, which were low in the testing of the survey. Dr. Provenzale responded that was a different process because the veterans had to actually go into the VA. She said refusal conversion will be important and is the point of the pilot, so strategies can be developed to enhance the recruitment process. Dr. Steele suggested that a lot of veterans may not be interested in giving their entire medical and research records, but would be willing to complete the survey and give blood. She asked if veterans could participate without giving their

records. Dr. Provenzale said she understood the point, but commented on how the records would enhance research. She clarified that they will only be given access to all the records, but would not collect them all. She stated it was a tradeoff and that perhaps veterans should be asked if that would impede their participation.

Dr. Jesse said opening up the access to Dr. Provenzale's data is important and stated that it is something he has been pushing for in the VA. He stated that open data allows for transparency and it also allows for others to think of new things that perhaps the investigator did not think of to include in the study analyses.

Dr. Steele stated that only the pilot study was discussed and asked if a larger study would occur if the pilot study worked. Dr. O'Leary said that he expected the pilot study to be a run in to the real study. He stated that the VA has been committed to a full study since the beginning, but they want to ensure that they get it right from the beginning. He said the pilot study will allow for glitches to be identified and that unless the project is a failure (which he does not expect) than he would not dream of anything other than a full commitment. Dr. Provenzale said that she would be available throughout the day along with a colleague who could answer questions and take contact information if veterans were interested in participating or learning more about the study.

Chairman Binns welcomed committee member Mr. Anthony Hardie who joined the meeting and invited him to make a comment. Mr. Hardie thanked the Committee who had worked so hard for many years and Paul Sullivan who helped create the original Committee charter. He stated that he was deeply disturbed by the actions and the non-actions of the VA. He said that last June (the last time the VA allowed the Committee to meet) the Committee concluded that it had no confidence in the VA with regards to GW illness research. Mr. Hardie said shortly thereafter the VA began working to destroy the Committee. He stated that he has been involved in GW veteran issues for 18 years and noted that the Committee has created recommendations in reports that have been systematically ignored by the VA. Mr. Hardie commented on the strategic plan that was whitewashed by the VA last year and noted that the IOM case definition panel has now been created for chronic multisymptom illness, which will lump in GWI with other conditions when it should not. He stated that the creation of the panel was in contravention to what was discussed in the VA Gulf War strategic plan.

Mr. Hardie stated that it was clear that the recommendations of the Committee are not taken seriously by Secretary Shinseki or anyone else in the department and he feels that the investigation into the charges brought up by Dr. Coughlin were not taken seriously or being done properly. He said the VA staff is not being held accountable and the department is not under any appropriate amount of control. Mr. Hardie felt that Mr. Riojas comments were inappropriate and noted that the Committee is the one shining hope for GW veterans. He stated that he appreciates all that the Committee has done, but feels that there is no longer a need for veterans to be on the Committee. He said that he does not feel that he has a role on the Committee any longer and noted that he was appreciative of the Congressionally Directed Medical Research Program (CDMRP) where he continues to serve and where veterans are taken seriously and funding continues to increase. Mr. Hardie stated that it was a travesty that the Committee continues to make recommendations that go nowhere, or if they are heard at all they are simply white-washed and changed. He said that he will no longer be serving on the

Committee and invited other GW veterans in the room to join him as he walked over to Capitol Hill to meet with members of Congress. Chairman Binns thanked Mr. Hardie for his service.

When the meeting resumed, Dr. Sullivan introduced the next speaker, Dr. Fiona Crawford.

Lipidomic and Proteomic Profiles of GWI Animal Models and Clinical Translation
Dr. Fiona Crawford, Tampa VA Medical Center

Dr. Crawford thanked the committee for inviting her to speak and stated that her overall approach has been to develop mouse models of exposures to GW agents that can be used to identify therapeutic pathways and peripheral biomarkers. She discussed two different animal models that her lab has developed and the use of lipidomics and proteomics as potential markers (Appendix A – Presentation 3). Mouse Model A, an adaptation of Dr. Abdel-Rahman's model, is a 28-day paradigm during which mice receive pyridostigmine bromide (PB), permethrin, DEET, and stress daily. Treated mice demonstrated higher rates of anxiety and poorer motor control, and demonstrated changes in neuropathology, specifically in increased glial fibrillary acidic protein (GFAP) levels, which is an indication of astrocytosis. Dr. Crawford indicated that mouse model A demonstrated immediate central and peripheral effects of exposures, but mouse model B demonstrated the effects of exposures 20 years later, which parallels GW veterans' exposures. In this model, mice are exposed to PB and permethrin daily for 10 days, and are then tested over a number of time points for the next 150 days. No immediate effects were seen, but mice demonstrated higher rates of anxiety 30 days after the exposure paradigm. Initially, exposed mice performed better on learning and memory tasks, but they performed significantly worse by the final time point. Dr. Crawford indicated that this pattern was often noted in humans possibly due to cholinergic stimulation from the PB exposure.

Dr. Crawford then discussed proteomics, which allows scientists to take complex mixtures of samples that can be analyzed to separate digestive protein peptides, based on their mass and charge which allows for a broad picture of what is occurring in the proteins. Dr. Crawford's lab uses quantitative proteomics, meaning they put one tag on the exposed mice samples and another tag on the unexposed mice samples and then mix the samples together to get a relative quantification of the proteins present in the brains of the exposed and unexposed mice. The results yield a list of proteins that are significantly regulated in response to exposure. Dr. Crawford discussed the list of biological functions that were significantly and differently regulated in the exposed mice versus the control mice that included lipid metabolism, cell movement, and immune cell trafficking. Dr. Steele asked Dr. Crawford to clarify again, that all the results are 150 days out following a 10 day exposure of the mice. Dr. Crawford responded that Dr. Steele was correct. She stated that the lab has another cohort of mice that were tested at different time points throughout the 150 days as well.

Dr. Crawford then discussed her lipidomics work, explained basic background information on lipids and how they are formed, and then discussed the work flow process of analyzing lipids in her lab. Significant increases were seen in the brains of mice from Mouse Model A in several phosphatidylcholine and sphingomyelin lipid species, though no significant overall differences were found. The same brain effects were seen in mice from Mouse Model B, including a significant overall effect. Plasma effects were the opposite, showing decreases in phosphatidylcholine and sphingomyelin species. Increases in fatty acids were seen in both

Mouse Model A and Mouse Model B. Dr. Crawford stated that there is a clear effect on lipids, but the research is just starting and her lab has not processed all of the data yet. She finished discussing future steps and hypotheses that her lab plans to conduct.

Dr. Sullivan noted that it was interesting that effects were seen much further out after the initial exposure paradigms and asked if the animals appeared to be demonstrating accelerated aging. Dr. Crawford said it was an interesting question and noted that the mice have not shown any particular effects of aging, but also noted that they have not let them live long enough to truly assess this. She indicated that there was a possibility of increased mortality, but she had yet to analyze that data and noted that some of the effects were ones that would be expected in aged mice and that it may be accelerated aging. Dr. Crawford said that taking away the poison does not cause the effects to subside and there is instead a persistent chronic effect.

Dr. Steele stated that she was impressed by Dr. Crawford's work and noted that she was taken by the observation that things look better at first and then they are worse. She said that there are studies showing that there are delayed effects at low level exposure, a trend which appears to occur over and over, yet no one has thoroughly evaluated that concept. Dr. Steele said that there are human trials of PB that have shown improvements. She asked Dr. Crawford what she might speculate is going on with the acetylcholine cascade event following the exposure. Dr. Crawford said that there is clearly a cholinergic effect and is currently trying to study that effect in more detail. She stated that what Dr. Steele said in the beginning about clinical studies is important and highlighted how critical it is for basic science and clinical researchers to collaborate to ensure that research remains on the right track.

Dr. Bloom stated that her work was impressive and said that he wants to know the sequence with which the changes emerged, specifically reference the 10 days exposure with effects seen 150 days later. He said it is important to fill in the gap between the 10 days and the 150 days and see what correlates with the behavior. He noted that will allow Dr. Crawford's group to look for mediators or modulators of the systems that have gone wrong. Dr. Crawford agreed and said that there needs to be a time course determined.

Dr. O'Callaghan noted that there is an age-related increase in GFAP and astrocytosis which develops late, which is not necessarily associated with the process that would be expected. He discussed the idea of a lack of response from microglia due to aging and not necessarily a loss. He noted that adrenal insufficiency has been found to develop over time. He asked if Dr. Crawford had looked at any other processes that may be occurring. Dr. Crawford stated that it was a good suggestion and that it needed to be done noting that astrocyte function and markers of astrocytes need to be looked at.

Dr. Heng stated that in the field of genetics there is always a fear of change and the idea that change is bad. He said that the change or the adaptation in the short term is good, but you pay the price in the long term cost. He noted that under stress if there are no changes death will occur, but stated that if processes are altered too much negative long-term consequences can occur, such as the development of cancer. He asked Dr. Crawford if she had compared the proteins on an individual level to examine the level of diversity. Dr. Crawford stated that it had not been done and that they have only been focusing on the comparison of overall changes between the

exposed and the unexposed groups, but noted that individual diversity could be examined. She said one assumption of animal studies is that the animals are similar or sort of "clones" which are then translated to humans that have much more variability.

Dr. Golomb noted that it is assumed when changes in lipidomics or proteomics are seen it is often translated as corrupted, but noted that changes can be seen in healthy individuals because the changes are adaptive. She said when seeking therapeutic approaches to normalize individuals, it is important to be cautious to not normalize processes that allow the function of the individual. Dr. Crawford agreed noting that it was a good point, and stating that it would be taking into consideration.

Dr. White stated that it is becoming more and more of a challenge to fund animal work because there is a lot of pushback regarding treatment and people. She said that she is a big fan of animal work because there are a lot of questions that can be answered, especially at the pre-therapeutic stage like Dr. Crawford's studies. She noted the importance of keeping the work going at the same time as human studies, and thanked Dr. Crawford for being a great example of animal studies. Dr. Crawford noted she would love to work with other groups looking at the proteomics of other animal models of exposure such as sarin and noted that it would be important work.

Dr. Steele noted that it is unique that Dr. Crawford is using two models of GWI. She stated that she was having difficulty understanding whether there were different results with the different models. Dr. Crawford said that direct comparisons had not been done, but said that she believes that there may be something different found in the different models.

Chairman Binns said that the research is exciting and demonstrates a lot of good progress has been made. He noted there have been many cases over the years where the VA has stopped funding a study and CDMRP has continued to fund it. He said Dr. Crawford's work is the first he has seen in which work that was funded by CDMRP is now being picked up by the VA, which he noted is a step in the right direction. He asked whether the substances themselves are still present in the animals in the down streaming stage. Dr. Crawford said they are currently getting together the procedure to look at that, which is something that is long overdue.

Chairman Binns thanked everyone and adjourned the meeting for lunch.

Dr. Sullivan welcomed everyone back and introduced the next speaker.

