I hereby certify the following minutes as being an accurate record of what transpired at the October 27-28, 2003, meeting of the Research Advisory Committee on Gulf War Veterans’ Illnesses.

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

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

Consultant to the Committee
Jack Melling

Guest Speakers
Maria Araneta
Betty Mekdeci
Han Kang
Carrolee Barlow
Wilkie Wilson
Nelda Wray
Hermona Soreq
Steven Berkowitz
Michael Kilpatrick
Robert Sheridan
Eugene Oddone
Susan Perez
Denise Hynes
Clare Mahan
Meeting Agenda

Monday, October 27, 2003

8:30 – 8:45  Welcome, introductions, and opening remarks  Mr. Jim Binns

8:45 – 9:30  Birth Defects and Pregnancy Outcomes Following Service in the Gulf War  Dr. Happy Araneta
Dr. Araneta, Assistant Professor at the University of California at San Diego, will present information from her studies on birth defects in children of Gulf War veterans. Her presentation will include the first release of the results from her study “Conception and Pregnancy During the Persian Gulf War: The Risk to Women Veterans” to be published in the November, 2003, issue of Annals of Epidemiology.

9:30 – 10:15  Information From a Registry of Birth Defects in Children of Gulf War Veterans  Ms. Betty Mekdeci
Ms. Mekdeci is Executive Director of Birth Defects Research for Children, a non-profit organization that maintains a registry of children of Gulf War veterans with birth defects. She will present data from the registry, as well as preliminary information from a cooperative study of Goldenhar Syndrome in children of Gulf War veterans.

10:15 – 10:30  Break

10:30 – 11:15  Findings on Birth Defects from the National Survey of Gulf War Veterans  Dr. Han Kang
Dr. Kang is Director of VA’s Environmental Epidemiology Program and the War-Related Injury and Illness Study Center in Washington, D.C. He will present new results on birth defects from VA’s National Survey of Gulf War Veterans, including medical record corroboration of birth defects reported by Gulf Veterans.

11:15-11:45  Discussion

11:45-12:00  Update on Published Research  Dr. Lea Steele

12:00-1:00  Lunch
1:00 – 1:45

**NTE and Identification of Possible Molecular Targets of Neurotoxic Exposures in Gulf War Veterans**

Dr. Barlow, currently with Merck Research Laboratories, will present work conducted with colleagues at Salk Institute that demonstrated the effects of organophosphate pesticides on neuropathy target esterase (NTE), including the role of NTE genetic variability. This research may have profound implications for our understanding of the effects of these chemicals on humans. Dr. Barlow will outline the potential for genomic research to identify targets for treatments of potential benefit to both ill Gulf War veterans and others at risk of future terrorist or military chemical attack.

**Dr. Carrolee Barlow**

1:45 – 2:30

**Neurotoxins and Gulf War Illness: An Overview of VA’s Research Enhancement Award Program (REAP)**

Dr. Wilson, VA Senior Research Career Scientist and Professor of Pharmacology at Duke University, will describe the work of VA’s Neurotoxins and Gulf War Illness Program, which will examine proteins expressed in patient and animal samples following exposure to neurotoxins. This research has the potential to identify biomarkers that identify exposed individuals, as well as molecular targets for treatment interventions.

**Dr. Wilkie Wilson**

2:30-2:45

**Break**

2:45 – 4:30

**Update on VA Gulf War Illness Research Programs**

Dr. Wray is VA’s Chief Research and Development Officer, and will update the committee on recently funded deployment health studies. She will also present information on plans for VA’s Neuroimaging Resource Center and the Gulf War illness pilot project from the San Francisco VA.

**Dr. Nelda Wray**

**VA Study of AChE-R in Gulf War Veterans**

Dr. Soreq, of Hebrew University in Jerusalem, and Dr. Concato, Chief of Epidemiology at the West Haven VA, will present initial results of a VA study to determine whether ill Gulf War veterans have high levels of a mutant form of the enzyme acetylcholinesterase (AChE-R), shown in previous studies to be associated with exposures to AChE-inhibiting chemicals such as those encountered during the Gulf War. Dr. Soreq’s laboratory has developed a novel treatment that may be effective in treating this abnormality.

**Dr. Hermona Soreq**

**Dr. John Concato**

4:30-5:00

**Public Comment**

5:00

**Adjourn for the day**
Tuesday, October 28, 2003

8:30 – 9:45
**Department of Defense Research on Gulf War Veterans’ Illnesses and Chemical Defense**
Dr. Kilpatrick will present information on DOD’s research on Gulf War illnesses and deployment health, and an overview of DOD research relating to medical chemical defense.

Dr. Michael Kilpatrick

9:45 – 10:30
**Additional Findings from the VA ALS Study and Update on the ALS Registry**
Dr. Oddone, Director of the Health Services Research Center at Duke University, and Principle Investigator of VA’s study of ALS in Gulf War Veterans, will present more detailed results of analyses from that study, and will update the committee on VA’s ALS Registry.

Dr. Eugene Oddone

10:30-10:45
**Break**

10:45 – 11:15
**Monitoring the Health of Gulf War Veterans Using Existing VBA Data Systems**
Ms. Perez is Assistant Director for Data and Information Services at the Office of Performance Analysis and Integrity at VA’s Veterans Benefits Administration. She will present information on benefits claims data resources and how they might be used to monitor the health of Gulf War veterans.

Ms. Susan Perez

11:15 – 11:45
**Monitoring the Health of Gulf War Veterans Using VHA Data and Information Resources**
Dr. Hynes directs the VA Information Resource Center, and will present information on the databases and resources available at VA’s Veterans Health Administration, and how they might be used to monitor Gulf veterans’ health and clinical care.

