THE IMPLICATIONS OF THE U.S. DEPARTMENT OF VETERANS AFFAIRS' LIMITED SCOPE OF GULF WAR ILLNESS RESEARCH

HEARING

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON VETERANS' AFFAIRS
U.S. HOUSE OF REPRESENTATIVES

ONE HUNDRED ELEVENTH CONGRESS

FIRST SESSION

JULY 30, 2009

Serial No. 111–39

Printed for the use of the Committee on Veterans' Affairs

U.S. GOVERNMENT PRINTING OFFICE
51–878 WASHINGTON : 2010

For sale by the Superintendent of Documents, U.S. Government Printing Office
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CONTENTS

July 30, 2009

THE IMPLICATIONS OF THE U.S. DEPARTMENT OF VETERANS AFFAIRS' LIMITED SCOPE OF GULF WAR ILLNESS RESEARCH

THURSDAY, JULY 30, 2009

U.S. HOUSE OF REPRESENTATIVES,
COMMITTEE ON VETERANS' AFFAIRS,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
Washington, DC.

The Subcommittee met, pursuant to notice, at 10:00 a.m., in Room 340, Cannon House Office Building, Hon. Harry E. Mitchell [Chairman of the Subcommittee] presiding.

Present: Representatives Mitchell, Walz, Adler, Hall, and Roe.

OPENING STATEMENT OF CHAIRMAN MITCHELL

Mr. MITCHELL. Good morning and welcome to the Subcommittee on Oversight and Investigations of the House Veterans' Affairs Committee. This is a hearing on the Implications of the U.S. Department of Veterans Affairs' (VA's) Limited Scope of Gulf War Illness Research. This meeting is held on July 30th. This meeting will come to order.

I want to thank everyone for attending today's Oversight and Investigations Subcommittee Hearing entitled, "The Implications of the U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research."

It has been upward 19 years since the United States deployed nearly 700,000 servicemembers to the Gulf in support of Operations Desert Shield and Desert Storm. When these troops returned home, some reported symptoms that were believed to be related to their service and possible exposure to toxins, agents, and chemicals. However, the amount and combination of these chemicals used during this period is unknown, and conflicting research has created a real challenge for being able to prove a veteran's symptoms resulted from service-connection.

As a result, there are many veterans with undiagnosed illnesses and multiple symptom illnesses relating to their service in the Gulf War who are still suffering from chemical agent exposure, and are finding themselves fighting the VA to have Gulf War Illness recognized as a service for compensation.

As many of you know, in May of this year, this Subcommittee held its first of a series of hearings to address this issue. During that hearing we examined the impact of toxins and pesticides used during the Vietnam and Gulf Wars. And with a growing chorus of

concern over the accuracy of existing research, I believe it is time for us to take an in-depth look at the scientific research surrounding Gulf War Illness research.

Today's hearing will focus on how the current research is progressing, including taking a closer look at the reports offered from the Institute of Medicine, the IOM, and the Research Advisory Committee, the RAC. In addition, the hearing will examine the VA's role in treating Gulf War Illness.

There are few things that I would specifically like to examine today. First, did VA and IOM meet Congressional mandates and the essence of Public Laws 105–277 and 105–368 to include animal and human studies, along with evaluating diagnosed and undiagnosed illnesses? Second, were methodologies used by the IOM equivalent in both Agent Orange and Gulf War studies? And third, I would like to examine the methodologies utilized in the production of the RAC report.

We have learned, and will continue to learn, that Gulf War Illness research is a challenge, but a missing link appears to be a lack of documentation of exposure and compounds that exposed our veterans.

Additionally, we are waiting for science to bridge the gap between self-reported illnesses and diagnostic evidence, just as we did with Agent Orange veterans.

Our last hearing on this issue shed light on the fact that we aren't doing enough for our Gulf War veterans and that they continue to fight for what they deserve.

Today, I am hopeful that we will examine this issue with open minds and get one step closer to a consensus amongst Congress, VA, scientific bodies, and most importantly, our veterans.

For today's hearing, we have brought experts from all fields to discuss this important issue. I am hopeful our panelists here today will discuss the merits of the RAC report in comparison with IOM methodologies and the results of both, as well as discuss the best course to ensure that this important research will benefit veterans.

I am anxious to hear from the VA what actions they have taken in response to the RAC report, and more importantly, how the questions surrounding Gulf War research affect our veterans and how the VA plan to move forward.

While I praise all of our panelists here today for the research work they are doing on behalf of our Gulf War veterans, we must find a way to give these veterans the answers they have been looking for since returning home from theater almost 20 years ago.

Before I recognize the Ranking Republican Member for his remarks I would like to swear in our witnesses. I would ask all witnesses from all three panels to please stand and raise your right hand.

[Witnesses sworn.]

Thank you. I would now like to recognize Dr. Roe for opening remarks.

[The prepared statement of Chairman Mitchell appears on p. 47.]

OPENING STATEMENT OF HON. DAVID P. ROE

Mr. ROE. Thank you, Mr. Chairman, for yielding time.

As you indicated in your opening statement this is the second of a three-part series of Gulf War Illness research. The focus entitled to this second hearing is Implication to VA's Limited Scope of Gulf War Illness Research. While I am not sure that the VA has limited scope in the area of Gulf War Illness research, I appreciate you calling this hearing to further evaluate the research that has been completed and reviewed, not just by the Research Advisory Committee on Gulf War Veterans' Illnesses, but also by the National Academy of Science and the Institute of Medicine. I understand that both organizations are represented here today as witnesses.