Neuroimaging Biomarkers in Gulf War Illness

Mr. Rakib Rayhan, Georgetown University

Mr. Rayhan thanked the Committee for inviting him to the meeting and passed along Dr. Baraniuk's regards, who was unable to attend the meeting. Mr. Rayhan stated that he would be discussing Dr. Baraniuk's lab's neuroimaging data over the past two years (Appendix A – Presentation 4). He discussed an overview of health symptoms, imaging techniques, and described the lab protocol which aimed to determine whether exercise-induced symptoms are related to central nervous system dysfunction in GW veterans. He described the participant characteristics noting that all of their GW veterans meeting the 1998 criteria for CMI also meet

the 1994 chronic fatigue syndrome (CFS) criteria. Dr. Golomb asked if they selected the veterans for CFS or if it was by chance that each veteran met criteria for CFS. Mr. Rayhan said they did not select for CFS. GW veterans with CMI and CFS reported higher levels of pain and fatigue, and had a lower dolorimetry (pain) threshold compared to controls. Brain imaging studies showed increased axial diffusivity was seen in the left corticospinal tract and increased mean diffusivity in the superior longitudinal fasciculi on diffusion tensor imaging (DTI), which has been shown to control working memory. The primary outcome of the study was increased axial diffusivity in the right inferior frontal occipital fasciculi (IFOF), which has significant correlations with fatigue, dolorimetry pain testing, and McGill pain scale total scores. Mr. Rayhan explained that the right IFOF connects regions of the brain which have been implicated in pain and fatigue, and the perception of pain.

Mr. Rayhan then discussed exercise induced changes, re-emphasizing the hypothesis that stressing the system would reveal underlying CNS regions responsible for the post-exertional malaise that veterans reported experiencing. Data included functional MRI (fMRI) BOLD imaging with the two-back test, voxel based morphometry (VBM), pain measurements, and other physiological measures. There were two distinct responses to the exercise noting that 10 veterans had orthostatic tachycardia after exercise, but the response subsided after a full day of rest. The group of veterans that did not have an increase in tachycardia following exercise demonstrated an increase in tender points on dolorimetry pain testing. The control group did not have any changes in either measurement following exercise.

Dr. Golomb asked if either of the results remained significant if the veterans were not separated into two different groups. Mr. Rayhan said that he thought the increase in tender points would remain significant, but noted that the actual analysis had not been done. He continued noting that the veterans also filled out the self-reported Chalder Fatigue Questionnaire. The group with the post-exercise tachycardia had a primary loading on the cognitive constructs, while the group with the increase in tender points had a primary loading for the physical constructs.

Mr. Rayhan discussed the pre-exercise brain imaging noting that the increase in tender points group higher activation in the anterior insula, a region that is related to pain, and the tachycardia group had increased activation in the left cerebellum, a pattern seen in those with Alzheimer's disease and multiple sclerosis (MS). Both groups of GW veterans performed worse on the two-back test during the pre-exercise imaging compared to controls. Following exercise, the controls showed normal working memory. The group of veterans with an increase in tender points demonstrated an increase in activity in the superior frontal, which moved to the medial frontal gyrus, a region implicated in the processing of pain. The group with the post-exercise tachycardia did not demonstrate any blood flow on the BOLD imaging, which was suggested to indicate a possible neurovascular deficit that was preventing blood flow to these regions. Mr. Rayhan then discussed volumetric differences found on the VBM analysis. The group with post-exercise tachycardia demonstrated atrophy in the brain stem, the region in the brain that regulates heart rate and blood pressure. The group with an increase in tender points demonstrated reduced volume in a region of the superior gyri and the precuneus, which has been implicated in pain processing. Mr. Rayhan noted that they hope to replicate the study in a larger group.

Dr. Golomb asked if there was a difference in two-back performance after exercise between the two groups and Mr. Rayhan said that there was not. He believed that both groups had been able to compensate allowing for their similar performances. Dr. Golomb noted that the groups performed the same cognitively after the exercise, but there were results demonstrating no blood flow. Mr. Rayhan agreed and noted it was a limitation of the study and further explained the process for determining blood flow from the VBM.

Dr. Meggs asked if these results had the potential to be a diagnostic test for GWI. Mr. Rayhan said they are at the beginning stages, but that he hopes so. Dr. White said that there is a lot of hope for biomarkers and for imaging to be a potential biomarker. She stated that she thought that a big limitation of these studies were that all of the veterans also had CFS. She pointed out that most of patients with GWI do not have CFS, and these studies are looking at a particular subset that may not translate to the other GW veterans. Dr. Steele agreed with Dr. White and noted that it is unusual for all of the veterans to meet criteria for both CMI and CFS and stated that there was something not quite representative of the sample. She indicated that it is difficult to interpret the results due to that fact. Dr. Rayhan agreed and said that they realized the limitations and said they acknowledge the fact that it may not be relevant to other subsets of GW veterans.

Dr.Golomb said that with a tiny sample it is possible that the baseline characteristics may not look different, because it requires a huge difference to yield any significant results. She noted the results may be different in a larger sample and said it would have been nice if the sample was one to one matching instead of being proportionally matched. Mr. Rayhan agreed, but stated that they had difficulty recruiting for the study because it required a four night stay to participate.

Chairman Binns asked about the criteria for CMI compared to CFS and said that the results depend on who is filling out the forms as some of the criteria sound similar. He stated it is not like taking a temperature, which is standard and objective. Mr. Rayhan agreed and said that they tried to address that problem and they are hoping that they can identify biomarkers allowing people to look beyond the criteria. Dr. Golomb stated the science cannot move beyond the criteria unless it is assured that the sample is inclusive. Mr. Rayhan agreed and stated that was a limitation. He noted that the most important take away point was that there was a lot occurring in the central nervous system and the groupings are not necessarily steadfast. Dr. Sullivan agreed with Mr. Rayhan and said it was important to investigate the change in the CNS especially looking at changes in the white matter. She stated that it will be important to replicate in a cohort without CFS as well.

Dr. Sullivan thanked Mr. Rayhan and introduced the next speaker, Dr. Julia Golier.

Mifepristone Treatment Trial of Gulf War Multisymptom Illness

Dr. Julia Golier, Bronx VA Medical Center

Dr. Golier thanked the Committee for inviting her and stated that she would be presenting the results of a randomized controlled trial of mifepristone, a selective type II glucocorticoid receptor agonist, in GWI (Appendix A – Presentation 5). She stated that her past work had consistently demonstrated altered HPA activity in GW veterans not related to PTSD, and while the mechanisms of mifepristone are not completely understood, the overall effect is the

recalibration of the HPA axis. Dr. Golier demonstrated the study design, a crossover study where subjects were randomized into two six week treatment phases with a one month washout. A dose of 200 mg a day was used, which has been shown to be well-tolerated. Participants were GW veterans who met criteria for multisymptom illness defined by the Kansas definition. Dr. Golier described the primary, secondary, and descriptive outcomes, which included clinical outcomes, neuropsychiatric outcomes, and neuroendocrine outcomes. In total, 32 veterans completed the study and Dr. Golier described their demographic characteristics and their baseline self-report data.

Veterans demonstrated an expected increase in plasma cortisol and plasma ACTH in response to the mifepristone. No differences were found in clinical outcomes for physical or mental health outcomes. An improvement in verbal learning was seen for neuropsychological outcomes, which was measured by the Hopkins Verbal Learning Test. Non-significant differences were seen in PTSD improvements measured by the PCL total score, most notably it was decreased in hyperarousal. Dr. Golier stated that overall the drug was well tolerated; there were significant improvements in verbal learning and a trend towards improvement in PTSD symptoms.

Dr. Golier said she was hoping to ask the veterans if they would take a drug that improved their list learning, but did not make them feel better. Dr. Sullivan asked if the veterans reported improvements in their memory. Dr. Golier stated that the veterans did not perceive a memory improvement. She said now research has to decide if it is worth studying mifepristone at higher doses, for longer duration, and whether to further study its mechanism of action or investigate other treatments that target glucocorticoid signaling.

Dr. O'Leary asked if Dr. Golier was considering doing a longer trial to see if the improvements in list learning remain after 6 months or a year. Dr. Golier stated that they are currently doing another trial, looking at a shorter duration in higher dose, which is consistent with most of the literature. She said they originally did the lower dose for a longer period of time, because GWI has so many symptoms and has been occurring for so long. She noted that there were virtually no adverse events and the drug was well-tolerated.

Dr. Golomb stated that she has found in her studies that objective cognitive tests did not correlate with subjective tests, and noted the importance of longer training for cognitive tests before the trial starts to help overcome a lot of the variance in training which can obscure the power to detect significant differences.

Dr. O'Callaghan stated that he is getting ready to start a trial of mifepristone in a GW animal model for hypersensitivity to cortisol induced neuroinflammation. He noted that he is going to implant pellets of mifepristone in the animals and said he would let her know what the results are.

Dr. Sullivan asked if the analysis included those who had PTSD and whether it would change the analysis. Dr. Golier said that she had selected out those with PTSD to determine whether that would have an effect on PCL scores. Dr. Golomb noted that things like pulmonary sleep problems produce some of the problems for PTSD, which is common in GW veterans. Dr. Golier stated that a full clinical evaluation was completed to screen those issues out.

Dr. Steele agreed with Dr. Sullivan that it would be interesting to see the results with psychological comorbidity and those without. She asked if the two phases were combined to look at the changes between drug and placebo. Dr. Golier said that those were the results that she had initially reported, where the verbal learning effect was seen. Dr. Steele asked if there was any type of measure for the veteran's global impression of health or other symptoms such as fatigue. Dr. Golier said there were no differences in symptoms based on the Kansas criteria.

Dr. Sullivan thanked Dr. Golier and Dr. Steele commented that there have barely been any pharmaceutical trials and said it was a bold move to try something noting that it made a lot of sense. Dr. Sullivan agreed and said that it made a lot of sense to try it and they both commended her for her work.

Chairman Binns adjourned the meeting for a short break before beginning the treatment discussion.

Committee and Panel Discussion: Treatment Development Discussion

Dr. Sullivan began the treatment panel discussion. She stated that there are currently not any known treatments for GWI or specific symptoms which have been scientifically validated. She noted that identifying viable treatments is a top priority, but it has been slow do to an incomplete understanding of the pathobiology of GWI and a previous lack of treatment funding. Dr. Sullivan noted that treatment trials started to occur in the past five years or so, which are beginning to publish data. There were four papers recently published regarding treatment of GWI including those from Dr. Amin regarding continuous positive airway pressure (CPAP), Dr. Conboy's treatment trial of acupuncture, Dr. Golomb's initial paper on CoQ-10 study, and Dr. Baraniuk's research with carnosine.

Dr. Sullivan explained that there were different treatment approaches that could be used for GWI including symptom-based treatments or treatments focused on proposed mechanisms of GWI and noted that both approaches are necessary. Symptom based therapies currently being investigated in GWI include acupuncture, CPAP, Exercise Resistance Training, pain medications, mindfulness, and nutraceuticals. Mechanism-based treatments could include glial modulators, innate immune modulators, anti-inflammatories, antioxidants, axonal transport stabilizers, and single treatments for multiple GWI symptoms. Dr. Sullivan noted that as pathobiological mechanisms are proposed more mechanistically based treatments have been funded. She presented slides showing symptoms based treatments, mechanism based treatments, and pre-clinical treatment studies that are currently being funded by the VA and CDMRP. Most clinical trials are currently ongoing and results are not yet available, as well as some animal model studies that will provide proof of concept.

Dr. Sullivan then discussed potential new treatment avenues such as flavonoids, glial modulators, other pharmaceuticals, and complementary or integrative therapy, noting that they could potentially be discussed during the treatment panel discussion. She stated that she also wanted to open the discussion to what the most promising scientific treatments to develop and what the best process would be to develop new ideas. Dr. Sullivan noted that a consistent case

definition should be used for comparable results and felt that GW veterans and practitioners should be surveyed for ideas. She asked whether there should be a clear goal for the number of treatment trials funded and whether more pilot studies should be encouraged as discussion topics for the panel.