Dr. Denise Hynes

11:45 – 12:15
**Q&A, Discussion**

12:15 – 1:15
**Lunch**
1:15 – 1:45  **Anthrax Vaccinations and Health Outcomes in the National Survey of Gulf War Veterans**
Dr. Kang will present results from VA’s National Survey of Gulf War veterans on a subgroup of veterans known to have received the anthrax vaccine in association with Gulf War deployment.

1:45 – 2:00  **Federal Trials of the Anthrax Vaccine**
Dr. Jack Melling

2:00 – 3:30  **Committee Business**
Mr. Jim Binns

3:30 – 4:00  **Public Comment**

4:00  **Adjourn**
Welcome, introductions, opening remarks
Mr. James H. Binns, Jr., Chairman

Chairman James Binns called the meeting to order at 8:30 a.m. He welcomed the participants and attendees.

Birth Defects and Pregnancy Outcomes Following Service in the Gulf War
Maria Rosario (Happy) G. Araneta, PhD
Assistant Professor, University of California at San Diego

Chairman Binns introduced the first presenter, Dr. Maria Rosario Araneta, to speak on her studies of birth defects and pregnancy outcomes following service in the Gulf War. (See Appendix – See Presentation 1.) Her presentation included the first release of the results from her study “Conception and Pregnancy During the Persian Gulf War: The Risk to Women Veterans” to be published in the November, 2003, issue of Annals of Epidemiology. A discussion took place following Dr. Areneta’s presentation.

Dr. Golomb inquired about research showing problems that may not become apparent until children are older, including such concerns as behavioral problems. Dr. Araneta indicated that her studies had not been able to capture these problems given limitations associated with birth certificate data. She indicated that this type of problem had been recognized by CDC, which has considered monitoring possible birth-related problems through age six.

Dr. Haley complimented Dr. Araneta on the contributions of her studies. He asked if the study had compared birth defect rates in civilian versus military hospitals, since those who were ill might have left the service earlier. Dr. Araneta responded that the anonymous nature of birth defect registries prevented an ability to differentiate between births in military versus civilian hospitals.

Dr. Steele asked if rates of birth defects among female and male parents might be evaluated together rather than separately, as reported in Dr. Araneta’s data. Dr. Araneta replied that when rates in males and females were combined, three types of heart-related birth defects were significantly elevated.

Dr. Cherry noted that the rate of all birth defects combined was similar in the two groups. Dr. Araneta noted that overall birth defect rates in the U.S. had been fairly consistent over the last 20 years but that important discoveries about risk factors for birth defects requires that different types of birth defects be evaluated individually.

Dr. Golomb observed that separating the results for veterans who consider themselves ill would be useful to see if rates differed in ill vs. healthy veterans.

Mr. Graves suggested that future studies should consider differences in characteristics and locations of deployment.

Mr. Binns asked Dr. Araneta what future studies she would recommend. Dr. Araneta replied that she would recommend case control studies to evaluate these abnormalities and that future studies should also incorporate information related to exposures.

Mr. Binns asked what physicians should tell Gulf War veterans who may have concerns about having children. Dr. Araneta advised that veterans should be counseled to speak with their physicians and to take
folic acid three months prior to conception, as is recommended for any prospective parent with possible exposure risk.

Dr. Steele asked if Dr. Araneta had determined whether rates of birth defects had differed in different years following the war. Dr. Araneta replied that they had not looked at that.

Information From A Registry of Birth Defects in Children of Gulf War Veterans

Ms. Betty Mekdeci
Executive Director, Birth Defects Research for Children

Mr. Binns introduced the next speaker, Ms. Betty Mekdeci, Executive Director of Birth Defects Research for Children, a non-profit organization that maintains a registry of children of Gulf War veterans with birth defects. She presented data from the registry, as well as preliminary information from a cooperative study of Goldenhar Syndrome in children of Gulf War veterans. (See Appendix – Presentation 2.)

Following the presentation, Mr. Smithson asked how many of the veterans who are fathers of children within the birth defect registry are ill themselves. Ms. Mekdeci replied that she hasn’t analyzed that yet, but the data were included in their questionnaire, and she will do it.

In response to a methodology suggestion, Ms. Mekdeci reiterated that the purpose of the registry is not the same as that of a research study.

Dr. Steele asked whether the questionnaire asked about exposures in theater. Ms. Mekdeci responded yes, but that many veterans don’t know for certain what they were exposed to. Mr. Smithson wondered whether the questionnaire asked about veterans’ locations in theater. Ms. Mekdeci said it did not, but that this information could be obtained in follow-up efforts.

Dr. Steele asked what denominators were used to estimate crude rates. Ms. Mekdeci replied that the information was obtained from Dr. Araneta’s study.

Dr. Pellier asked if it is correct that Ms. Mekdeci had data on 40,000 families. Ms. Mekdeci clarified that information was available on 3,437 veterans’ families. Dr. Pellier observed that, in the pharmaceutical industry when looking at the adverse effects of a drug, the comparison is done in relation to the overall population. He indicated that approach might be applied to the birth defect registry by comparing Gulf War veterans to the entire registry population, including Gulf War veterans. Ms. Mekdeci said that she would be interested to read references on this approach.

Dr. Cherry asked to what extent the cases in the registry included cases identified in Dr. Araneta’s studies. Dr. Araneta replied that there were five in the Gulf War group and two in the nondeployed group.

Mr. Binns asked if Ms. Mekdeci planned to evaluate whether ill veterans are more likely to have children with birth defects than well veterans. Ms. Mekdeci said she could do that. Mr. Binns asked what research Ms. Mekdeci would recommend. Ms. Mekdeci emphasized the need to identify and assist families of female veterans who have children with birth defects.