As a follow up to our first meeting, we have received responses to questions for the record from Dr. Roberta White from Boston University, Dr. Lea Steele from Kansas State University, Paul Sullivan of Veterans for Common Cause, as well as the VA. I appreciate that we received their responses prior to today's hearing. Their input from the last hearing is important information that we have to process today.

On Tuesday afternoon, the Committee also received the Secretary's "Annual Report to Congress on Federally Responsive Research on Gulf War Veterans' Illnesses for 2008." This report is also important for us to review as it reflects the large body of work that is continuing on this matter.

In fiscal year 1992 through fiscal year 2008, the VA, the U.S. Department of Defense (DoD), and the U.S. Department of Health and Human Services (HHS) funded 347 distinct projects relating to health problems affecting Gulf War veterans. As of September 30, 2008, 288 of these projects were completed, and 59 projects were either new or ongoing. I am pleased to have received this report prior to today's hearing.

I am looking forward to a lively discussion today, as we have representatives here from several different scientific backgrounds representing different studies on Gulf War Illness and possible causes.

I am pleased, Mr. Chairman, that you have decided to include in this hearing the Institute of Medicine representatives who have compiled large volumes of material on Gulf War Illness, possible causes, and comorbid diseases, which may or may not have come from exposure during the first Gulf War.

I am interested in learning whether these same exposures were also present during the current conflict and what we can expect as the authorizing Committee, as to new presumptions for exposure in both conflicts.

I would like to remind my colleagues as we proceed that we must, throughout this series of hearings, keep an open mind as to the reports and studies being presented to us, and the way ahead for us as the authorizing Committee for benefits and services provided to our Nation's veterans.

Again, Mr. Chairman, I appreciate your diligence in pursuing these hearings, and yield back my time.

[The prepared statement of Congressman Roe appears on p. 48.]

Mr. MITCHELL. Thank you. Mr. Walz, would you care to make an opening statement?

Mr. WALZ. No, Mr. Chairman, thank you again, and thanks for the Ranking Member for holding this hearing.

Mr. MITCHELL. Thank you. I ask unanimous consent that all Members have 5 legislative days to submit a statement for the record. Hearing no objection so ordered.

If the first panel would please come forward. Joining us on the first panel is Dr. Lynn Goldman, Professor at the Johns Hopkins University Bloomberg School of Public Health. She is also a Member of the Committee on Gulf War and Health at the Institute of Medicine of the National Academies. Dr. Goldman is accompanied by Robbie Wedge, Senior Program Officer at the Institute of Medicine. Also joining us on the first panel is Jim Binns, Chairman of the Research Advisory Committee on Gulf War Veterans' Illness, and Dr. Lea Steele, Former Scientific Director of the Research Advisory Committee on Gulf War Veterans' Illness and Adjunct Associate Professor at the Kansas State University School of Human Ecology.

I want to remind all panelists if they could please keep their statements to 5 minutes. Your complete written statement will be submitted for the record. And I would like to recognize in this order first Dr. Goldman, then Mr. Binns, and then Dr. Steele. Dr. Goldman?

STATEMENTS OF LYNN GOLDMAN, M.D., MPH, PROFESSOR, BLOOMBERG SCHOOL OF PUBLIC HEALTH, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MD, AND MEMBER, COMMITTEE ON GULF WAR AND HEALTH, INSTITUTE OF MEDICINE, THE NATIONAL ACADEMIES; ACCOMPANIED BY ROBERTA WEDGE, M.S., SENIOR PROGRAM OFFICER, BOARD ON THE HEALTH OF SELECT POPULATIONS, INSTITUTE OF MEDICINE, THE NATIONAL ACADEMIES; JAMES H. BINNS, CHAIRMAN, RESEARCH ADVISORY COMMITTEE ON GULF WAR VETERANS' ILLNESSES; AND LEA STEELE, PH.D., ADJUNCT ASSOCIATE PROFESSOR, KANSAS STATE UNIVERSITY SCHOOL OF HUMAN ECOLOGY, MANHATTAN, KS, AND FORMER SCIENTIFIC DIRECTOR, RESEARCH ADVISORY COMMITTEE ON GULF WAR VETERANS' ILLNESSES

STATEMENT OF LYNN GOLDMAN, M.D., MPH

Dr. GOLDMAN. Thank you very much, Mr. Chairman, and thanks also to Mr. Roe and the Members of the Subcommittee for holding this hearing today on your concerns about veteran's health.

As you know my name is Lynn Goldman, and I am a professor of environmental health sciences and epidemiology at the Johns Hopkins University, and I did also serve in government for 6 years as assistant administrator for EPA's Office of Prevention, Pesticides and Toxic Substances. But in this regard, I have chaired two of the Institute of Medicine Gulf War and Health Committees. One of the books here is our report on "Gulf War and Health: Review of the Medical Literature Relevant to Gulf War Veterans Health," and another is our report on fuels, combustion products, and propellants. Also, I was a member of the committee that produced the report on insecticides and solvents. And so I am here because of my experience as a volunteer. Also, I am a member of the Institute of Medicine.

I am going to focus on four points:

First, the overall process that the Institute of Medicine uses for these studies and how these reports are reviewed.

Second, how these IOM committees have determined whether a given agent might be related to a given health effect, relevant to both the Gulf War and the Agent Orange studies that have been conducted.

Third, how these scientific studies incorporate the published literature, including animal studies, in the reviews.

Fourth, how what we know about exposures in the Gulf War might affect our reviews.

So let me begin with study process. I think that you are well aware of the fact that the IOM is a division of The National Academies, that it is a non-governmental institution that was chartered by Abraham Lincoln to provide independent scientific advice to the Nation, and that the IOM assembles volunteers who produce consensus reports that are highly scholarly in nature.