Dr. Sullivan asked the panel members to discuss their current treatment trials before beginning the discussion.

Dr. Meggs began and explained his randomized double-blinded crossover trial which assessed two medications: low dose naltrexone and dextromethorphan. Both of the medications have previously been shown to down regulate microglial activation and reduce neuroinflammation. The participants were randomized to either take naltrexone or placebo for three months followed by a month washout period. The participants then took either naltrexone or placebo for three months. The procedure was the same for dextromethorphan. Dr. Meggs described the inclusion and exclusions criteria for his study. He also noted that roughly 50 people had been enrolled and/or completed the study, and noted that there was one more year left for the treatment trial. Outcome measures included visual analogue scales of mood, quality of life measures (SF-36), and cognitive tests (Connor's Continuous Performance Test), and each participant also had physical exams and laboratory measures as well. Dr. Meggs said that he had not formally analyzed the outcome data yet, but was encouraged when veterans reported feeling better and improvements in memory, noting some had expressed a desire to continue the medication once the trial was completed.

Dr. Sullivan said the study sounded very positive and asked how many participants they were hoping to have and whether he was combing the two medications in the drug trial. Dr. Meggs said the target was 60 people and that they were not combining the two drugs together because combining them would limit the number of individuals who could take the medications because of interactions with other medications. Chairman Binns asked what the dose level was for the naltrexone trial. Dr. Meggs said the low dose naltrexone is 4.5 mg and the dextromethorphan is a sustained release pill taken twice a day which is 100 mg. Chairman Binns referenced a study of low dose natrexone in fibromyalgia stating the researchers found participants not responding to the lower doses would find a higher dose of up to 9 mg effective. Dr. Golomb noted that a recent paper discussing treatments for autism gave naltrexone an A rating. Dr. Steele and Dr. Golomb asked about the FDA investigational new drug (IND) process and Dr. Meggs discussed his experience. Chairman Binns noted that this project all started with a presentation in 2006 to the Committee by Dr. John Huong with the National Institute of Environmental Health Sciences (NIEHS), and it was exciting that a year from now data will be available on this promising treatment trial. Dr. Davey asked if phase I or phase II studies were done with either of the medications in this particular population. Dr. Meggs said that the two medications are generic medications on the market that were shown to be safe and effective so those prior studies were not required. Dr. Steele asked what mechanism the study was funded under by the CDMRP and Dr. Meggs said it was a clinical trial.

Dr. Golier explained her intranasal insulin treatment trial funded by the CDMRP, which is being completed in conjunction with Dr. Sullivan and Dr. Maxine Krengel at the Boston VA and Boston University School of Public Health. Prior research has shown that intranasal insulin can

prevent progression of verbal decline in Alzheimer's disease, improve memory and mood in healthy participants and decrease the cortisol response to stress. The study is a phase II A, two-site trial looking at two doses of intranasal insulin. The design is an eight-week crossover trial with a one month follow up period. Dr. Golier stated that it may be worth discussing primary outcomes, but said a main outcome will be neuropsychological testing, specifically memory and attention for this treatment trial. Other outcomes will cover aspects of physical and mental health. Dr. Golier said the study had not started recruitment yet and explained that an obstacle was receiving the actual device from the manufacturer. She noted that an IRB concern was participants' glucose levels decreasing requiring researchers to monitor for signs of hypoglycemia.

Dr. Steele asked if any blood measures will be taken in this trial. Dr. Golier said that basic blood measures will be monitored such as glucose levels, but currently it is just the treatment trial and no other biological measures are included. Dr. Sullivan noted that there is a lot that they wanted to do, but right now there are not enough funds to do those additional aspects. Dr. White stated that the computerized versions of CPT are good for treatment outcomes because it can measure a much more precise range of answers. She stressed the importance of breadth and specificity for the tests suggesting computerized versions of CPT, finger tapping, and working memory tasks. Dr. Golier noted that computerized tests also ensure consistency of administration across sites. Committee members discussed issues of outcome measures and suggested that it may be helpful to have a meeting or add an appendix to the new RAC report for these types of issues. Difficulties with case definition and who will continue to qualify as a healthy control as the population continues to age was also discussed. Dr. Steele and Dr. Golomb discussed complications that can occur with crossover trials, specifically noting that medications may have lasting benefits. Dr. Golomb explained some problems she has had with crossover trials, but also noted the benefits and stated that a single crossover is easier to manage compared to a multiple crossover trial.

Mr. Rayhan discussed the double-blinded placebo randomized control study with carnosine from Dr. Baraniuk's lab at Georgetown University. Carnosine is an antioxidant that may benefit veterans with GWI as some believe that it is a reactive oxygen disease. There were 25 GWI participants in the carnosine trial with 12 veterans in the carnosine group and 13 veterans in the placebo group. He noted that the carnosine group had a significant increase in their Digit-Symbol Substitution Test score and a decrease in diarrhea symptoms. The dose started at 500 mg with an increase over the three month trial so that by the end of the trial participants were taking a dose of 1500 mg.

Dr. Golomb asked if a lot of other measures were assessed as well. Mr. Rayhan said a lot of other measures were looked at, but nothing else changed post-treatment. She asked if it was a parallel design study and Mr. Rayhan said that it was. Dr. Golomb noted that it was a small cohort. Dr. Sullivan asked if Dr. Baraniuk had any ideas for the next step for this treatment study to expand to a larger study. Mr. Rayhan said that he was not sure what Dr. Baraniuk had planned next. Chairman Binns asked if any of the veterans wanted to continue the medication, and Mr. Rayhan said a couple of patients did express interest, most notably because of the improvement in diarrhea symptoms.

Dr. Jesse asked about what treatments have appeared to be effective in veterans with GWI other than the Co-Q10 trial. Dr. Sullivan stated that only Co-Q10 has appeared effective so far, which is why treatment trials are so important in this field. Dr. Jesse asked if anyone has looked at statins in terms of treatment. Dr. Golomb stated that GW veterans are a group that would likely do very badly on statins. She noted that in the presentations today there was additional evidence of probable mitochondrial problems. Any conditions linked to higher rates of mitochondriopathy are predictors of worse outcomes with statins including diabetes, high triglycerides, and any of the metabolic disorders. Dr. Golomb said statins tend to cause a much worse clinical state that stays with patients for the rest of their lives with only a chance of a small improvement once they stop taking the statins. She said that GW veterans would potentially be a catastrophic group to use statins on as a clinical agent. Dr. Jesse said that the positive aspects of statins would seem to affect the same aspects as the Co-Q10. Dr. Golomb stated that statins are antioxidants in younger healthy people and they are pro-oxidents in a subset of older people. She noted the pro-oxidant effects are tied to the adverse effects which are linked to every condition with a known relationship to higher mitochondrial problems.

Dr. Sullivan thanked Dr. Golomb and noted that the discussion would move from the clinical treatment discussion to the pre-clinical discussion.

Dr. O'Callaghan noted that animal models allow for direct examination of brain tissue at multiple time points. The use of animal models allows for persistent, molecular, cellular, and functional effects associated with individual or combined exposure from the GW to be evaluated. He said that with animal models you can look at treatments that either treat symptoms or that target underlying mechanisms. Diisopropyl fluorophosphate (DFP) causes neuroinflammation and is used as a sarin surrogate to create a "sickness" behavior mouse model. Dr. O'Callaghan stated that early on they tried to apply corticosterone, an anti-inflammatory, as a treatment and said that it unexpectedly made the DFP induced neuroinflammation markedly worse. He said he used this model of physiological stressor of corticosterone and a nerve agent as an animal model of GWI that can be used to test specific hypotheses and treatment interventions.

Dr. O'Callaghan explained that his current preclinical treatment trial of minocycline. He stated that minocycline has been used in man for many years as an antibiotic and is well tolerated even in high doses. Minocycline has shown strong anti-inflammatory properties in rheumatoid arthritis and in multiple animal models of inflammation. Dr. O'Callaghan noted that minocycline recently failed miserably in a large ALS clinical trial, but noted he did not think it was unexpected because minocycline is anti-inflammatory and does not necessarily get to the neuroprotective or neuroregenerative aspect required at that stage of ALS neurodegeration. He stated that so far minocycline has been shown to suppress some, but not all mediators of neuroinflammation in the GW mouse model. Data was collected during a short-term time point, a middle time point of 90 days, and then 180 days which is a close mimic to the 20 year time point for GW veterans. Multiple brain regions and other tissues have been studied as well as serum markers that are currently being analyzed. Dr. O'Callaghan stated that when PB and DEET are added to the model the neuroinflammation is not worse, but the effect of the minocycline is diminished.

Dr. Sullivan thanked Dr. O'Callaghan and agreed that it was important to point out that minocycline may still be effective in GWI even though it was not effective for ALS. Dr.

O'Callaghan noted that he views this is a symptom-based treatment because they are treating the neuroinflammation, which is not necessarily the underlying cause of GWI. Dr. O'Leary stated that minocycline has been found to be most effective earlier on in the treatment of rheumatoid arthritis. He asked how that plays out in Dr. O'Callaghan's experiment. Dr. O'Callaghan said that minocycline only treats the neuroinflammation, which does not treat the damage. He stated that it is the damage that causes the neuroinflammation. Treating the neuroinflammation does not necessarily mean that it will mitigate the disease or treat the damage. He noted that a disease like rheumatoid arthritis is already on going so if you do not treat early than you cannot protect against the neuroinflammation as it contributes to the underlying pathology.

Dr. Steele stated that there was a large clinical trial of doxycycline in GWI, which has a similar mechanism of action. She said the case series done around that reported great results, but there were mixed impressions during the clinical trial. There were benefits after a few months, but long term there were not any. Dr. Golomb noted that there were a lot of odd things about the study that may have affected the results. Dr. O'Leary noted that minocycline is much more effective at crossing the blood brain barrier than doxycycline. Chairman Binns noted that the principle investigator of the doxycycline trial had criticized his own study noting that they used doxycycline without investigating potentially more effective similar options.

Dr. Sullivan asked Dr. Crawford to discuss some of the preclinical work being done at the Roskamp Institute, as well as discuss the translation to clinical from preclinical treatment development.

Dr. Crawford stated that her lab has taken two different approaches to examine neuroinflammation and immune dysfunction. She said that they had examined the effects of permethrin and PB on specially bred (CD40 receptor deficient) mice. She indicated a lot of variability in behavioral data and noted that they still needed to look at changes in the brain. Dr. Crawford stated that they have also done work with an anti-inflammatory nutraceutical, a kappa B inhibitor. She said they tested the compound in mice and just finished analyzing the behavioral data. She noted that it appears as though the mice are performing worse and not better. She indicated that they would like to try another anti-inflammatory with a different mechanism of action.

Dr. Crawford then discussed the treatment development process. She asked Mr. Rayhan if they looked for any evidence that there were actually antioxidant effects in the patients. Mr. Rayhan said that they did not measure any antioxidants or antioxidant effects specifically in their study. Dr. Crawford said as they move through a pre-clinical development stage, that all those things are considered including blood brain barrier penetrance issues. She noted that once things move into clinical trials it is still nice to have some sort of surrogate biomarker or some sort of measure of response. She emphasized that this allows researchers to determine if the treatment did not work or if it did not work because it did not affect the intended target. Mr. Rayhan stated that they did do brain scans before and after with the carnosine, but stated that they have not had the chance to analyze the data. Dr. Crawford stated that it is good to have something that may indicate if a treatment would be effective if altered in some way such as increasing the dose or extending the treatment period.