The meeting adjourned for a brief break.
**Findings on Birth Defects from the National Survey of Gulf War Veterans**

Dr. Han Kang, MD, PhD  
Director, VA Environmental Epidemiology Program/War-Related Injury and Illness Study Center  
Washington, D.C.

Mr. Binns introduced Dr. Han Kang to present findings on birth defects from the National Survey of Gulf War Veterans that included recent results of medical record reviews done to determine the accuracy of veteran-reported birth defects in the study. (See Appendix – Presentation 3.)

After his presentation, Dr. Golomb observed that birth defect risks related to some exposures might increase over time, so it would be useful to do a similar data collection at a more recent point in time.

Dr. Haley complimented Dr. Kang for another great contribution to the literature. It was important to note that the veterans’ self-reports appeared to be supported, and it would also be important to evaluate details related to the 17 that were not confirmed.

Mr. Robinson said he appreciated that self-reported surveys of veterans had been validated. He said he is receiving a large number of self-reports of veterans with multiple sclerosis. He also indicated that a recently released study implied that media perceptions affect self-reports.

Dr. Cherry noted that the only Achilles heel of the study would be if nondeployed veterans had higher rates of problems that had not been followed up. Were more self-reports not followed up in non-Gulf veterans? Dr. Kang replied that 33% of conditions were not followed up in non-Gulf and 40% of conditions were not followed-up in Gulf War veterans.

Dr. Araneta said that a military birth defects registry had been established in 1998 that was based on ICD-9 codes on birth certificates from military hospitals and births in civilian hospitals that had been paid for by the military. She indicated that this is a passive birth defect surveillance system, which typically underestimates birth defect rates by about 40%.

Dr. Kang said that the rate of birth defects in the nondeployed population in his study was similar to that found in the general population, suggesting that there had not been a problem of under-reporting in this group.

Ms. Mekdeci suggested asking parents for help in getting medical records.

Mr. Binns asked what future research Dr. Kang would recommend. Dr. Kang noted that the birth numbers were so small from Phase III of the National Gulf War Veterans Health Study that it was not possible to draw conclusions related to birth defect rates. To settle the issue, the study would have to have a considerably larger sample size, but that would be very expensive.

Mr. Binns asked if Dr. Kang has data to know whether the Gulf War veteran parents in his study were well or ill, and if it appeared that rates of birth defects had changed over time. Dr. Kang indicated that data collected for his study would allow them to look at both questions.

Dr. Haley suggested that selection bias might be reduced by looking at birth defects among all children in the family, not only the ones born first since the war. He also encouraged Dr. Kang to provide information on the total number of births in his cohort to other researchers who wish to study this problem. Dr. Kang thanked him for these suggestions.
Dr. Steele reviewed the recommendations regarding birth defects from the Draft Executive Summary of the Committee’s upcoming report. Mr. Robinson suggested recommending active surveillance for birth defects to the military and noted that there are unspent funds available at DOD for future deployment health research. Dr. Araneta recommended that the State of California be allowed access to military hospital records. Dr. Steele asked about the nature of California’s birth defect surveillance program. Dr. Araneta replied that it is a uniform system based on CDC codes.

Ms. Knox said that there should be a pamphlet to advise veterans who are considering having families about birth defects research.

Dr. Barlow asked if the Committee has authority to recommend better classification of birth defects.

Dr. Araneta said that there should be pregnancy-testing requirements prior to deployment. Ms. Knox indicated that those requirements currently are in place.

Dr. Steele noted that there is a very large study in Britain of birth outcomes among U.K. Gulf War veterans. Dr. Araneta said that the study results would be published in February 2004. Dr. Cherry said that the study includes all British deployed troops.

Mr. Smithson said that both ill and well veterans are concerned about whether veterans are at greater risk for having children with birth defects.

Dr. Araneta said that CDC is exploring the use of expanded ICD codes for birth defect surveillance.

Dr. Golomb observed that doctors often have so many requirements that they provide information on birth defects coding very quickly, resulting in high error rates for birth defects identified on birth certificates.

Ms. Mekdeci said it was important to follow through and look at defects that emerge later in a child’s life.

Dr. Golomb cautioned that more research might change current impressions, just as findings from the research presented at this meeting differ from what was known two years ago.

**Update on Published Research**

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

Mr. Binns welcomed Dr. Steele in her new dual capacity as scientific director of the Committee staff as well as Committee member. Dr. Steele presented an update on research published since the last Committee meeting. (See Appendix – Presentation 4.)

In the discussion that followed, Dr. Haley observed that there were two problems with the Hotopf study. First, it measured total serum paraoxonase levels, which are the wrong thing to measure. It should have measured the Q allozyme. Second, the case definition used in the study was far too broad and included people sick for any reason. This would result in the case group likely including people who are mildly symptomatic or ill for reasons unrelated to service in the Gulf War.

Regarding the Riddle article in Military Medicine, Mr. Robinson said that Dr. Mark Brown told him this information had been “state of the art” when this paper was put together several years ago. Dr. Golomb reviewed the premises cited in the article and showed they were no longer considered accurate. Mr.
Robinson said he had asked Dr. Brown if he planned to publish a retraction, and that he said he would if asked. Mr. Robinson suggested that the Committee should recommend a retraction. Mr. Graves agreed. Ms. Knox said that this publication is what military and VA physicians are reading.

Regarding the “Consensus Statement” paper, Dr. Meggs asked whether the authors mentioned that one of the common threads in many of the scenarios described was exposure to toxic elements. Mr. Robinson said that his veterans’ organization had been aware of this effort to substantiate the stress theory. He expected that there would be objective evidence of illness in World Trade Center firefighters, too. Dr. Golomb agreed and pointed out that firefighting is also associated with toxic exposures.