In the case of these particular reports, the expertise that would be brought together would be medical experts and toxicologists, people who know about the substances, know about the illnesses, and understand the animal studies that are relevant to this. These members come from universities and not-for-profit institutions, and they are balanced in terms of being free of biases and conflicts of interest.

Our work is completely independent of the agencies that sponsor this work. They are not allowed to participate in the work or have access to the work. If we do ask them for information that has to be given publicly. Everything has to be out in the open.

So what does a committee do? We review all the relevant literature we can find, we work toward reaching consensus about conclusions, and we draft a report. The Institute of Medicine has a very complicated peer review process with oversight by an external team. I, as the chair of the committee, would have had nothing to do with that process. Another group brings in a variety of experts who review the report and provide comments. Then those comments are returned to the committee. Each comment has to be addressed. Finally, somebody who is independent of our process has oversight over the process to assure that the committee has responded to comments before the report is finalized and made public.

So this is a very extensive process of peer review. At no point during that review process is the sponsor given any access to or allowed to affect either the analysis or the conclusions of the report.

Each Committee has its own way of working. In terms of the Gulf War and the Agent Orange reports, there are two guide posts that these Committees have used. One is the statements of work that are given to the IOM by the sponsoring agency, in this case the VA. The second is the legislation. Certainly in the case of committees I chaired, at each and every meeting we would review both of those, because they are important guides to the direction we should go.

How do we develop categories of evidence? Generally these committees have used five categories, such as sufficient evidence of a causal relationship, extreme for an association, limited suggestive evidence of an association, inadequate insufficient evidence to de-

termine an association, and limited or suggestive evidence of no association. These categories have come about through the practice of scientific bodies over the years, not only by the Agent Orange committees, but also by a group called the International Agency for Research on Cancer. These are ways that scientists can organize our thoughts through a lot of criteria for deciding if a relationship is causal.

One thing that has been misunderstood is how the criteria that they have evolved over time. In the Gulf War studies, for example, a new category of sufficient evidence of a causal relationship was introduced. This category is important. For example, you know that fire trucks are associated with fires, but not because they cause fires. In reviewing scientific evidence, we need to look at chains of events, to understand causal chains look at what precedes an adverse event so that we can make a determination of causality as opposed to association; things that occur together are not necessarily in a causal chain. In science there are specific ways that this is done.

Another thing that I think has been confusing has been the role of human versus animal studies. In this context, we realize that a phrase that has been introduced in some of these studies, "in human studies," has been misunderstood. Basically, when we talk about a causal association and when we are looking at human evidence, we want to make sure that the association isn't due to factors like chance, bias, or confounding. Because epidemiology studies are rife with those problems. And so where the criterion says that causality will be determined on the basis of whether in epidemiology not due to chance, bias, and confounding, some people have findings are taken that to mean, therefore, IOM committees are not looking at animal studies. That is not true. And all of these reports have included examination of relevant animal studies, these studies have been given weight, and there have been experts on these committees that are very knowledgeable about these studies.

Each and every animal study hasn't been reviewed and every report because some of these chemicals, for example, Benzene, have thousands of animal studies. For Benzene has a chapter in every toxicology textbook; we know a lot about Benzene and we can summarize all of that. We don't have to go back and read every single study that is been conducted over the last 50 years on Benzene to know what Benzene does both to animals and humans. And so there is also some judgment involved in terms of which studies are reviewed, how they are included, and the value of the information that is provided by those individual studies is a part of this process.

And the last point I want to make has to do with the exposures in the Gulf War and how that has affected all of the work of these committees. The legislation lists a number of chemicals and biological agents that the IOM was asked to consider, not because there was any specific evidence of how many people might have been exposed to those, but because it was known that those had been used in the Gulf, had been in the arena, and there was some potential for human exposure. No one committee could review all of those substances. So the IOM held some meetings with veterans to try

to identify the agents about which they were concerned, and then developed a process to prioritize those for review.

But this issue of exposure has continued to be a problem. This is not like Agent Orange, where you can go back years later and find traces of dioxins in people's bodies. Among the substances that we reviewed, most are fleeting; they do not leave an imprint that today we can identify. Maybe some day we will, but today we don't have a way of testing whether you were exposed to particulate matter from an oil well fire 20 years ago. Oftentimes, the studies that we reviewed could not provide clear evidence. For example, a soldier might know that they had a vaccination, but they don't know what it was. And, even if they know which vaccination it was, they don't know which lot it came from. But these are the kinds of things that we want to know when we do epidemiology. The records may be there somewhere, but they haven't been in a place where epidemiologists have been able to use them.

And for some of the potential exposures, such as, for example, the bombing and the fire that happened at the Sarin gas plant fire, we have only been able to use models to understand what the exposures might be. It is very difficult to model a fire where you don't know the quantity of the material that was there and you don't know the temperature at which it was burning. You have some information about the weather and the wind speed and so forth, but some of the basic parameters for modeling are missing. And so it is very difficult to determine what the exposures may have been.

The bottom line is although these committees have looked at the health effects of potential exposures as charged by Congress, it is very difficult because of the lack of real exposure information for any scientific body to use to make firm cause-and-effect conclusions about exposures to individuals or even groups of individuals in the context of specific health outcomes.

Last, I should mention that there is an updated review of the literature on Gulf War veterans that is under way at the IOM. I don't know very much about it, I am not involved with it personally. Again, I would like to thank you for the invitation to talk to you today. Thank you very much.

[The prepared statement of Dr. Goldman appears on p. 49.]

Mr. MITCHELL. Thank you, Dr. Goldman.

Mr. Binns.

STATEMENT OF JAMES H. BINNS

Mr. BINNS. Thank you, Chairman Mitchell, Ranking Member Roe and Members of the Committee.