Dr. Steele stated that she had seen literature comparing the relationship between nicotinic receptors and neuroinflammation and asked Dr. O'Callaghan and Dr. Crawford their thoughts regarding Dr. Kevin Tracy's work. Dr. O'Callaghan said that the data Dr. Tracy presented is opposite of what he has found with DFP because it was expected to be anti-inflammatory and not pro-inflammatory. He said that he did not think it would have a cholinergic effect. Dr. Golomb noted that some other researchers have theorized that some nictonic receptors should be neuroprotective.

Dr. Steele moved on to ask Dr. Davey about a large data set collected by Dr. Han Kang which was difficult to analyze, and asked about the possibility of the VA Office of Public Health (OPH) sharing data records with other investigators. Dr. Davey said that she could look into that particular analysis. Chairman Binns asked if OPH would be able to join the VA Office of Research and Development (ORD) to determine if there was a way to share data with other qualified researchers. Dr. Davey commented that it is something OPH would like to look into. She stated that after giving investigators a chance, releasing it for public use may be a good idea. Dr. Steele commented that other organizations share data and asked if there was a mechanism in place for the VA to share de-identified data. Dr. O'Leary stated that there are data use agreements and that they are currently working on maximizing data use agreements and determining how to go about sharing data in a public database. Dr. Jesse said part of the problem is that the investigators for each project control who has access to the database and noted that OSTP has put out some guidelines. He said that protecting patients is the priority and said they are currently working on agreements that would allow a researcher to come into a controlled VA environment, which would also allow them to ask the questions necessary about the data.

Chairman Binns asked if there were any ideas about ways in which to build processes other than individual investigator proposals to try and generate treatment ideas faster. An audience member stated that the veterans should be polled. Dr. Sullivan stated that a large survey is occurring through Boston, which asks those questions and that Dr. Golomb is also conducting a similar project, but no data is available yet for either study. Dr. Jesse stated that patients could also be queried, but said that they have been spending about a year and a half trying to determine what that means, and determining who the patients are. He stated that it may be coming to fruition soon and said it may be possible for the Committee to be involved in the process.

Chairman Binns stated that there has been an idea since about 2004 that would involve the creation of a group to investigate treatments. He noted the idea was that clinicians do not have time and are not always involved in research. The group would investigate the procedure heard about from a veteran or other clinicians, and then would develop research studies from those ideas. Dr. Steele stated that there was a request for applications (RFA) out in 2005 that was similar to that concept. She said it would essentially bring together everything about treatments for GWI or for conditions that are similar to GWI. She noted that UT Southwestern was funded partly for this reason, but their concept ended up being different in the end.

Dr. Steele stated that sitting at a table together and discussing these topics seems to be effective. Dr. Jesse agreed and proposed the idea of potentially have meetings or virtual meetings about treatments in GWI to facilitate further discussion. Dr. Golomb stated that it would also be helpful to have periodic meetings between researchers currently working on treatments to bounce ideas

off of each other and ensure that data will be interpretable and comparable. Dr. O'Leary noted that he thought the new report the Committee was working on would help facilitate the development of treatments, and he agreed that phone calls between investigators would be helpful. Chairman Binns stated a hybrid may be best with a couple of people at VA working on it full time, and others joining in virtually periodically. Dr. Jesse noted that at times it is best to start out with a face to face meeting, but agreed that technology has allowed for good virtual meetings as well. Dr. Davey noted that for other diseases there have been meetings where everyone came together, pharma, researchers, and academics, and noted that its success has stood the test of time.

Albert Donnay, a member in the audience then stated that the VA needs to have a policy on record retention, noting that in the past some investigators have made their own decision about discarding a data set. He noted that it is not difficult to archive data sets, and would allow for new researchers and graduate students to access data sets. He emphasized the need for objective outcome measures, and suggested the study of oxygen treatment could be useful. Dr. Golomb noted that she had considered using oxygen treatment in the past. Chairman Binns thanked everyone for their contribution and moved on to the committee discussion portion of the meeting.

Committee Discussion

Dr. White began the discussion talking about the 2013 RAC report, noting that it was discussed during the teleconference meeting, when the Committee reviewed a preliminary draft. The outline has been revised for the current version of the report, with the goal of updating the findings since the 2008 report. She reviewed the outline of the report, noting that Dr. Steele, Dr. O'Callaghan, Chairman Binns and her own group will be working on completing the report and stated who would be working on which section. Dr. White stated that there were currently detailed tables compiled for the report and she was hopeful that a draft would be done by August, with a finalized report in the fall. She said that the timeline will depend on the ability of the Committee to meet. She stated that it is a large effort, but noted it will be shorter than the 2008 report. Dr. Bloom asked to be provided with a bibliography of all the human brain data in one place, stating that it will be helpful for the IOM panel that he will be serving on.

Dr. Sullivan then discussed the VA GW Research Portfolio. She noted that GWI research has traditionally been underfunded; noting that traumatic brain injury (TBI) in OEF/OIF veterans had received significantly more funding in the last 5 years than the total amount of funding for GWI research over the past 22 years. Therefore, funds need to be used for the most relevant and important topics with regard to GWI research. Dr. Sullivan showed a slide listing the criteria for inclusion into the VA Gulf War research Portfolio and noted that there has been disagreement in the past over what should and should not be included in the portfolio. She discussed VA expenditures and noted that it varies for what the Committee considers GW specific research versus peripheral research. She noted that there was a trend in the last couple of years of an increase in specific GW research and less peripheral research. Dr. Sullivan noted that there had been some questionable inclusions such as expensive scanners or machinery that were not currently being used for research with GW veterans. She concluded that for inclusion in the portfolio the studies should predominantly include GW veterans, topics should be prioritized

according to the VA GW strategic plan, and pre-clinical studies should be directly relevant to GWI. Dr. Sullivan stated that she feels the numbers can be further improved if the Committee makes a solid recommendation of what should be included in the GW portfolio.

Chairman Binns appreciated being shown the criteria, because he felt that the criteria needed to be addressed to resolve the issue. He asked if studies that include multiple eras of veterans should be included in the portfolio, noting that maybe it should reflect the percentage of GW veterans' participation. He referenced the ALS brain bank, noting 1 in 60 is a GW veteran, but all of the money for that project was included in the GW portfolio. Dr. Golomb agreed and stated that there are conditions elevated in GW veterans, but that all the studies on those conditions should not be included in the portfolio, unless it is specifically addressing the condition in GW veterans. She noted that funding for those topics could come from other sources, but funding for GWI will not come from other sources. Dr. Sullivan supported Dr. Golomb's statement. Chairman Binns stated that some things may have been included because there were not many projects in the pipeline. He said that now is the time to re-set the strategy however, and to build a better GW program as there are more proposals and ideas currently than any time in the recent past. Dr. Jesse said that he was not aware that there has ever been a cap on GW funding. He asked if the Committee has ever felt that strong proposals have not been funded.

Chairman Binns said that he thought there were several good proposals that had not been funded in the past and noted that was a good segue to the next topic and moved on to discuss strategies for getting more good proposals funded. He noted that in the early 2000s the problem was that the proposals were reviewed by standing merit review panels. He said the people on the panels did not know anything about GWI, except the belief that it is caused by stress, causing proposals to not be funded. He stated that he does not know what the mechanism is for funding now. Chairman Binns felt that there was a good and bad example of funding in the last round of grant reviews that he was aware of. He said the good example was the funding of the light therapy project in Boston, but the bad news was that Dr. Georgopolous was not funded because the people on the Committee did not understand the concepts that he was proposing to study. Dr. Golomb and Chairman Binns noted that he was a good example of someone who works in the VA, who is highly knowledgeable, highly credentialed, and who has interesting preliminary findings but was not getting funded. Chairman Binns asked for ideas on how to improve the merit review panel process.

Dr. Golomb stated that it would be nice to have a mechanism for funding studies and giving priority to studies that would have a greater impact, even if the group had mixed investigators and it was not just VA employees. Dr. Steele stated that there used to be a separate grant review panel for GWI research reviews. Dr. Kalasinsky stated that there is still a GW specific review panel. He said that he recruits people for that, stating that there are core members and then ad hoc reviewers, noting that he asked Dr. Sullivan for some recent recommendations. He pointed out that the list is public information and noted that there are a lot of qualified people currently doing the reviews. He expressed that they go to great lengths to have GW knowledgeable people on the panel, and he noted that they also have people specifically in place for clinical trials that go to great lengths to determine if the trial would be successful. Dr. Sullivan said that it is good to hear that when investigators take the advice of the reviewers, and then resubmit their proposals, that they stand a chance of then getting them funded. Dr. Kalasinksy agreed that was

good and noted that investigators are allowed two resubmissions of their proposals. Dr. Sullivan stated that she did give names for the review panel, but noted that she had heard from some researchers that some comments from reviewers were inappropriate. She specifically cited an example where she was told that one reviewer said "there is no such thing as GWI so why would there be a treatment for it." She noted someone like that should not be on a GW review panel. Dr. Kalasinksy stated that he has never seen a review like that and it must have occurred before his time at VA. He stated that he could get the Committee the list of reviewers for the past year if that would be helpful.

Dr. White commented that in her experience on CDMRP panels, there were times when reputable investigators got interested in doing GWI research, but did not have enough background knowledge and their proposals were not developed enough to be funded. She said to develop new researchers in the field; it would be a good idea to provide some mentoring in GW research and to demonstrate good GW proposals to them. She noted that it could just be basic ideas such as case definition, and how to choose subjects. Dr. O'Leary agreed with Dr. White and said that when possible they will reach out to investigators when they see a promising idea. He noted that some investigators are more receptive than others. He stated that when a veteran is willing to put their body on the line for a clinical trial, they want to ensure that the trial has a sound design and is safe. Dr. Jesse agreed noting that there is a difference between having a good idea and turning the good idea into a good executable protocol. He said maybe one of the things that the Committee could partner with is to identify good ideas that may not get funded the first time, and work with them to make it fundable. Dr. Golomb agreed that it may be helpful to even create a document with an outline of essential parts of GW research for potential investigators.

Dr. Golomb asked further about the funding of studies noting that there was at a time that the VA was only interested in funding large studies to ensure appropriate power. She noted that they did not fund smaller studies that may give information as to whether a larger scale trial would be effective. She stated that since VA would only fund large studies, only a few could be funded because they were so costly. She asked if the VA will now fund smaller projects. Dr. O'Leary said that they do want to have enough power, but said that smaller studies are important to determine feasibility of practice as well. He stated that the VA was open to smaller trials, but cautioned researchers to be careful with their effect sizes. Dr. Davey said that she sat on an NIA panel and noted that they discussed setting aside funds to mentor new researchers.

Chairman Binns asked if it was appropriate to put in an appendix on how to design a proper GW research study in the new report. Dr. Sullivan stated that it was something that they could work on separately with Dr. Kalasinksy that could be given to research investigators. Dr. Steele said that there was some of that type of information in the 2008 report, but it was presented more as methodological advice. She thought it may be helpful to provide clearer guidelines for research investigators. Dr. Golomb agreed with this suggestion.