The meeting adjourned for a lunch break

**NTE and Identification of Possible Molecular Targets of Neurotoxic Exposures in Gulf War Veterans**

Dr. Carrolee Barlow, MD, PhD
Director of Molecular Neurosciences, Merck Research Laboratory, San Diego, CA

Mr. Binns introduced the first speaker for the afternoon, Dr. Carrolee Barlow, who presented results of work conducted with colleagues at Salk Institute that demonstrated that neuropathic target esterase (NTE) is a target enzyme for organophosphates known to cause adverse neurological effects in humans. (See Appendix – Presentation 5.) This research may have implications for understanding the effects of these chemicals on humans and the potential role of genetic variability of this enzyme. Dr. Barlow also outlined the potential for genetic research to identify targets for developing treatments of potential benefit to both ill Gulf War veterans and others at risk of future terrorist or military chemical attack. Discussion followed.

Dr. Golomb asked if NTE is expressed in blood or saliva. Dr. Barlow said it is important to determine this in humans.

Dr. Soreq noted that AChE activity was also somewhat different in the NTE heterozygotes. Dr. Barlow thought this might be attributed to the small numbers in the study and thought it might not occur if a larger number were studied.

Dr. Pellier asked if Dr. Barlow had looked at NTE in the gut. Dr. Barlow said they had not, although they would be sending the mice to other researchers. Dr. Pellier asked if Dr. Barlow thinks that NTE is providing some type of maintenance of neurons and wondered if she had any related insights into other neurodegenerative diseases like Alzheimer’s. Dr. Barlow said her sense is that Parkinson’s may be linked to NTE.

Dr. Haley asked why the system doesn’t recover when NTE levels are restored. Dr. Soreq stated NTE is a signaling enzyme.

Mr. Binns asked if Dr. Barlow could explain in layman’s terms how the genetic research approach she described might lead to treatments. Dr. Barlow explained that once researchers find a gene and understand what its function is they can then screen pharmaceutical compounds to see what can affect the gene’s product. She related that the gene for an orphan disease was identified by her group in 1998, and that they have now reached the point that they have identified a very promising drug compound. This was the timetable for an orphan disease affecting 1,000 children in the U.S., which is nowhere near the size of impact potentially associated with a better understanding of NTE.
Neurotoxins and Gulf War Illness: An Overview of VA’s Research Enhancement Award Program (REAP)

Dr. Wilkie Wilson
VA Senior Research Career Scientist
Professor of Pharmacology, Duke University,

Mr. Binns introduced the next presentation by Dr. Wilkie Wilson providing an overview of VA’s Research Enhancement Award Program (REAP) on neurotoxins and Gulf War illness. Dr. Wilson described the work of the VA-funded program, which will examine proteins expressed in patient and animal samples in relation to neuronal hyperexcitability and exposure to neurotoxins. This research has the potential to identify biomarkers that identify exposed individuals, as well as molecular targets for treatment interventions. (See Appendix – Presentation 6.)

Following the presentation, Dr. Golomb reported on a case of overexposure to organophosphates that was associated with seizures.

Dr. Barlow noted that she asked Dr. Steve Heineman at Salk Institute to look at NTE knockout mice to see if they were more susceptible to kindling. She also sent mice to Dr. Abou-Donia at Duke.

Mr. Robinson asked whether the PTSD difference mentioned by Dr. Wilson is caused by genetics or other protective mechanisms.

Dr. Golomb said that studies have shown that exposure to high levels of stress can affect the nervous system in a way that makes it hyperresponsive to later exposures.

Dr. Wilson observed that it might be beneficial to further study choline as a possible protective compound against the effects of exposure to acetylcholinesterase inhibitors.

Dr. Golomb said it is important to determine if it might be used now to provide benefit to individuals who have already been injured.

Mr. Robinson commented that Special Forces troops are specially trained in measures to help them deal with extreme stress.

The meeting adjourned for a brief break.

Update on VA Gulf War Illness Research Programs

Dr. Nelda Wray, MD, MPH
Chief Research & Development Officer, U.S. Department of Veterans Affairs

Mr. Binns introduced the next speaker, Dr. Nelda Wray, VA’s Chief Research and Development Officer (CRADO), and thanked her for her assistance in arranging for several of the speakers at the meeting.

Dr. Wray briefed the Committee on recently funded deployment health studies. She also presented information on plans for VA’s Neuroimaging Resource Center and a Gulf War illness pilot project from the San Francisco VA. (See Appendix – Presentation 7.)
VA Study of AChE-R in Gulf War Veterans
Dr. Hermona Soreq, Hebrew University, Jerusalem, Israel
Dr. Steven Berkowitz, VA Cooperative Studies Program

Mr. Binns introduced Dr. Hermona Soreq who presented information on and preliminary results from the VA-sponsored study of acetylcholinesterase and other enzyme levels in Gulf War veterans. (See Appendix – Presentation 8.) Dr. Soreq’s presentation was followed by a related presentation provided by Dr. Steven Berkowitz of VA’s Office of Research and Development. The presentations were followed by discussion with Committee members concerning the study.

Mr. Robinson noted that there are blood samples for 900 veterans of Task Force Ripper, including both pre and post-Gulf War I samples. located at DOD. Dr. Craig Hyams would be familiar with the current disposition of these samples.

Dr. Cherry stated that the study design was not necessarily related to exposures in the Gulf War since someone with anxiety in the non-deployed group should be similar to someone with anxiety in the Gulf group.

Dr. Meggs asked whether the study was considering other symptoms of Gulf War illness besides anxiety such as cognitive dysfunction, memory loss, etc. Dr. Berkowitz replied that he was not sure of all the variables being studied and measures being used. They had measured anxiety with the Spielberger scale. Dr. Golomb stated that that scale is not useful for anxiety associated with physiological illness.