The Research Advisory Committee on Gulf War Veterans' Illnesses is a public advisory body of scientists and veterans mandated by Congress and appointed by the Secretary of Veterans Affairs.

In a moment you will hear from Dr. Steele how the committee's approach to reviewing the science in its 2008 report differed from that used in the Institute of Medicine reports. I will discuss the legal background of the reports.

It is important to understand that neither the Research Advisory Committee report, nor the Institute of Medicine reports, are origi-

nal research. Both of them are summaries—reviews of what others have done.

And the reason the IOM is involved in this subject is because in the same law that established the Research Advisory Committee, Congress directed VA to contract with the IOM to prepare reports to guide the Secretary of Veterans Affairs in determining Gulf War veterans' health and disability benefits.

Now Congress was very specific as to how it wanted these reports done. Congress directed VA to have the IOM review the scientific literature for 33 hazardous substances to which troops were exposed in the war to see if any of these substances were associated with an increase risk of illness. That is not a cause that is associated with an increase risk of illness, that is what the law required.

If there was sufficient evidence of an association—again, not a cause, an association—the Secretary of Veterans Affairs was directed to prescribe a presumption of service-connection for Gulf War veterans' benefits. Because most studies of hazardous substances are done in animals, the law required that both human and animal studies be considered in reviewing this association specifically. And because Gulf War veterans' illnesses often do not fit conventional diagnosis, the law required that undiagnosed illnesses should also be considered.

In addition, because veterans were often exposed to combinations of substances, the law required that the report should consider combinations of exposures, yet the IOM reports themselves state "Only evidence from human studies was considered, combinations of exposures were not considered, and undiagnosed illnesses were not considered in reviewing whether there was a sufficient association."

The result is that the committees of scientists who worked on the IOM reports were attempting to put together a puzzle that was missing half the pieces. Most of these scientists had no idea they were not following the law, I am sure. They were undoubtedly told that they were following standard IOM methodology. The Gulf War reports state that the methodology comes from earlier IOM reports ordered by Congress related to Agent Orange exposure in Vietnam. However, a close examination shows that the Agent Orange methodology was subtly changed in the Gulf War reports. One word, the word "human" was inserted in the definition of whether there is sufficient evidence that a substance is associated with an increased risk of illness.

The effect of this change is that animal studies were not considered in the conclusion that governs the presumption of service-connection, even though the law specifically required them to be considered in that conclusion by both the IOM and the Secretary. Whether they were considered elsewhere in the reports, and they were, is of no consequence.

As to how that could have occurred, I would refer you to my written testimony which includes correspondence between VA and IOM staff prior to the start of one of the reports. These documents show that discussions between VA and IOM staff placed conditions on the report that predetermined its outcome before the IOM committee to prepare it was ever appointed.

Today I am pleased to report that the VA official involved in those discussions has recently left VA. I am also encouraged that the new Secretary of Veterans Affairs is manifestly committed to transforming the culture at VA headquarters to better serve veterans.

So I hope that change is on the way, and look forward to the testimony of the Department of Veterans Affairs this morning. Change is sorely needed.

I have worked for three previous Secretaries of Veterans Affairs, all honorable men, but have sadly seen VA staff continue to minimize the serious health problems of Gulf War veterans. Because of the stature of the IOM, its reports have misled not only the secretaries of Veterans Affairs, but also researchers, doctors, Congress, veterans' families, and veterans themselves.

In December, VA ordered a new IOM report to review the report of the Research Advisory Committee. Thus after waiting 18 years for VA to acknowledge that they are ill due to toxic exposures, Gulf War veterans are now waiting for a committee that has not reviewed all the evidence to review the report of a committee that has. Recognizing the impossibility of this task, IOM staff have stated that its committee will not review the RAC report, but VA continues to say that it will.

What is clear is that the VA IOM relationship is in urgent need of reform. The Institute of Medicine is the high court of American medical science. Manipulation of its processes by the government is a serious breach of public trust with implications far beyond this subject.

[The prepared statement of Mr. Binns, appears on p. 52.]

Mr. MITCHELL. Thank you. Dr. Steele.

STATEMENT OF LEA STEELE, PH.D.

Dr. STEELE. Thank you. Good morning, I am Dr. Lea Steele, I was asked to testify this morning on the differences between the IOM's Gulf War reports and the report of the Research Advisory Committee on Gulf War Veterans' Illnesses, or the RAC.

I was previously scientific director of the RAC and I oversaw the Committee's review of the research for this report. As you know, many veterans returned from the 1991 Gulf War with symptoms that weren't explained by medical or psychiatric diagnoses. This problem has been called Gulf War syndrome, undiagnosed illnesses, or just Gulf War Illness. It is important to distinguish this undiagnosed illness problem from diagnosed diseases like cancer or diabetes.

Gulf War Illness refers specifically to this complex of symptoms. Typically a combination of chronic headache, difficulties with memory and concentration, widespread pain, and other abnormalities that occur together as a multi-symptom condition.

To begin, I will just briefly remind you of some of the major findings of the RAC report. Based on a detailed analysis of nearly 2,000 studies and reports the RAC concluded that evidence clearly indicates that Gulf War Illness is real, that it affects at least one in four veterans of the 1991 Gulf War, and that few veterans have recovered over time.

The evidence most consistently points to two primary causes. First, a small white pyridostigmine bromide pills or PB, that was given to protect troops from the affects of nerve agents. And second, pesticides which were used in large quantities during the war. Several other factors like low level exposure to nerve agents could not be ruled out as contributing to this problem. Studies consistently show that Gulf War Illness was not caused by psychological stress or being in combat.