Dr. Steele discussed the issue of funding smaller studies, noting that she had heard of researchers getting rejected for their smaller studies due to a lack of pilot data. She emphasized the need for a funding mechanism for pilot studies within the VA, like the CDMRP has. Dr. Kalasinksy said the VA does not necessarily require preliminary data, but stated that if preliminary data does not exist there needs to be a good explanation of why the project should be done. He stated the Dr.

Steele was correct and that there is no pilot treatment RFA through VA because the numbers are usually very small and a positive effect is not normally seen. He also stated that if there is not enough evidence that a treatment is safe, than it will not be funded. Dr. Kalasinsky stated that if there was evidence that the treatment was safe, than the researcher should apply to the full trial RFA. Dr. O'Leary stated that most of the VA regular merits are the size of what many think of as pilot data, at least in the terms of FDA submissions. He said that there does not need to be a special mechanism, because the mechanism in place is already accommodating what is needed.

Dr. Jesse clarified that the VA has not held back good research because there is not enough money. He agreed however, that there was probably a sense that the VA has been less than accommodating for some of the research that has been funded. He noted it might be because they have not worked with investigators enough to make a great idea work. Dr. Jesse said that having the Committee put out clear guidelines for GW research would be helpful.

Chairman Binns stated that this discussion had been helpful and stated that Dr. Kalasinsky definitely deserved credit for the time that he has put in and the improvements that have occurred since he started his position overseeing the GW research program. Dr. Sullivan clarified that the problem was not that the funding had been capped. She stated that the problem was including studies not directly relevant to GWI, because the VA has said they have put in a lot of money in the research, but has yet to see positive results. Chairman Binns stated that VA could put a portion of the funds representative of the portion of GW veterans in the study in the portfolio. Dr. Sullivan stated that she felt that the study should only be included if the majority of the participants were GW veterans. Dr. Golomb agreed and stated that the majority of the participants should be GW veterans for it to be included in the portfolio. Dr. White stated that basing it on proportions was difficult, but also said the term majority subjects was not a clear term. She said there could be studies in which GW veterans were compared to another patient population, but the study was still focused on GWI. She expressed that the studies should be included in the profile if the main idea or hypothesis is focused on GWI and clarifying something about GWI.

Chairman Binns stated that he hopes the VA will reconsider the charter changes, and felt that all the Committee recommendations had been and continue to be regarding research, which is clearly in the charter. He thanked everybody for their participation and adjourned the meeting for the day.

DAY 2

The June 18th, 2013 meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses (hereinafter referred to as the Committee) was held in the Sonny Montgomery Room (Room 230) at the U.S. Department of Veterans Affairs Central Office, 810 Vermont Avenue, NW Washington DC.

Welcome and Introductory Remarks
Mr. James Binns, Committee Chair

Chairman Binns called the meeting to order at 8:30 AM. He stated that the program for the first half of the morning was to review the VA Gulf War Portfolio. He introduced Dr. Victor Kalasinsky and Dr. Robert Jaeger.

Dr. Jaeger introduced members of the VA staff including Dr. Jesse, Dr. O'Leary, Dr. Kalasinsky, and Dr. Davey. He stated that the level of VA representation is indicative of the VA's level of concern. He felt that all the presentations would have good tiding for GW research in terms of proposals being funded and studies being done. He took a moment to recognize Dr. Joel Kupersmith, who recently stepped down as the Chief Research and Development Officer. He stated that Dr. Kupersmith made many contributions to raise the profile of GW research.

Update of VA ORD Gulf War Research Portfolio
Dr. Victor Kalasinky, Designated Federal Officer

Dr. Kalasinsky stated that the GW Research Strategic Plan was approved in February, noting that it was a modified version of the one that was seen by the Committee last June. The strategic plan was posted on the VA website and every Committee member received a copy. He said there would be an annual review of the strategic plan, and modifications will be made as needed. Dr. Kalasinsky noted that the strategic plan included many of the topic areas that the Committee had been recommending that the VA focus on over the years and he noted that the VA is moving forward to implement those recommendations.

Dr. Kalasinsky then discussed the proposals that came in for the October 2012 GW review panel and the February 2013 review panel. He noted that 15 proposals were submitted in October and 4 were recommended for funding and 17 were submitted in February and 3 were recommended for funding. He said that ORD was getting increased numbers of proposals and increased numbers were being funded. He noted that his office works with the PI if the project is close to being funded so they know exactly what they need to do for the next round of grant reviews. He noted that another review panel was coming up in July. Dr. Kalasinsky noted that there were 22 applications for review for the next panel and two had been removed for administrative reasons. Dr. Sullivan noted that it was quite an improvement in the number of proposals submitted and asked why two of them were previously taken out for administrative reasons. Dr. Kalasinsky noted one was not appropriate for the RFA and the other project had a PI who had not gone through proper eligibility approval. He stated that only 5 of the 32 proposals from last year were resubmissions, meaning that there were new researchers applying.

Dr. Kalasinsky showed a list of active projects noting that the Committee had previously seen most of them before as they were currently ongoing studies. He pointed out that three projects were newly funded and were projects that had finally gotten started since the February teleconference. He noted there were other projects that were close to receiving their funding and that he was just able to list the topics of those projects. Dr. Kalasinsky reminded the committee that once the projects were recommended for funding the projects needed to clear IRB and IACUC, but said these particular projects were just waiting on the last of the paperwork so he

could mention them. Dr. Steele asked if they were already listed on clinicaltrials.gov. Dr. Kalasinksy said they may be, but that they cannot be released to the public until everything was approved and completed. He noted that the VA does not list them on clinicaltrials.gov, but rather the PI lists them there. Dr. Jesse clarified that these have been approved and that funding is contingent upon each site getting IRB approval among other approvals. He stated that they would be officially announced once the sites were cleared to begin the project.

Dr. Kalasinsky displayed the criteria used for inclusion in the GW research portfolio and then demonstrated the funding over the last ten years. Funding in 2011 was $5.6 million and $6.7 million in 2012. He stated that the estimated funding for 2013 was currently around $7.8 million.

Dr. Kalasinsky stated that there was a contract with the IOM for the GW case definition project. The project officially started on the first of May and will run for a year. The panel has been selected and there is a public meeting June 29th where Dr. Kalasinky and Dr. Jaeger will be presenting some information, as well as some of the Committee members. Dr. Kalasinsky summarized some topics already discussed such as the CSP #585 and GW Era Cohort and Biorepository project and noted the Biorepository brain bank in Boston officially started last July. He stated that the VA is planning a joint program review with the DoD, which will probably start in July. The GW Veterans' Illnesses Task Force report has been posted online for the 30 day comment period and will be modified according to some of the comments. He noted the report to Congress was currently being worked on.

Dr. Sullivan asked if physical copies of the annual report to Congress are still made or if they are only online now. Dr. Kalasinksy said there were no longer going to be physical copies and that the report was now a PDF on the VA website. Dr. Steele asked if the joint program review will just be an administrative meeting between the VA and the DoD. Dr. Kalasinsky said that it was strictly a VA and DoD administrative review. Chairman Binns asked if ORD was the point of contact with IOM for the case definition panel and asked who drafted the charge, noting that it used language from the previous charge that was drafted by OPH. Dr. Kalasinksy stated that the ORD was the point of contact and said he had drafted the charge noting that he did use the same language, but added to it. Chairman Binns commented that the VA's actions appear to be contradictory at times. He stated that in the last 18 months there had been a lot of positive improvements that the Committee is appreciative of, but noted that there were other actions by the VA that seemed to undermine their own work. He noted the continued attempt to imply that GWI is a psychological problem fundamentally works against everything else the VA has been attempting to do. He emphasized that the Committee does appreciate the progress that has been made. Dr. Sullivan agreed. Dr. Jesse stated that they would come back to this topic, but he would like to finish up the other presentations first.

Dr. O'Leary stated that he wanted to add something to the presentation. He noted that in conversations with local veterans it has become clear to him that they should consider expanding health services. He said they need to focus on the development of health services, and noted the need for research to help improve clinical care. Dr. O'Leary noted that they were really looking forward to the new RAC report and praised the 2008 Committee report. He said that he feels the report and recommendations from the Committee will help them focus the GW research program. He noted that it may help to target researchers to have them redouble their efforts to

expand knowledge on certain topic areas. Dr. O'Leary stated that he wants to be able to fund every strong proposal that they receive, and that the Committee should not mistake where the VA is now with where the VA wants to be. Chairman Binns said that Dr. O'Leary's comments were encouraging.

Dr. Jesse asked Dr. Davey to start her presentation. Chairman Binns stated that the Committee was happy to have OPH back, noting their importance to GW research.

Update of OPH Gulf War Research Program
Dr. Victoria Davey, VA Office of Public Health

Dr. Davey started her presentation with a discussion on the follow-up survey study of a national cohort of GW and GW era veterans. She explained that the project is on its third phase and serves as a comprehensive assessment of health and wellness, meaning it goes beyond the scope of chronic multisymptom illness (CMI). Domains include physical health, mental health, woman's health, and functional and social status. The study was designed to provide a population level assessment of overall health and to provide a sub study of medical records validation review. Dr. Davey showed a slide demonstrating the overall timeline of the project and explained that data collection will end July 1, 2013 and initial reports will be anticipated in mid-2014. The current response rate was about 49%, which was an increase from the 2005 response rate. More deployed veterans have responded than non-deployed veterans, and most of the respondents have been males.

Dr. Davey moved on to discuss the medical records validation sub-study, noting that the plan was to contact a random sample of 2000 veterans asking them to participate. Veterans who reported a doctor's visit or hospitalization and reason over the last year will be eligible for the sub-study. They will attempt to have a proportional amount of paper and web-based respondents, and Dr. Davey noted that the goal is to have about 50% outpatient and 50% hospitalization records. The veterans self-reported medical conditions will be verified in the medical records to assess the degree of agreement, which will serve as a validation measure of the self-report survey.

Dr. Davey discussed the sub-study of veterans expressing suicidal ideation, noting that it was both a clinical outreach as well as a study on veterans who expressed suicidal ideation in their survey. She explained that suicidal ideation was measured by the PHQ9 and a mental health clinician followed up with anyone expressing suicidal ideation. The clinician team was composed of social workers and psychologists, and was coordinated by the Washington DC WRIISC. As of June 1st, 11 percent of respondents expressed suicidal ideation. All of the veterans expressing suicidal ideation were called and most were reached. About 3.6 percent were immediately transferred to the VA crisis line and the others were provided with resources as necessary including the crisis line phone number, connection to local resources, and mental health education. Dr. Davey stated that a manuscript had been submitted for publication to a peer-reviewed journal. She noted that this extends previous work done by the VA and may have future implications for the relationship between survey researchers and survey respondents.

Dr. Davey moved on to discuss the Post War Mortality Study from Neurologic Diseases. The study is a follow up of the mortality of specific neurologic diseases of the entire population of GW veterans and GW era veterans. The conditions studied were clearly delineated in records including brain cancer, multiple sclerosis, Parkinson's disease, and ALS. The cohort was previously examined at 2, 7, and 13 years after the war, with those results already published. Information was collected from the National Death Index and medical records were collected with consent from the next of kin. Adjusted rate ratios were calculated and compared to ratios in the US Population. Dr. Sullivan asked if they were able to get information from every state to create the national ratio, noting that it had been a problem in the past. Dr. Davey stated that she would have to check, but that she believed that they were able to. Dr. Golomb asked if only the primary cause of death was looked at because most people with ALS die from respiratory problems. Dr. Davey said that she would check, but believes they also looked at the second and third cause of death.