Mr. Binns asked if the group of Gulf War veterans whose samples were being studied include those with pain, cognitive difficulty, and other symptoms other than anxiety. Dr. Berkowitz said yes. All of those data were collected, including all symptoms endorsed by the veterans.

Mr. Graves commented to Dr. Soreq that when she had last presented information on AChE-R to the Committee, he believed that her work was on the verge of leading to treatment options for those with excess levels of AChE-R. He asked about the current status of those efforts. Dr. Soreq responded that treatments tested for a particular condition must be shown to be relevant to that condition. Dr. Berkowitz stated that by the end of the study, we will know if AChE and AChE-R levels are related to Gulf War illness.

Mr. Binns asked if they would have data in February on just anxiety or on the full range of symptoms. Dr. Berkowitz replied that he would expect to have the full range.

Mr. Graves asked why VA had focused this study on anxiety in the first place. Dr. Berkowitz replied that Dr. Soreq had previously done work in a U.S. population that showed an association of anxiety with AChE-R.

Dr. Cherry then asked why the study was not addressing the central hypothesis put forward by Dr. Soreq and the Committee when the study was recommended. Dr. Berkowitz replied that the hypothesis of the study was that anxiety may have produced veterans’ symptoms. Dr. Cherry reiterated that that had not been the hypothesis put forward by the Committee and recommended for study.

Dr. Golomb stated that studies have clearly shown that a relatively small number of ill veterans have anxiety.
Dr. Haley observed that the Iowa study, from which this group of veterans was drawn, was conducted by piecing together questions from various studies. As a result, they have reported findings that are very different from other studies, including a higher estimate of problems with anxiety than has been found in other studies. The interest of the Committee was that enzyme levels be assessed in the larger group of veterans who have Gulf War illnesses, but do not have anxiety. Dr. Berkowitz said that these individuals should be factored out.

Dr. Golomb said that many Committee members were uncomfortable with what Dr. Berkowitz was saying. In the past, when researchers have found symptoms of psychological difficulties in ill veterans, the findings were used to say that Gulf War illnesses are the result of stress. The Committee had been interested in evaluating physiological parameters of Gulf War illness. Dr. Berkowitz said that it is important to isolate the differences associated with each factor. Dr. Golomb replied that the approach described by Dr. Berkowitz would not be capable of doing that, since it relies on the assumption that anxiety caused the physiological symptoms when the physical symptoms could have, in fact, caused anxiety symptoms experienced by ill veterans. Dr. Steele agreed, indicating that the study design was the tail wagging the dog and that there was no evidence from previous research indicating that anxiety had caused all the other symptoms experienced by veterans.

Dr. Barlow said that although she is an outsider, she understands where the Committee’s concern is coming from. It was important that the populations to be studied be properly defined, and then that the data be allowed to speak for itself. Dr. Berkowitz replied that even if the premise of the study was erroneous, the study findings might still provide the justification for a clinical trial.

Dr. Golomb asked Dr. Soreq if she thought that the primary issue of interest for Gulf War illnesses related to anxiety. Dr. Soreq replied that she thinks that the most prominent link with AChE-R is with neuromuscular disease.

Dr. Cherry said she thought we were looking at a marker for exposure but that the purpose of the study had somehow been twisted, changed to a test of anxiety. Dr. Barlow commented that “healthy individuals with anxiety” was not a tight definition for a population to be studied. Dr. Steele said the Committee had expected the purpose of this work was to measure whether veterans with Gulf War illness had elevated AChE-R levels. Dr. Golomb reiterated that anxiety, as a symptom, is present in a very low number of ill veterans. Dr. Barlow said that because ill Gulf War veterans do not look anything like a group of people with anxiety disorders, she thought the anxiety aspect of the study should be scrapped.

Dr. Berkowitz replied that as far as he knew, all of the data would be looked at.

Dr. Haley said there needed to be a protocol people agree on.

Dr. Pellier asked if VA and the study leaders would submit an analysis plan to the Committee. Dr. Berkowitz replied that he would have to discuss that with the research leadership and the principal investigators. Dr. Cherry asked if the committee could see the current analysis plan tomorrow. Dr. Berkowitz said he did not have a copy of the analysis plan.

**Public Comment – Day 1**

Mr. Binns stated that the next agenda item was the public comment period and called on the individuals who had signed up to provide comments.
Alison Johnson said that in a study of multiple chemical sensitivity (MCS) in Atlanta, 1.8% of those with MCS reported having psychiatric symptoms before they developed MCS and 38% reported having psychiatric symptoms after they developed MCS. She also reported that results of using neurotin for MCS have been terrible. She indicated that some individuals with MCS had reported good results with its use early on but had later crashed, and that the drug had been difficult to withdraw from.

Denise Nichols said that, if you talk to the vets, they are still generally being treated as psychiatric patients in the VA system. It also concerned her that the death rate was still going up. She wondered how many who died were given psychiatric treatments when they should have been given medications for their medical problems. She knew, for example, of individuals put on heavy psychiatric medication when they had chest pains. An ill friend who went with her to a conference and forgot his medications was much better when he did not take the drugs. She asked to know what doctors are seeing at the specialty clinics where Gulf veterans are sent. She said she was not asking for a study, just information and communication.

Mr. Binns thanked the members of the public for their comments.

The meeting adjourned for the day at approximately 5:15 p.m.

The meeting reconvened the following day, October 28, 2003, at 8:30 a.m.