We also reviewed the evidence of other types of health problems, only a few diagnosed conditions have been linked with Gulf War service. Although serious, these conditions affect relatively few veterans. The biggest problem by far is the undiagnosed Gulf War Illness problem.

The differences between the RAC report and the IOM reports are not subtle, and they are not explained by minor variations in our review methods or how individual studies were considered or weighted. Rather they reflect major differences in the types of questions addressed by the two reports and the scope of evidence that was used to answer those questions.

I can illustrate this by comparing the RAC and IOM findings on PB, the anti-nerve gas pill. PB was widely used by the military only in the 1991 Gulf War. Based on multiple sources of evidence, the RAC found that PB was causally associated with Gulf War Illness; in other words, it is one of the causes of Gulf War Illnesses. This evidence includes studies of Gulf War veterans that provide unambiguous results. All six studies indicated that PB was significantly associated with Gulf War Illness. Studies also found a dose response effect. That is, veterans who took PB for a week or longer had higher rates and more severe illness than veterans who took less PB.

We also considered results from animal studies showing that repeat low dose PB exposure over a sustained period produced brain effects that are not seen with brief or single dose PB exposure.

PB's association with Gulf War Illness is also consistent with what investigations tell us about the patterns of PB use during the war.

So all of these different types of evidence are consistent, and combined they support a clear association between Gulf War Illness and PB, and especially prolonged use of PB.

The IOM report on the other hand found that PB is associated with short-term effects, but there was insufficient evidence to determine if it is associated with long-term effects.

IOM's findings were based largely on clinical research in humans, which generally studied effects of PB taken over a short period, not more than a few days, and had no long-term follow up. Their findings did not consider the many studies of Gulf War veterans or the other PB research I mentioned.

IOM findings did not address in PB is associated with undiagnosed illness, and this was true for most exposures evaluated by IOM. Findings considered only limited types of evidence and did not specifically address if the exposure was associated with health problems that are found in Gulf War veterans.

My written submission lists 12 general types of research that the RAC considered in its findings. The IOM findings relied in large

part on just two of these categories of evidence. The other types were not considered by IOM or just considered in a very limited way.

For example, the hundreds of detailed epidemiologic findings on associations between Gulf War Illness and Gulf War exposures were scarcely considered by IOM. And as Mr. Binns has indicated, IOM findings did not take into account results of the many animal studies of exposures and combinations of exposures.

IOM also made little use of the many government investigations of exposures. For example, the report from DoD on over 60 different pesticide products used by Gulf War personnel concluded that at least 40,000 troops were overexposed to pesticides in theater.

Now aside from these global differences, there are many specific differences in the evidence considered. For example, on the question of how many Gulf War veterans have been affected, the RAC report found, based on findings in 6 out of 7 studies, that between 25 and 30 percent of Gulf War veterans have a defined pattern of multi-symptom illness over and above the background rates found in comparison groups. IOM findings indicate an excess of just 13 percent, about half, based on results from just one of the seven studies.

Another example relates to a highly publicized IOM finding that there is no unique Gulf War Illness. This has been widely misinterpreted to indicate that there is no Gulf War Illness problem at all or that there are just random symptoms in different veterans.

The RAC report examined the many studies that showed a consistent pattern of symptomatic illness in diverse groups of Gulf War veterans, and it concluded that Gulf War Illness is unquestionably a real and definable problem, whether or not it is considered unique from different perspectives.

So now returning to the big picture. What are the actual implications of these differences? Are they really important? Based on our review of the research, I believe they are.

The IOM Gulf War and health reports were intended by Congress to be an authoritative assessment of evidence on both diagnosed and undiagnosed health problems in Gulf War veterans, and specifically to determine if these problems are associated with the many exposures in the Gulf War. But IOM's reports do not provide findings of that type, and they could not based on the evidence considered.

In particular, government officials who rely on IOM findings will know very little about the undiagnosed, but widespread problem of Gulf War Illness, its characteristics, its impact on veterans, and its relationship to exposures during the Gulf War.

In short, the major differences between findings of the IOM reports and the RAC report are not because the RAC and IOM reviewed the same studies, but came to different scientific conclusions about the evidence that result from major differences in what evidence was considered and what questions were addressed. Thank you.

[The prepared statement of Dr. Steele appears on p. 57.]

Mr. MITCHELL. Thank you. Let me just ask very quickly, and maybe it is more appropriate for another panel. Is there a use for PB today? What is PB used for?

Dr. STEELE. PB, it is a drug that is used for myasthenia gravis, it has been used since the fifties. During the Gulf War it was not approved by the Food and Drug Administration (FDA) yet for use as an anti-nerve gas pill, it was given an investigational drug approval just specifically for the Gulf War. Since that time, it has been approved for use as an anti-nerve gas agent against one nerve agent called Soman, but that nerve agent was not present in the Gulf War.

Mr. MITCHELL. Thank you. Does each Committee believe that our veterans are suffering from a multi-symptom illness that is commonly referred to as Gulf War Illness? Dr. Goldman.

Dr. GOLDMAN. Yes, the Committee I chaired that wrote Volume IV did conclude that, and concluded that the rate of such multi-symptom illnesses among Gulf War veterans is much higher than the rate among people who were deployed at the same time who were not in the Gulf.

Mr. MITCHELL. Okay. And the RAC?

Dr. STEELE. Most definitely

Mr. MITCHELL. Okay. Dr. Goldman, what do you see as the difference in the conclusions, not the process or methods, between the IOM report and the Gulf War on Health Volume IV and the health effects of serving in the Gulf War and the RAC report? So not the difference in conclusions, the methodology or methods.