Dr. Davey noted that the medical records were currently being reviewed and some preliminary analyses were being done. She stated that the next step was to expand the data to the latest available National Index Records and to also include OEF/OIF/OND veterans who also had neurologic mortality. Dr. Steele stated that it was great that the mortality study was moving along and noted that in the past the deployed veterans were compared to non-deployed veterans, since veterans tend to be healthier than the average population. She also asked if they would do a sub-grouping analysis similar to what was done in the past where veterans who were downwind from the Khamisiyah plume and veterans highly exposed to oil well fires were studied separately as well. Dr. Davey said that she does not think that was being done. Dr. Steele noted that the major findings from the previous studies were related to these specific groupings.

Dr. Davey then discussed the Health Surveillance for a New Generation of U.S. Veterans which is a study of OIF/OEF veterans. The study surveys 30,000 deployed and 30,000 non-deployed on health, exposures and functioning. Data collection occurred in 2009-2011 and data analyses and manuscript preparation are currently underway. Analyses already completed included a method overview, prevalence of respiratory health outcomes, development of statistical weighting, and infertility history. Rev. Graves asked why she was presenting information on OEF/OIF and asked if they were going to be grouped together with GW veterans. Dr. Davey stated that it was a separate study and that she was keeping the Committee up to date on current projects and feels that there is a lot that could be learned from this study. Dr. Golomb emphasized the need to keep the two groups separate and Dr. Steele asked if they were collecting any information on chronic multi-symptom illness and if so how the rates compared to GW veterans. Dr. Davey said she would have to check. She mentioned that analyses were currently underway for the new generation study that included TBI, PTSD, illness and functional status, complementary and alternative medicine (CAM) therapies, and prevalence of military sexual trauma. Dr. Davey then showed a list of planned analyses for this study.

Dr. Davey summarized that the findings from all the studies help the VA understand the postwar experience for GW veterans and OEF/OIF veterans who may have service related illnesses. She said the studies help in the development of policy and the design of further studies. Ongoing projects include collaboration with the Millennium Cohort Study, the Veterans Health Examination Survey which looks at the health of all veterans compared to the US population and

will allow sub-analysis of more specific cohorts, and the continued longitudinal follow-up of deployed cohorts.

Chairman Binns stated that he was impressed with the follow up of veterans who had suicidal thoughts and noted that he thought it was included because of Dr. Coughlin's insistence. He said Dr. Coughlin reported issues not addressed in the study under sworn testimony which called into question the construction of the study and the attitude of some of the VA staff. Chairman Binns asked if Dr. Davey has looked into any of the charges that Dr. Coughlin had made. Dr. Davey stated that Dr. Coughlin was instrumental in bringing attention to the rates of suicidal ideation, but noted that he did not lead the study design. She said she cannot comment on the investigation following Dr. Coughlin's testimony and said that it was still ongoing. She stated that if she thought any of her staff swayed research they would no longer be doing that research and noted she believes she has a group of ethical researchers. Chairman Binns said most of what Dr. Coughlin said rang true to him and asked about another issue regarding the national survey study contract noting that he was told in a prior Committee meeting by OPH staff that changes could not be made to the survey due to costs that would be incurred. Dr. Davey stated that the primary pressure was getting a scientifically sound survey out in a timely fashion though there were some contractual pressures. Dr. Jesse stated that he did not think that issue would be resolved today and said the important thing was that the survey was moving forward and was as complete as possible.

Dr. Meggs asked if the survey asked questions about sleep, fatigue, attention and memory problems and chronic pain. Dr. Davey said she would get the Committee the survey. Dr. Steele stated that it was great that the response rate was high, but noted her concern at the high rate of suicidal ideation. Dr. Sullivan stated that she agreed and thought it was an important thing to have the call back and referral process in place. Dr. Steele again emphasized the importance of the sub-group analysis in the mortality study and Dr. Sullivan agreed particularly mentioning the significantly increased rate of brain cancer mortality within sarin exposed groups.

Dr. Sullivan then asked if the children's health study data had been lost. Dr. Davey said no one in her office was around during that study, but they have done a search for it. She stated that there was a registry of children and spouses and a separate study through the ORD. She said the ORD study was intact, but it appears as though the registry data was lost during a transition. Dr. Davey said the more robust data was preserved. Dr. Jesse noted that it was not OPH that lost the data, but a server issue and said an exhaustive search was occurring to try and recover the data. Dr. Steele commented that while the data exists, a paper has never been published on the children. Dr. Davey stated that there was a DoD report that discussed some of the data. Dr. Jesse noted this conversation relates back to the previous day's conversation on open data and the ability of others to analyze exiting data sets. Dr. O'Leary stated that they would talk about it and if possible they would try to figure out how to increase the availability of data. He said it was not an instantaneous process, but they would work together and try and figure it out. Dr. Davey stated that she thought there were some papers on the children's data.

Dr. Sullivan asked if Dr. Davey knew when the next Gulf War Review would be coming out noting the veterans use it and find it helpful. Dr. Davey said she did not know and would have to ask her staff.

Chairman Binns stated that they had now set aside time for Dr. Jesse to speak.

Discussion of Overarching VA Approach to Research
Dr. Robert Jesse, Principal Deputy Under Secretary of Health

Dr. Jesse commented about the process of the Committee's meetings. He said that Dr. Kalasinsky's comments were not meant to be cagey or dodging, but he noted that there were issues that cannot be talked about publicly. He noted in the future it might be wise to also have portions of the meeting that are a closed session so more in-depth conversations about grants and funding can occur. Chairman Binns stated that he thought that was an excellent idea and noted that the Committee could hold executive sessions. He said that the law says that the Committee should review proposed grants and ideas, but currently the Committee is only informed once something is accepted and becomes public knowledge. Dr. Jesse noted that when there is a closed session that it would need to go in the federal register. He said that a closed meeting would allow for greater openness between the Committee and VA staff. Dr. Steele said that she thought it was an excellent idea. Chairman Binns added that the VA needed to have a proactive stance about raising issues while they are still open for discussion, noting that the Committee is finding out about projects after they have already been approved and no longer open for discussion or any type of alteration. He said the Committee is unaware of projects so the VA should note when the Committee might want to have an executive session at the next meeting to discuss an issue.

Dr. Jesse stated that is a communication issue, and noted that it is a good segue to the next thing he wanted to discuss, the IOM case definition panel. He said he saw the agenda and noted that the Committee would have representation at the meeting, but he asked if the Committee wanted to discuss their feelings on the scope of work that was written. Dr. Steele noted that case definitions are challenging, but essential. She stated that it has been a long time and currently there are about 10 case definitions for GWI. Writing a case definition for something that does not have biomarkers, and will therefore be based on symptoms is a complex task that requires individuals who are very familiar with the research. She said the panel should be composed of people who have done research on GWI, have worked with the clinical population, who know what works and what does not, and who know the analytically different research methods that could be used to fine tune the symptom pattern. Dr. Steele said that as part of the strategic plan process there was a group convened to go over those considerations and to make recommendations around how a case definition should be developed. She noted that was mostly retained in the final strategic plan, emphasizing the two essential elements that there should be a comprehensive analytic approach and an expert consensus process after the analytic results. Dr. Steele said that assigning the project to the IOM, which basically does literature reviews, goes against both processes outlined in the strategic plan. Dr. Steele stated that the IOM has never done a case definition until last January when they identified a definition for multisymptom illness for the treatment report that they prepared. She said that they did not even explain how they created that definition.

Dr. Jesse stated that his understanding is that the IOM is good at convening experts, but noted that he cannot speak to the analytic piece. Dr. O'Leary stated that IOM is independent so the VA

trusts their judgment, noting that the VA cannot tell them what to do. He said the IOM does have good analytical capabilities available to bring in data. He said that what the IOM will choose to do is something that he cannot predict, since IOM has so much independence. Dr. O'Leary said he believes the IOM will have a reasonable approach, but noted that he cannot guarantee it will occur in a way that the Committee or ORD would prefer.

Chairman Binns stated that the contract does not direct a data or analytic review and agreed that IOM would have the capability to do that. He said the contract language is virtually the same as the contract language that was used in the previous IOM treatment report, which is open-ended directing the consideration of all literature in any population of similar symptoms. Chairman Binns stated that it will create a case definition that is so broad that it will capture almost any condition. He noted that it will be impossible to distinguish between groups during research. He said that this is what VA directed IOM to do. He also noted that the panel they convened are experts in other fields, but are not experts in GWI. Only three of these IOM panel members have ever done GW research and those that have were primarily on the side of suggesting that GWI is the same thing that happens after every war. Chairman Binns said some of the other members have served on other panels that produced reports saying that there was not enough evidence to determine that exposures are linked to illness. Finally, he stated that there was also a former president of the American Psychosomatic Society on the IOM panel, as there has been on the last 5 panels.

Dr. Steele stated that she has never heard of a case definition being developed by people who do not do work in the topic area, especially when it is a clinical definition that lacks biomarkers. Dr. Jesse agreed that creating a clinical case definition is complex. He asked what the Committee's impression is of the intent of the public hearing the IOM panel is holding next week. Chairman Binns stated that IOM received a lot of criticism last time surrounding the treatment panel and noted that they were trying to include a more representative group to speak to this panel. He noted that it does not change the fact that the assignment of the panel was wrong and said that it will not change anything fundamentally in the end.

Dr. Bloom said that he has served on panels before and emphasized that it is not written in stone that the panel has to do exactly what the original statement of task states. He stated that if the sponsor indicates that they are expecting certain requirements then those requirements can be fulfilled. Dr. Bloom and Chairman Binns both agreed and stated that what is required was for the sponsor to interact with the panel staff and to initiate that process. Dr. Bloom said the original statement of task could still be modified.

Dr. Jesse stated that it appears as though the Committee members attending the panel meeting had a significant amount of time to speak. He said that if necessary the VA can speak with IOM after the public hearing. He said that the VA's primary interest is getting a good case definition. Dr. Jesse stated that the current broad definition is probably helpful to the veterans in order to establish the disease as an entity in terms of practice. He noted that the broader the definition the easier it is to say that someone has it. Dr. Golomb stated that it is impossible to do research with a definition that does not distinguish between anyone. Dr. Jesse said that he was trying to make a distinction between a research definition and a medical or clinical definition. Dr. Golomb stated that she thinks it would be appropriate to have a different definition for a clinical setting and for

a research setting. Dr. Jesse stated that it was an interesting nuance that needed to be discussed further.

Rev. Graves said that he would not consider it a nuance, but a large issue. He discussed a study that found no differences between deployed troops and non-deployed troops and then talked about a nearly identical study that found significant results when distinguishing forward troops who were exposed to sarin with troops positioned further back. He said if a case definition is so broad that it washes out results than no one will benefit from it because every study will show that they are the same as the general population. Dr. Jesse said that it is a nuance because now they are trying to define it by different populations. He said a similar argument occurred during the Agent Orange discussion and noted that the records from DoD were not clear enough. He stated that differences in exposures are a whole different issue. Dr. Jesse said that he fully agrees that the case definition needs to be developed with the perspective of driving good science and research. He stated that he thinks that will eventually drive the ability to treat patients.