**Department of Defense (DOD) Research on Gulf War Veterans’ Illnesses and Chemical Defense**

Dr. Michael Kilpatrick, Deputy Director, DOD Deployment Health Support Directorate

Dr. Robert E. Sheridan, U.S. Army Chemical Defense Institute

LTC (Dr.) Brian Lukey, Director, U.S. Army Military Operational Medicine Research Program

Mr. Binns introduced Dr. Michael Kilpatrick. Dr. Kilpatrick presented a briefing on DOD’s medical research program, including research on Gulf War illnesses and deployment health, and an overview of DOD research relating to chemical defense. (See Appendix – Presentation 9.) This was followed by a presentation by Dr. Robert E. Sheridan of the Army Chemical Defense Institute (See Appendix – Presentation 10.) A discussion followed during which LTC Brian Lukey joined Drs. Kilpatrick and Sheridan in responding to questions about the DOD programs presented.

Mr. Binns asked LTC Lukey and Dr. Sheridan about funding levels for their programs. He noted that one of the researchers who presented to the committee the previous day, whose research has been funded by the Chemical Defense Institute for many years and is highly regarded, had been advised that no funds were available to continue the research. This situation appeared to make no sense at a time when the country is more concerned about chemical defense than at any previous time in its history.

Dr. Sheridan replied that funding for medical chemical defense research was down this year compared to last year and that the overall trend over several years had been flat. In FY2003, the program funded only intramural projects, and was not able to fund all intramural studies planned. In the current year intramural projects are competing with extramural, but funds are still very tight because many of last year’s studies are committed over two years.

LTC Lukey noted that the scientific panels that advise on his programs’ research have all expressed the judgment that their various areas of research are inadequately funded.

Dr. Golomb commented on the importance of drawing and maintaining whole blood samples before and after the current deployment in Iraq and future deployments.
Mr. Robinson asked LTC Lukey if the pre- and post-Gulf War I blood samples from Task Force Riper could be used for testing. LTC Lukey replied that he would be interested to see what tests are available and that it is important that the best tests were identified before using scarce stored blood.

Dr. Steele asked why the Department of Defense was no longer funding research on Gulf War Illnesses at the very time when the research is beginning to provide important insights. It would also seem that Gulf War veterans are a large group that can be studied to provide important insights in relation to future deployment and domestic concerns. Dr. Kilpatrick replied that there is some continuation of Gulf War-related research.

**Additional Findings from the VA ALS Study and Update on the ALS Registry**

Dr. Eugene Oddone, MD, MHSc
Director, Health Services Research Center, Duke University

Mr. Binns introduced Dr. Eugene Oddone to present additional findings from VA’s ALS Study and to update the committee on VA’s ALS registry. (See Appendix – Presentation 11.) A discussion followed.

Mr. Binns asked if results of the interviews regarding exposures showed any relationship between exposures and ALS, noting that there have been at least two anecdotal reports of ill Gulf War veterans developing ALS after secondary exposures to pesticides. Dr. Oddone replied that Dr. Peter Spencer had not found any associations of ALS with deployment-related exposures. His analyses did not address exposures after deployment.

Ms. Knox asked if Dr. Oddone’s team still had the blood samples from the study. Dr. Oddone replied yes.

Mr. Robinson said that veterans calling in to the National Gulf War Resource Center are reporting multiple cases of multiple sclerosis (MS). Might the ALS Registry also look at MS in the future? Dr. Oddone reported that his group had also received calls on MS but that there was no one to hand them off to in the VA system. Mr. Smithson asked if they are maintaining a list of MS patients. Dr. Oddone stated that they were not documenting MS cases at this time.

Dr. Golomb added that she had also heard of cases of MS among Gulf War veterans. Dr. Steele stated that there is an online group of Gulf War and other veterans who have MS, but that there were currently no research efforts focused on the question of MS rates in Gulf War veterans.

Dr. Pellier commented that the ALS study is very important. It provided the first tangible evidence of neurodegenerative disease in Gulf War veterans. He thinks it would be useful to look at all neurodegenerative diseases including ALS, MS, and Parkinsons Disease. Dr. Oddone said they could widen the scope of the effort to include MS and Parkinsons and that such an effort should not triple the total cost.

Mr. Graves asked if anyone has contacted the Kuwaitis to see if they had been affected by excess rates of neurodegenerative diseases. Dr. Oddone said they hadn’t, but that it was a good idea. Mr. Graves said that Kuwait might also be a source of funding for that type of research. Mr. Robinson said that the Kuwait government had put out a call for researchers to do health studies on Kuwaitis.

Dr. Steele asked if they were also including veterans with ALS who had died in order to construct an epidemiologic curve. Dr. Oddone said that initial calculations suggested that the epidemiologic curve had already peaked.
Dr. Steele asked about cases of neurodegenerative diseases referred to the registry that had ultimately not been verified as ALS cases, and what had been the types of conditions in this group. Dr. Oddone said that he could get that information.

Dr. Cherry asked about DNA findings evaluated for the study. Dr. Oddone said he did not have that information, but it would be included in a future manuscript.

Dr. Haley asked if there has been discussion of a brain bank to archive tissues of patients who had died. Dr. Oddone said yes, that they had obtained cost estimates on rapid autopsies that had been about $5,000 per patient. He said they would be working with patient groups.

**Monitoring the Health of Gulf War Veterans Using Existing VBA Data Systems**

*Ms. Susan Perez*  
Asst. Director, Data & Information Services, Office of Performance Analysis & Integrity  
U.S. Department of Veterans Affairs

Mr. Binns introduced Ms. Susan Perez. She presented information on benefits claims data resources at the Veterans Benefits Administration (VBA). (See **Appendix – Presentation 12**.) In particular, she presented data that had been requested by the Committee concerning: (1) the number of veterans who had submitted disability claims and had served in the Gulf War, and the number of veterans who had submitted disability claims who had been in the military during the Gulf War but had not deployed to the Persian Gulf theater; (2) the demographic and military profiles of the two groups; and (3) the number and proportion of individuals from the two groups who had submitted claims for three conditions: ALS, multiple sclerosis, and tinnitus.