Dr. GOLDMAN. What I think is the most important difference, is that the RAC felt very strongly that they could prove a causal association between PB and the Sarin gas exposures and multi-symptom illness. If you look collectively across these IOM reports you would not see such a conclusion.

Mr. MITCHELL. And this was mentioned in both of them. In your testimony, Dr. Goldman, you stated that inserting the word "human" into the association of evidence was used as a clarifier.

Dr. GOLDMAN. Correct.

Mr. MITCHELL. Was there some reason or confusion about the Agent Orange findings since the word "human" was not inserted in those reports? And does this take away from the scientific word of the study?

Dr. GOLDMAN. Well the Agent Orange committees did not have a category of association for causality. For determining causality, we have in epidemiology the set of postulates that we use called the Bradford-Hill criteria that the association needs to be met before we say it is cause-and-effect. There are a lot of findings in epidemiology that are associations but that aren't actually cause-and-effect. So when that category "causality" was added, that is when Committees said, that for human studies we need to make sure that it is not a result of chance, bias, and confounding.

Now, I have here one of the reports that I was on, on fuels and combustion products. This is the chapter where the animal studies reviewed. And I can show you these reviews, chapter after chapter. So when I hear in testimony that these committees did not review animal studies and when I chaired and served on some of these Committees and I can show you in these books that were published

years ago that these studies were reviewed, I think that there may simply be a disagreement here about that. Because the animal studies certainly were reviewed for these reports.

Mr. MITCHELL. Would either one of you like to comment on that?

Mr. BINNS. Yes. I have a page here from Gulf War on Health Volume I, page 72, that is this one, and it states, "For its evaluation and categorization of the degree of association between each exposure and a human health effect, the Committee only used evidence from human studies." So for that assessment of the degree of association, the Committee only used evidence from human studies.

The requirement in the statute does not state that causality needs to be showed. Yes, our report did go so far as to say we felt it was causal, but the issue here is whether the IOM followed the statute. The statute does not require causality. It says, "That the Secretary should make a determination whether there should be service-connection based on whether there is evidence that a positive association exists between exposure of humans or animals and the occurrence of a diagnosed or undiagnosed illness in humans or animals." It is very clear, and it is just for an association.

And it further states, and this is from the law, "An association between the occurrence of an illness in humans or animals and exposure to an agent, hazard, medicine, or vaccine shall be considered positive for the purposes of this subsection if the credible evidence for the association is equal to or outweighs the credible evidence against the association."

So even a tie goes to the veteran if the evidence were equal. And if there is any evidence over that it definitely triggers a presumption. It does not require causality. It has nothing to do with the Hills postulates.

Dr. GOLDMAN. Actually the Committees read the law the same way that Mr. Binns just cited, and those were the discussions we had at the beginning of every Committee meeting. But one sentence has been taken out of context. If you look at the paragraphs that that sentence is a part of there is a lot of explication of how animal studies were reviewed. In Volume I—I was not on that Committee—you can see descriptions of the studies and they say, "that the Committee used animal and other non-human studies, particularly as a marker for health effects that might be important for humans." The remainder of the paragraph goes on and on about how that was done.

Now you can't ask a dog about a headache. So for conditions that are based only on symptoms, you are going to have trouble elucidating much about those from animal studies. However, you can find out a tremendous amount about how substances are absorbed and what they are doing. There is no group of scientists who would ever say we should ignore information. It is just that you can't make a conclusion about symptoms because you can't ask animals about symptoms. But there is no way that annual studies were ignored by these Committees.

Mr. MITCHELL. Thank you. My time has expired.

Dr. Roe.

Mr. ROE. Thank you, Mr. Chairman. Obviously this is a very, very complicated issue, and you will excuse me, since last night I didn't read all of the material. I did get through a lot of the mate-

rial. And I don't know how we are ever going to come to a conclusion here because of what Dr. Goldman has said, and she is correct. And Mr. Binns, I know you are going straight to the law.

When you are looking at science and you use animals, and I have done scientific research, we can cure cancer in animals, in mice, but it doesn't work in humans. So you have to use both, I agree with that, you can find out. And as Dr. Goldman said, when you are doing animal research, you can't very well go to a human and say let me draw the chemicals out of your brain, which you can do to a mouse or a rat or whatever in the lab.

So it is going to be impossible to ever, I think, because you don't know what the exposure was. And I read in here somewhere where the military, the DoD, didn't even know what immunizations were given to the troops when they went. I find that astonishing to me that you could go. Although I remember when I got mine going in the service, probably like most guys, and now women, you just lined up in a line and they fired away, and if you happened to have a shot record you got it with you, and I have no Earthly idea what happened to mine. So I can understand why a soldier wouldn't know what immunization they were given.

Do you think it would be a benefit to have a third party, although it may not at this point, to look at the two conclusions that were drawn? Because I know in work I have done, sometimes I thought I was going one way and ended up another.

And Mr. Chairman, when you don't know how much—like in the case of Sarin gas—how much someone got, there is no way to ever know. There is not any way you are going to draw a conclusion. Would you all comment on that, please?

Dr. GOLDMAN. My personal view, and this is not necessarily the view of the IOM or anyone of its Committees, is that there needs to be a re-examination of how that whole scheme has worked in terms of the law, and the idea of service-related illness, as well as the hurdles that the veterans have had to leap over in order to be able to document service related illnesses and what they have had to do in order to receive the services that they need.

It might make sense to take all the IOM's Gulf War conclusions, and look at what the VA has done with them and how this work has or has not actually benefited the veterans. Because I think at the end of the day, that is the critical issue, not the subtle differences in the way these Committees might have reviewed these studies, but what can be done to actually benefit the veterans and their health I think that is the major issue.