Chairman Binns stated that a fundamental issue was that the definition be linked to GW service. The term chronic multisymptom illness sounds like it covers irritable bowel syndrome (IBS) and a lot of other conditions. He stated that the term was initiated by Dr. Fukuda to describe the illness within the terms of GWI. He said that the VA needs to interact with IOM and stated that it should not be done after the meeting. He noted they have their own portion of the meeting and they can change the statement of work then. Dr. Steele stated that VA should withdraw the statement of work. Dr. O'Leary stated that the government made the decision and it went into a contract. He said that if they are discussing altering the contract it probably cannot be done in a public forum. He expressed that they would have to check with the lawyers, but he emphasized that he cannot break the law. He said that they are willing to engage in a discussion, but they are going to do it within the parameters of the contract. Dr. Jesse stated that the Committee should ask Mr. Jonathan Gurland, the ethics advisor, if there is a way the Committee can legally be involved in contract discussions early in the process, which would allow the Committee to advise the VA and help them make good decisions. He said that he will probably tell them it must be done in closed sessions and the Committee would then be held to confidentiality until the process was approved.

Dr. Bloom stated that he felt that the VA could approach the panel and tell them that they met with the RAC and that the original statement of work provided does not meet the needs of the strategic plan and that they would like to modify it. He noted that it could be done in close session with the panel staff and does not need to involve any type of public discussion. He said the panel staff could then go back and get the statement of task changed. Dr. Jesse said that he thinks that could be done. He noted that he thought it was equally important and more powerful to have them raise their concerns at the public meeting. He stated that they could talk to IOM and say that they want to speak to them after the meeting because information will be presented that may change how the contract will move forward. He noted that it will put them in listening mode, and he stated IOM may have information for the Committee to hear. He stated that it was possible that the panel was planning to approach it in a way that would satisfy the Committee's needs. Dr. Jesse said he would have no problem doing that.

Dr. Steele said she understand his point but expressed that there were still core issues, notably that the panel needs to be comprised of GW experts. She stated that the panel was comprised of very distinguished people, but IOM did not create a panel of GWI experts. She indicated that some people have a little experience, but overall the level of expertise is far removed from any other case definition panel previously formed. Dr. Jesse stated that they should bring that up in the public meeting because then it becomes a matter of public record. He said that the panel could bring in new members, add consultants, or do whatever they wanted. He indicated that if he had a month it was potentially possible to revamp he statement of work, but that he only has four days.

Chairman Binns said that he can appreciate the time limits, but said that at the end of the day it is a contract issue between the VA and IOM. He noted that it will come down to the VA telling IOM what they want. He said the Committee has to rely on the VA to tell them to change it, not for the Committee members to persuade IOM to do it. Dr. Jesse stated that the point of the public meeting is to bring issues to light because things are not entirely written up yet and it is a chance for change. He said the contract is to do it, and the next step is how it will get done. He agreed that if it is done incorrectly VA is essentially throwing away money. He encouraged the Committee to bring their voices and he will ensure that the panel is in listening mode. He noted that he would then have a conversation with them after the public meeting. Dr. Jesse expressed that this was the best he can offer at this time.

Chairman Binns had one last comment since Agent Orange was mentioned. He said that it was an IOM study that first linked Agent Orange with illness. He noted Congress also asked IOM to review 33 toxic substances as determine if any of them could produce the symptoms in GW veterans. The rationale was that IOM had recently been through the process with Agent Orange so there would be confidence in the standards they followed. Chairman Binns stated that they changed the standard however, and animal studies have been excluded from consideration, although the law expressly states that both human and animal studies are to be considered. Chairman Binns stated that this has been pointed out, but nothing has ever been done. He stated that he feels IOM has not been historically separate and independent from the VA. He emphasized that VA is going to have to take the lead to tell them to do things differently.

Dr. Meggs stated that Committee has consistently asked tough questions such as why important questions were removed from the survey and replaced with questions geared toward psychosomatic illness. He said the Committee continues to ask difficult questions such as why is the case definition panel being handled this way, and why there are psychiatrists on the panel, but not GW physicians. He asked if the Committee was told they were going outside their mandate because they ask these hard questions. He noted that when Dr. Steele asked for examples, no examples were given.

Dr. Jesse said he thinks the Committee should ask those hard questions in order to do what the Committee is intended to do which is to provide advice to the Secretary on GW research. Dr. Jesse said scientists are used to asking hard questions because that is how scientists work. He noted the Committee will never be criticized by him for asking hard questions. He stated that in terms of stepping outside the bounds, that question was asked of Mr. Riojas and not him. He said that question is directed at a level that is above him and he cannot comment on that. He agreed

that the Committee deserved an answer and he hopes they get an answer, but that he will not be the one to provide it. He told the Committee to never stop asking the hard questions and to never stop trying to advance the science. He noted that he felt the discussions have been eye opening and he said that it is his job to make sure the Committee functions as it is supposed to in order to best help the veterans.

Dr. Jesse then commented on the psychosomatic piece noting that he thinks there is a bit of an issue around the topic. He discussed a study he was involved with called sad heart, which looked at the relationship between depression and healing after a heart attack, and commented on other studies which look at prayer and depression. He said the relationship between the brain and the rest of physical health is incredibly important. Dr. Jesse said to be careful because everything interacts and other things could be occurring along with the biological underpinnings that are currently being investigated and discovered. He stated that psychosomatic is an archaic term and discussed his fascination with changes in white matter, and things such as the blood brain barrier. He commented that a lot of hard basic scientists are now talking about the mind-brain connection that is not fully understood, but is known to have an impact on physical health. He agreed that the cause cannot be assigned to psychosomatics, but said that at the same time it is an important connection.

Dr. White stated that she completely agreed with Dr. Jesse and said that she does not like the mind-brain dichotomy. She noted however, that she felt that in the history of GWI there has been a real dichotomy and the cause has been attributed to psychological factors. She said she truly believes that physical illness and environmental exposures affect how people feel and think, and the Committee does not have a problem recognizing the fact that the illness or the effects can make you depressed. However, she pointed out the history of people attributing psychological issues as the cause is the problem.

Dr. White said that it was a really important thing when addressing the veterans and the Committee to think about the history of the dichotomy in GW research. Dr. Jesse said the term dichotomy is part of the problem. Dr. Golomb noted that no one was opposed to integrative medicine, but said the problem was when only the psychological aspects were considered. She said that studies have shown that depression with somatic components have a mitochondrial foundation. She said it is important not to jump to the conclusion that when there is a psychological factor that has been linked to an outcome that it means that the psychological factor is truly the cause without there being a fundamental underlying factor that may be driving both.

Chairman Binns stated that he felt that the real dichotomy is the position that nothing special happened in the GW and that is was just like any other war. He noted that something special had happened over there and that it was not stress, because as wars go, the GW was not that stressful. He said stress has been emphasized and that it is just something that happens in every war. Dr. Jesse said that he hoped that people were over that. Dr. Steele noted that she wished people were as well and said the members at the table do not believe that to be the case. Dr. Jesse said that part of the job of the Committee and VA ORD and OPH was to continue science that will dissuade members of the public from that notion. He stated that he felt the better part of the first day was an engaging day of science, and Dr. Sullivan stated that the Committee always tries to

provide that in the meetings. He said that the symptoms are real and not in the veteran's head and said that the biological aspects need to be better understood. He noted that cognitive behavioral therapy seems to be the answer to a lot of things, but noted that it may just mask the symptoms and not treat the underlying cause. Dr. Sullivan noted that the Committee was open to integrative therapies, but agreed that it does not treat the underlying cause. Dr. Jesse stated that it was important to continue to press the science from both ends.

Dr. Jesse then commented on how the VA handles unfunded grants. He commented that some grants have great ideas, but they are not written as good grants. He said that one thing the Committee could do in a closed session is to look through the grants that do not get funded. He noted that some may work better if they were combined or that some grants are too extensive in their work scope. He stated that it would help the Committee to begin to explore new ideas.

Rev. Graves stated that the Committee had asked the VA to preemptively intervene with the IOM prior to the public comment. He noted that if the panel was informed of what was coming and what might happen, it would have more time to collect documents and prepare. He said that it might lead to a more meaningful and robust discussion in private after the public meetings. Dr. Jesse said that his intent was that he would convey the message and tell the panel their concerns. Dr. Kalasinsky said that the contract asks the IOM to come up with a consensus definition for chronic multisymptom illness for the 1990-1991 GW, and noted that he felt that the Committee believes the charge was different from what it actually was. Chairman Binns said the language that was adapted from the previous treatment charge specifically says to consider information from other similar populations. He noted that if they do not get told to link the definition specifically to GW service only, then the results will be the same that were produced from the IOM treatment charge. Dr. Kalasinksy pointed out that there were other aspects of the charge that were being ignored such as discussions with researchers and clinicians and to establish a consensus case definition. Chairman Binns said that it was the same language.

Dr. Kalasinsky stated that there were currently about 10 definitions for GWI and expressed the thought that if there was a chance that those 10 people could come to a consensus on a definition it would have already happened. Dr. Golomb stated that it could happen if there had been a committee put in place to oversee the process. Dr. Steele expressed that the Committee had not come up with a case definition because the Committee strongly felt that it should be evidence based. She stated that a literature review does not establish an evidenced based case definition. She noted that a review of all the literature and of the already existing case definitions was completed in the 2008 RAC Report. She said that the next step should be an analytic enterprise and involve the input of experts in GWI. Dr. Steele stated that she even tells people not to use the case definition that she developed in the 1990s because they want to see the current symptom profile. Dr. Kalasinksy noted that Dr. Robert Haley used to be on the Committee and he and Dr. Steele were never able to come up with a consensus case definition. He stated that he felt if two people on the Committee could not come to a consensus then adding the others who have developed case definitions would not help. Dr. Golomb pointed out that they were never placed in a room and tasked with that objective. Dr. Steele agreed and said that it was not that they could not come up with a case definition and agree. She stated that she felt that they could come up with a consensus case definition if they discussed it and used all the available data to devise one.

Dr. O'Leary stated that case definitions are hard especially when things change over time, noting the difficulty of forming a case definition for cancer which seems simple. He said that to him, the case definition is useful and he does not want to underestimate it, but also suggested that a careful definition of inclusion and exclusion criteria for a study are important because they transcend case definitions over time. Dr. O'Leary also explained that the IOM can ask for additional studies or to make recommendations for specific work that should be done. He noted that the panel could make that recommendation immediately after the public hearing, which is why Dr. Jesse said it was important to introduce these ideas early on. He noted that it would help with the execution of the contract. He expressed the importance of defining patient populations; specifically defining what is happening and defining some of the potential meaningful outcomes, to make it easy for people entering the field to know what is important. He felt that moving forward on that would help advance GW work a great deal.

Chairman Binns stated that the Committee members will say their piece, but emphasized that the IOM panel will do what the VA tells them to do. Dr. Steele questioned the decision to give IOM the task since it was a process that they have not done before. She noted that other diseases with similar case definition processes have relied on experts and not tasked a panel such as the IOM. She asked what the rationale was and asked if it could be undone. Dr. Jesse said that he does not know if the assignment could be undone. He stated that IOM is generally considered as a trusted agent in working in these areas and said they are generally considered to be intellectually true and incredibly insightful. Dr. Steele asked why cardiologists have never tasked them with a case definition for angioplasty. Dr. Jesse replied that he did not think cardiologists would even be able to come up with a case definition for angioplasty. He noted that he cannot answer beyond that and said that at this point the VA can only frame the issue in ways that the IOM cannot ignore. Dr. Golomb stated that currently the task is not framed the right way. Dr. Jesse said that it can be changed to be the right way.