Figures reported in response to these data requests were shown in the presentation slides. Although no statistical analyses were provided, the figures did not indicate that a larger proportion of Gulf War veterans had submitted disability claims for MS than veterans who had not served in the Gulf War. Ms. Perez cautioned that this information was not a complete count of MS cases in either group and should not be over interpreted due to limitations inherent in data relating to disability claims.

A discussion followed. Dr. Steele commended Ms. Perez for her teams’ efforts in preparing the GWVIS reports and their demonstration of the different types of data available at VBA that might be helpful in monitoring the health of Gulf War veterans.

**Monitoring the Health of Gulf War Veterans Using VHA Data and Information Resources**

*Dr. Denise Hynes*  
Director, Information Resource Center, U.S. Department of Veterans Affairs

Mr. Binns introduced Dr. Denise Hynes, who joined the meeting by telephone from Illinois. Dr. Hynes presented information on the databases and resources available at VA’s Veterans Health Administration (VHA). (See **Appendix – Presentation 13**.) Due to technical problems with the teleconference equipment, Dr. Hynes was unable to hear questions from Committee members, so minimal discussion occurred following her presentation. Mr. Binns thanked Dr. Hynes for her presentation, and the meeting adjourned for lunch.
Anthrax Vaccinations and Health Outcomes in the National Survey of Gulf War Veterans

Dr. Claire Mahan
Environmental Epidemiology Service, U.S. Department of Veterans Affairs

Mr. Binns introduced Dr. Claire Mahan, who presented results from VA’s National Survey of Gulf War veterans including a subgroup of veterans known to have received the anthrax vaccine in association with Gulf War deployment. (See Appendix – Presentation 14.) A discussion followed.

Dr. Golomb observed that the apparent findings related to self-reported receipt of the anthrax vaccine may reflect instead those who received multiple vaccinations.

Dr. Cherry asked if they had controlled for confounding factors related to deployment. Dr. Mahan said they had controlled for a number of confounding factors, and that one important factor was that more than 70% of the subset of veterans with DOD shot records had been in the National Guard.

Dr. Haley noted that the study findings indicated a recall bias and asked if there might be a way to assess the degree of bias and adjust for it. Dr. Golomb stated that that probably couldn’t be done without having more information than was available.

Dr. Steele asked for information about who was in the subset of veterans with shot records, and where those records had come from, since it had generally been assumed that there were no records of who had received the anthrax vaccine. Dr. Mahan and an audience member from DOD indicated that there were records available for a few units.

Mr. Robinson noted that this data limitation illustrated the importance of careful monitoring of the health of current troops after they received vaccines.

Dr. Cherry said she had found similar results in her study of UK veterans. When analyses took into account other experiences in theater, preliminary associations of symptoms with the anthrax vaccine disappeared.

Federal Trials of the Anthrax Vaccine

Dr. Jack Melling
Director, Karl Landsteiner Institute, Vienna

Mr. Binns introduced Dr. Jack Melling, consultant to the committee, to present an update on federal trials of the anthrax vaccine. (See Appendix – Presentation 15.) A discussion followed.

Dr. Melling noted that studies of newer types of anthrax vaccines being studied often include a comparison group that receives anthrax vaccine adsorbed (AVA), the type of vaccine currently used by the military. Long-term evaluation of symptoms reported by participants in this arm of vaccine trials could provide the type of information the Committee thinks should be collected with respect to whether AVA is associated with long-term adverse effects.

In the discussion that followed Dr. Melling’s presentation, Mr. Robinson said that the U.S. Senate has passed a Sense of Senate resolution to stop the current vaccination program. Lawsuits are pending.

Dr. Steele asked Dr. Melling to explain the difference between AVA and the newer recombinant protective antigen (rPA) vaccines being developed. Dr. Melling replied that AVA is a 1950’s vaccine.
The organism is grown and filtered, and the protective antigen (PA) is isolated for use in the vaccine. The process results in a lower purity of PA, with the specific amount varying from batch to batch. The newer rPA vaccines use the gene that codes for the anthrax antigen and puts it into another organism. This process provides a higher purity and better control of antigen levels.

Mr. Robinson said that his understanding for the current deployment was that some blood samples were taken prior to the shots being given and that samples will be collected again at a later time. He believed that the Army was doing a limited surveillance for the vaccine’s effects and he understood this was being done at Walter Reed.

Dr. Melling said that the relevant parts of the new vaccine studies being planned had not been designed yet, and it might be possible for the Committee to find out more about the details and to make specific suggestions with respect to follow-up.

Mr. Robinson observed that the current vaccine is a different vaccine from the one used in Gulf War I. Dr. Golomb agreed, but said that if studies of the newer vaccine showed a problem, it had some relevance.

**Committee Business**

Mr. Binns stated that the next topic for consideration was committee business. Dr. Steele presented a proposed plan of work for the committee and staff over the coming year. (See Appendix – Presentation 16.) Committee members expressed approval of the plan and provided comments on various aspects of committee activities.

Dr. Golomb said that the topics chosen for meetings and speakers should include areas related to our hypotheses relating to the causes and pathophysiology of Gulf War illnesses.

Mr. Robinson emphasized that treatments were an important area to consider on an ongoing basis.

Mr. Graves asked what funding the committee had. Mr. Binns replied that the committee’s own budget remained at $400,000.

Dr. Melling suggested that speakers could be invited to make written submissions in advance of the meeting which could be posted to the website.