Mr. ROE. And Dr. Steele has been very, very clear, I mean I listened to her testimony now twice, and she believes that PB—and again, I should have done this last night but didn't—you don't see many myasthenia gravis patients, it is a pretty rare condition. But have you looked at the PB effects in that, Dr. Steele? Has anybody done that?

Dr. STEELE. Sure. The side effects—the acute side effects in myasthenia gravis patients are similar to what we saw as acute side effects during the Gulf War when people took the PB.

The issue is though that myasthenia gravis patients are severely deficient in their acetylcholine mechanisms, and so they take the PB in order to restore, you know, a higher level of acetylcholine so

that they can be normal. That is not the case in healthy young soldiers. They don't need to have their acetylcholine restored. And so the effects that we see in myasthenia gravis patients are quite different in terms of the biology of it.

So although, you know, the acute side effects are similar in the two groups, the long-term use of PB in myasthenia gravis does not tell us much about the long term use in healthy people. And we do have studies of that.

Mr. ROE. Yeah, just one quick question before my time expires. Dr. Goldman, is there any reason why—I mean, Dr. Steele and the RAC Committee is very—they think that PB is the cause. I think it would be very hard to draw the conclusion that it is. But why do they draw that conclusion and the IOM study doesn't?

Dr. GOLDMAN. Well, I think it could be they used a different process for determining causality. But even if PB is involved, which it could be in some of these illnesses, that some of the studies that are published for multi-symptom illness that show high rates among Gulf War veterans, or among groups of veterans who never deployed anywhere close to the Khamisyah location where the PB was dispersed. For example, veterans who were on aircraft carriers the entire time also have higher rates of illnesses.

Also, we did find in one of the Committees that I served on a limited and suggestive evidence for association with organophosphate insecticides that were over there. So there were many other things that were over there.

As I look at it, it is a very complicated picture. If you would only focus on the veterans, even if you did conclude causality, you would only focus on the veterans who were exposed or potentially exposed to Sarin or to PB, you would exclude others who may have been affected since the studies would indicate problems of multiple symptom illness among other veterans as well.

Mr. BINNS. Dr. Roe, if I may respond to your question. And first I believe that the figure that is generally accepted is 250,000 troops were exposed to PB. That is a figure that I believe some from DoD estimates. I have seen it from DoD.

Mr. ROE. A third of the troops were?

Mr. BINNS. Well that would be about something over a third. Yeah.

Dr. STEELE. About half of ground troops.

Mr. BINNS. The other question that you raised earlier though is an excellent one, and on the science I certainly defer to people like Dr. Goldman and Dr. Steele and to yourself as scientists. But Congress recognized that science might never be able to separate out these issues. Congress understood that these are difficult questions when you don't have accurate records and you don't have dose response and so on.

So knowing that, because this law was written well after the war. This law was written in 1997. They had to make some decisions as to who got the benefit of the doubt. And that is where I believe we have an answer already, which is not that we know absolutely what caused it or didn't, but within the terms of this statute they wanted animal studies considered. Congress makes it very clear. Animal studies is put in there about five times, both for what they wanted in the report conclusions and for what they wanted

the Secretary to consider. And then as I just described to you, they didn't require that it be conclusive or causal, they just required that it be equal to or greater statistical evidence that the veterans exposure could result in an illness, and they wanted to know undiagnosed illness exposures as well as diagnosed.

So I think that the statute did resolve it, and I think we do have an answer as to whether the statute was satisfied.

Mr. ROE. Thank you.

Mr. MITCHELL. Mr. Walz.

Mr. WALZ. Thank you, Mr. Chairman. I want to continue on this line, because I think this is an important point that Mr. Binns brought up. And I think from our perspective there is not a one of us up here probably in this room that doesn't have a relative, a friend, a constituent that hasn't suffered from this. And yes, we know that is anecdotal, yes, we know we want to apply the best research, but I do believe it was always the—the spirit of this statute was to get to that point. Because Dr. Goldman really got to the heart of this in saying what we are really trying to find out is how do we best care for them? How do we best develop a line of care? How do we best treat them? And that is one of the things that I would like to know.

Is it safe to say or have we come to this conclusion: If you were a warrior and were deployed during the Gulf War you have a much greater chance of suffering multi-symptom illnesses, that is a given, right?

Dr. GOLDMAN. Yes.

Mr. WALZ. Okay. So we have established that it is there. We have best attempts. And granted, I see a little difference in maybe Dr. Steele. Was it the methodology with the IOM study that you take most—

Dr. STEELE. No. In many ways the methodology of reviewing the science was very parallel.

Mr. WALZ. Okay.

Dr. STEELE. It is really about what areas of the science were considered and pulled together in order to come to our conclusions.

Mr. WALZ. Do you feel like the RAC study maybe got to the intent of the law was to find what Mr. Binns was talking about better?

Dr. STEELE. We had a different purpose for doing what we did, but in the end yes, we did consider all of the evidence that IOM was directed to consider, and we put it together to talk about associations between illness and exposures.

Mr. WALZ. Is anything coming out of this research? And again, this is for the next panels, but since you have been so involved in this is, is there any good research coming out for treatment out of the work that both of these panels have done, or this more trying to find association maybe?

Dr. STEELE. Right now actually the studies have shown that Gulf War veterans have not recovered over time for the most part, and we don't have effective treatments for this problem. But some of the research reviewed in our report talks about some of the biological findings that we are finding in Gulf War veterans, and we think this will point us to doing the right research for treatments.

Mr. WALZ. Okay.

Dr. STEELE. But right now, no.