Dr. Jesse stated that he did not think much more would come of the discussion and noted that he had another meeting to attend. He discussed that the Committee members do have a lot of time in front of the IOM panel and encouraged them to use it wisely. He stated that he can certainly put the IOM in listen mode and then have a discussion with them afterward. He said the whole reason for the public hearing was to make sure the panel was on the right track.

Chairman Binns thanked Dr. Jesse for his presence and his contributions to the discussion for the last two days. He agreed with Dr. Jesse that the good part of day 1 was productive and exciting science, and an illustration of why many of the members have ended up being involved a lot longer than they initially anticipated. He stated that scientific progress was being made and thanked Dr. Jesse for engaging in the meeting. Dr. Jesse thanked the Committee for having him and said that the discussions would continue. He told the Committee to feel free to reach out to him directly and said he will do his best to get honest answers and to get things moving forward. He asked how the meetings are scheduled. Chairman Binns stated that they canvas the Committee members for dates, but noted at this time it depends on which Committee members will be moving forward and who are being rotated off. Dr. Jesse again suggested that some time for a closed session should be planned, noting that it would have to be documented in the federal

register. He stated that he wanted the dialogue to be as open as possible and thanked the Committee for their dedication.

Chairman Binns adjourned the meeting for a short break before Mr. Jonathan Gurland began his presentation on ethics training for the Committee members.

Federal Advisory Committee on Ethics Training
Mr. Jonathan Gurland, VA Office of General Counsel

Mr. Gurland stated that he would discuss ethics training for Federal Advisory Committees, who are special government employees. He said the ethics rules apply to the Committee members, but they are not as rigorous as the rules applied to other government employees. He covered topics such as criminal conflict of interest laws and standards of ethical conduct.

Chairman Binns thanked Mr. Gurland for his presentation and moved on to the committee discussion.

Committee Discussion

Chairman Binns began the committee discussion with his summary of the discussions that happened over the last two days. He stated that the Committee believes that all of its findings and recommendations from prior meetings have all related to research and stated that the majority of them have remained unaddressed in whole or in part. Specifically he noted the most serious recommendations, which address elements of the VA that hold back research and progress. The recent change to the Committee Charter eliminating its oversight function and independence is a current example of the staff action. Chairman Binns stated that the Committee recommends that the charter change be rescinded. He noted that the Committee understands the necessity of an orderly turnover of some of its members, but emphasized the importance of membership not being selected by VA staff and the importance of having scientists and veteran advocates on the Committee. The membership of the Committee should reflect current scientific understandings of GWI and noted that no more than one third of the membership should be replaced in a given year. Chairman Binns noted that he hoped that the VA will keep more Committee members than they had previously announced.

Rev. Graves stated that since Secretary Shinseki began his administration none of the Committee members had ever received an official letter of their appointment to the Committee. He said if they want to start up something new then the VA should ask the members who would like to stay on the Committee and not just arbitrarily throw people off. He commented that the Committee has a history of knowledge and expertise that should be honored and utilized. Dr. Steele also mentioned that the Committee just lost two of its veteran members who resigned, which she thought important to mention.

Chairman Binns then discussed the Strategic Plan recently released that included some changes recommended in the June 2012 meeting. He then invited Dr. Steele to discuss the Strategic Plan. Dr. Steele stated that there were too many changes to discuss one by one so she just had some general comments. She noted that a lot of language was restored that had been taken out, which

is an improvement and made it more consistent with the initial draft the Committee originally approved. The recommendations about the Strategic Plan related to two things. First the current research activities of the VA do not really reflect the Strategic Plan in some key ways. Second, the Committee might want to make some recommendations which address the problems that still remain in the Strategic Plan. Dr. Steele said another issue was that the Strategic Plan only applied to ORD and it is not adopted by the entire VA. She summarized that the key issues of concern with the Gulf War Portfolio not being consistent with the Strategic Plan related to problems such as the IOM case definition panel and the current VA treatment research. She suggested that there should be some element in the Strategic Plan that prioritizes all the areas addressed and some language addressing how all the ideas will be implemented. She concluded that she believed that there was still a lot of room for improvement in the Strategic Plan and that the Committee would be pleased to help improve it.

Chairman Binns asked Dr. Kalaksinsky what the time table for the annual revision was and Dr. Steele asked how the annual revision was done. Dr. Kalasinsky said he does not know when it will be, but it will be reviewed once a year. Chairman Binns asked about the Gulf War Illness Steering Committee (GWISC's) involvement in the process. Dr. Kalasinksy said that he sent the report to the Steering Committee, but noted that issues with the sub-committees assignment had to be resolved. Dr. O'Leary stated that the VA was looking to move the Strategic Plan revision process, as well as other strategic plans for other groups, into the same time table as the ORD's time table for planning and budget executions. Dr. Steele asked about the process of the revision. Dr. Kalasinksy noted that they planned to involve both the Committee and the GWISC in the process. Chairman Binns suggested that the Committee make a general statement recognizing the current improvements, but stating that further improvements were also needed. He said that it may be beneficial to make more generalized suggestions instead of pointing out individual areas of the Strategic Plan. Dr. Steele commented again on the importance of prioritization and implementation. Dr. Kalasinsky reminded the Committee that it was a Strategic Plan and not an implementation plan. Dr. Steele stated that the plan could still include that, and noted that the working group she was part of was originally charged to give timelines and milestones.

Dr. Steele asked about the idea that the plan apply to the whole VA and not just ORD. Dr. Jaeger commented that he does not have the power to create a Strategic Plan for the entire VA. Dr. Steele pointed out that everyone involved in GW issues in the VA should be involved in the plan and not just ORD and indicated that recommendation was for the Secretary not ORD. Dr. Davey noted that the structure of the VHA has changed since the beginning of the plan and said that the department is attempting to become more integrated. Dr. Jaeger agreed and stated that he appreciated the comment that though the Committee may not like all the parts of the plan, having the Strategic Plan is better than having no plan at all.

Chairman Binns moved on to discuss the subject that the VA continually overstates the amount of money actually spent on GW research. He noted that there has been an improvement, but the numbers stated are still misleading.

Chairman Binns discussed the next topic which related to the IOM, which was in reference to the IOM treatment panel, and he specifically noted issues with the presenters who were invited to present at the public meeting. He stated that the VA presenters discussed inaccurate information

and noted that it led to the adoption of a working case definition of CMI that eliminated any GW service connection and did not address the established fact that GWI is not psychiatric in nature. Chairman Binns stated that the VA has now tasked the IOM with establishing a case definition of GWI, which will affect all future research. He commented that the Committee will make a recommendation that the case definition be given to a panel of experts who will use an analytical approach to develop a definition. Dr. Steele stated that the condition must be defined by its symptoms, but said that there is a lot of consistent data to help the process. She re-emphasized that the Committee does not support the VA's decision to assign the GW case definition to the IOM because it is not evidence based, it is not developed by an expert scientific process, and it will not involve most scientific experts working in GWI research, it does not involve key stake holders, and it is not the type of task IOM has done in the past. In conclusion, she stated the IOM should either alter their process or the task should be given to another panel.

Chairman Binns asked Dr. Bloom if he had mentioned that IOM may add members to the panel or have speakers present to the panel. Dr. Bloom stated that he believes the IOM could have a workshop to complete the consensus and then have the workshop report back to the panel. Chairman Binns asked if it would be like establishing a subcommittee. Dr. Bloom said that it would, and noted that the subcommittee could be an entirely different group of people to do the analytical work, because typical IOM panels only review literature. Dr. Steele commented that even if that were the case the panel would still have some complex details to work through. Chairman Binns agreed and said it would certainly be helpful to have more experts on the panel. Dr. White thought Dr. Bloom said they could commission out the analytic piece and hold a workshop with experts to work through the other details of the definition. Dr. Steele asked what the original IOM panel's job would be if that were the case.

Chairman Binns continued to address the recommendations from the last meeting, noting that he was omitting the issues that had since been resolved. He stated that the VA still had not contracted for the IOM study for the prevalence of MS in GW veterans that was ordered by Congress in 2008. Dr. Davey said they had contacted the IOM and determined that IOM would not be able to add to the body of knowledge because the studies that have occurred and are currently in process are already doing everything that IOM could do. Chairman Binns commented that his understanding is that there was an MS study done through the VA, but it was not a prevalence study. Dr. Steele added that it was not specific to the GW and Dr. Sullivan agreed. Dr. Davey stated that the VA was unsure of what to do with regard to this issue. Dr. Steele said that Congress would be happy if a good epidemiological studied happened and Dr. Sullivan agreed. Chairman Binns stated that it seemed as if the issue was not resolved, and Dr. Davey responded that she believed the mortality study and some other studies will help, but that it is still an ongoing process. Chairman Binns said that someday they should discuss if the mortality study should look at subsets of exposed groups and Dr. Davey agreed.

Chairman Binns moved on to the last topic, stating that VA continues to conduct a large survey of GW era veterans which omits the questions necessary to define GW illness and instead focuses on stress and psychological questions. He said one item that had been addressed is the increase in the VA budget, but qualified that the Committee was still not satisfied that all of the money goes to GW research. He stated that he will address the areas that have been fixed in the recommendations to be fair and noted that he will also add in new recommendations.

Dr. Kalasinsky asked that the recommendations be phrased in a way that the VA staff could concur or not concur, as they are often required to do once the recommendations are submitted. Chairman Binns agreed and also noted that some of the issues go above their pay grade, such as the change in the Committee's charter. He said that there were good things happening in the VA, but there were still some awful things happening. Dr. O'Leary commented that the rotation of the Committee members was a requirement of all committees and stated that sometimes the VA was not thrilled that it needs to happen. He also thanked the Committee for the gift of their time, noting that time is one of the few things one can give and never get back. He concluded thanking veterans for the gift of their service.

COL John Kent, who is with the office of the Secretary, commented that the office had been discussing ideas since Chairman Binns visited a few weeks prior and while the Committee's meeting was going on. He stated that in the next few weeks they would be working on ways to specifically reach out to GW veterans to have a more proactive dialogue with them about what their concerns continued to be. He said he did not know how it would play out, but there would be a concerted effort. COL Kent said that they wanted to engage in a meaningful dialogue, not just a lecture or a simple comment section to establish something more lasting. Chairman Binns stated that he would encourage them to address more than just research issues in that discussion noting that there were issues such as benefits, without any avenues for discussion. He noted that the veterans would probably be appreciative of the opportunity for direct discussions. COL Kent agreed and stated that they have been thinking about those issues. He stated that he was in charge of the GW Task Force Report, which just closed for public comment, and said that much like last year they received a large number of comments, suggestions, and ideas from veterans and other concerned parties. He also noted that some veterans left contact information, so the VA had a mechanism to reach out to some of them. He stated that a lot of the issues raised are ones discussed during the Committee meetings.

Chairman Binns commented that he wanted COL Kent to understand that the Committee members still sitting at the table were doing so in hope that the charter will be rescinded. He said that none of the members believed that the Committee could function without an independent staff and without the ability to review and speak frankly about the large issues related to GW research. COL Kent stated that his recommendation as a citizen is that the Committee should be very specific about what those issues are, what it is that the Committee thinks has happened, and what it is that the Committee needs. He said the more specific the recommendations the greater the likelihood of coming to an agreement, instead of creating an argument.

Chairman Binns thanked everyone for attending and brought the meeting to a close.