Dr. Steele suggested that the agenda might include public comments on only one day of each meeting, and invite members of the public who provide comments to submit them in writing for the permanent record.

Mr. Smithson asked about the visibility of the website and whether we could keep track of visits? Dr. Steele replied that she had asked VA to do this, and they were working on it.

Dr. Steele raised the subject of the degree to which the committee should consider issues arising out of the current Iraq deployment. Dr. Golomb said that the committee should stay focused on Gulf War I and that evaluating issues related to the current deployment could dilute the Committee’s efforts. The purpose for which the Committee had been established was the illnesses affecting Gulf War I veterans. Dr. Haley said Gulf War I has never ended for those ill veterans and that there may not be much we can do for Gulf
War II veterans at this point in time. Dr. Cherry said that we can keep informed of issues relating to the current war, but may not feel qualified to make recommendations.

Mr. Robinson noted that there are 600 soldiers currently at Fort Stewart with health problems from Afghanistan and Iraq and that the Committee could make recommendations based on lessons learned. Dr. Golomb agreed. Mr. Robinson said the U.S. Senate would be holding hearings on this issue and that others would be working on it as well. Given the considerable experience of some of the Committee members, it might be possible to make some simple recommendations related to things that should be done in relation to the current deployments. Veterans expect the Committee to provide information that helps 1991 Gulf War veterans and also helps make sure that the types of problems they have experienced do not happen again.

The consensus of the discussion was that the Committee would write a letter to Secretary Principi updating an earlier letter regarding lessons learned. Mr. Robinson indicated he would provide the first draft for Committee consideration.

Ms. Knox asked if there are samples of the anthrax vaccine used during the first Gulf War. Mr. Robinson’s understanding was that no samples had been saved.

Mr. Robinson said he is interested in choline as a prospective treatment. Dr. Golomb agreed.

Dr. Melling saw a need to provide current information to VA clinicians that might serve to “reprogram” them away from focusing so much on psychiatric explanations and treatments for Gulf War illnesses. Dr. Steele said this could be a topic for a future meeting.

Mr. Graves said information relating to oil well fires should be considered. For Gulf War veterans located in the middle of the oil well fires, it was like living in a fishbowl of oil rain.

Mr. Robinson said that sand also may have been a factor, and that it could have acted as a carrier for some of the other exposures of concern such as pesticides, infections, and depleted uranium.

There was applause following the discussion of the proposed topics to be addressed at 2004 meetings. The discussion then turned to communications maintained by the Committee. Dr. Steele described summaries of recently-published research and other matters of interest relating to Gulf War illnesses that would be provided to Committee members on a regular basis. Dr. Meggs said that members should continue to chat back and forth by email about emerging research information. Dr. Steele agreed that organized reports should not block the free flow of information. Ms. Knox asked if this information might also be provided to veterans. Dr. Steele indicated it could be put on the Committee’s website.

Dr. Cherry said that the upcoming report to the Secretary should include a focus on treatments. It also should reinforce the need to use and merge existing databases. Ms. Knox asked about the types of links needed between different data sources. Dr. Steele noted that to the best of her knowledge, the presentations made earlier in the day were the first opportunity for VBA to learn about databases available at VHA.

Mr. Robinson said that the Senate and House Armed Services and Veterans Committees should receive testimony on the Committee’s report. That may be the best way to launch it. The Secretary could request a hearing with those committees.
Dr. Golomb asked about the possibility of publishing a position paper in a medical journal. Dr. Steele noted that the PAC and NIH committees had published articles relevant to their major findings.

Mr. Robinson suggested seeking a Sense of Congress resolution.

Dr. Cherry said that an article in Military Medicine might be a good idea. A short piece would do, or a letter to the editor. Dr. Golomb said that one of the major journals is another option.

Public Comment – Day 2

Venus-val Hammack said that the publication U.S. Medicine is also commonly read by VA doctors. Regarding treatments and education through VA, Mark Brown had produced a guide for physicians on Gulf War illnesses, but half of the Persian Gulf coordinators at VA facilities do not have copies. She suggested that the Committee look at this guide, which is at least three years old.

Alison Johnson said a recent article in Sociology had some chilling information. Soldiers who applied to sick call were assigned to unpleasant duty. She offered her video and book for VA training and indicated they had been well received. She offered to make a master copy available for anyone to copy for free or to sell copies for $3.00. She is trying to raise $2,500 for insurance so PBS local stations can show the video.

Denise Nichols commented that the Committee had done some great work. However, the holiday season was coming up and the journals have had some discouraging reports. She wondered if the Committee could do an update, even on a website, of encouraging news such as the partial results from Israel? Suicides increase at the holiday season. Dr. Golomb asked if veterans put the word out to other veterans. Ms. Nichols said that there is a need to get the word out to VA clinicians, perhaps through teleconferencing. She said that VA should start turning things around for the veterans and that although the Committee had done good work with hard research and she was thrilled that treatments would be addressed, it was important to find a way to make a difference a little quicker for sick veterans. Ms. Nichols said that “where the pedal hits the metal” out there at VA hospitals, they still don’t get it. They think Gulf War illness is psychological and refer ill veterans to psychiatrists. Ms. Knox observed that she had a good point.

Mr. Robinson noted that the Committee has no presence in any VA publication. Dr. Steele said that information on the Committee had been published in VA’s Persian Gulf Review.

Dr. Cherry said that inviting written public comments was a good idea.

Mr. Robinson advised the Committee that the annual National Gulf War Resource Center conference would be held April 30, May 1, and 2, 2004 in Washington, DC. The conference would include a tour of the WRIISC Center and the clinical center at Walter Reed.

The meeting adjourned at approximately 4:00 p.m.