Dr. GOLDMAN. My view is that the studies that have been done to date haven't given us good information about either the natural history of these multi-symptom illnesses, nor how they evolve over time, nor the impacts of various types of treatment, including lifestyle and nutritional interventions that have been given The nature of these illnesses, just like many of the illnesses that I suffer from and many of you do as well, is that lifestyle factors, like smoking, caffeine, drinking, exercise, make a big difference in health. I think that this veterans could be benefited by more research. This is again just my personal opinion.

Mr. WALZ. Okay.

Dr. GOLDMAN. Future research could look at the time course of these illnesses, and also whether these undiagnosed illnesses turn into diagnosed illnesses. That is even something we don't know. That happens sometimes. People initially present with something you can't diagnose and then there is progression and it turns into something that can be diagnosed.

Mr. WALZ. That is an interesting point. Because my final question on my available time is, while I am deeply concerned that we get the care, we make this right, as we are equally concerned with Agent Orange, my fear always in this is have we learned anything? Did we repeat the same mistakes from Agent Orange to Gulf War Illness, and are we prepared to repeat the same mistakes for the returning veterans who are yet undiagnosed? That is where we should equally focus. And I would ask each of you if you think, have we missed the lessons learned here and do we need to start preparing right now?

Dr. STEELE. I can just briefly say that we learned some things but we didn't learn enough. And that is that in the current deployments in Iraq and Afghanistan we don't see these multi-symptom illnesses on a widespread basis that aren't explained by known things. We see other problems. We see head injuries, we see infectious diseases, things like that.

So we learned enough to one, not give everyone pyridostigmine bromide and overuse the pesticides. We made differences in policies that way that helped. But we still have a long way to go to try to properly assess veterans before they go, properly keep records of the exposures they encounter while they are in theater, and then assess them when they get back so that we can pick up these things at an earlier stage.

Dr. GOLDMAN. Yes I would agree that they are doing a better job now with pre-deployment examinations and post deployment examinations and a little more information about exposure. I would wish that there would be better records kept.

I think one of the biggest lessons though is that deployment even for a war that seems to be a short war, is a significant health event. And I think that part of what happened is that there was an under appreciation of what those veterans had gone through, and an expectation that they would be okay. In a sense, that they fell through the cracks.

Mr. WALZ. That is a great point. Well thank you all for the research you are doing, we truly appreciate it.

Mr. BINNS. If I could just offer one comment. Whether the recommendations of our committee's report, which includes several recommendations for further treatment research, are adopted or not, is at the moment in limbo because of this disconnect where VA has stated that it has referred our report to the Institute of Medicine for review, and yet my understanding from Institute of Medicine staff is that their current committee is not in fact reviewing our report.

So if you call could clarify that for me today now that we have everyone here, that might be a good opportunity to move things ahead.

Mr. MITCHELL. Yes. Go ahead.

Dr. GOLDMAN. I can try. At the same meeting that Mr. Binns and Dr. Steele presented I also presented to that committee and that is about all I know of that committee. But my understanding is that while they are covering the same ground, this is not a peer review of the RAC report. I think it might be a matter of semantics. They be producing conclusions in the same arena, but they are not doing it as a critique of the RAC. They are doing it as a parallel process, and that is the way that I understand that they have taken their charge, in a way is more a positive than a negative. I don't know quite how to put that. And perhaps we should have a response back from that committee, just for the record to just completely clarify what they are doing.

Mr. MITCHELL. If the Subcommittee will indulge me. Yes, Ms. Wedge, you are the chair of the committee that is updating this?

Ms. WEDGE. I am not, I am the study director for that, I am not a volunteer, I am an IOM employee. But I can clarify this. We are not reviewing the RAC report. We don't review reviews. So we are looking at original literature, much of which was included in the RAC report and anything new that has been published since the RAC report, and we are updating what was done in 2006, Volume IV, which was review of the literature. So we are to look what health outcomes have increased prevalence in deployed Gulf War troops compared with non-deployed Gulf War troops.

Mr. BINNS. If I can just add to that. The last part is specifically what that committee is charged to do. It says, "The committee will summarize the literature on the outcomes that were noted in the 2006 report; cancer, ALS, neurologic diseases, birth defects and other adverse pregnancy outcomes, post deployment psychiatric conditions. The committee will also review studies on cause specific mortality."

They are not going to review any of this literature on substances, the degree to which substances are associated with illness, that is not their charge. And it is as if someone were to look at the first, you know, pages 83 through 87 of the RAC report and say they were reviewing it. Yes, it will bear on those narrow topics that they are reviewing, but it has nothing to do with animal studies, with all of these issues we have been discussing today; nothing.

Mr. MITCHELL. Thank you. Mr. Hall.

Mr. HALL. Thank you, Mr. Chairman, and I would like to submit a statement for the record. Unfortunately I am double booked. There is a markup in another Committee that I have to go to shortly.

[The prepared statement of Mr. Hall appears on p. 48.]

First of all thank you and Ranking Member Roe for holding this hearing, and our witnesses for your testimony, and for your work.

Dr. Goldman, in your testimony you stated the VA did not play a role in IOM's examination of Gulf War Illness. Given the disagreements between your organization and the RAC and the delayed final product as a result, would you be open to at least limited involvement of the sponsor or the RAC in the study process?

Dr. GOLDMAN. Even if I were willing to allow this, my committee members wouldn't. If you bring a bunch of scientists together who are tops in their field, which is what these Committees consist of, they are not really accustomed to taking direction from government bureaucrats telling them how to do their work. If they thought that was happening, you wouldn't get scientists to volunteer to serve on a committee. Scientists take great pride in working independently; they take great pride in being skeptical. That is one of the reasons why the criteria for decisions changed over time.

Mr. HALL. Okay.

Dr. GOLDMAN. It doesn't work that way.

Mr. HALL. You have answered my question.

Mr. Binns, does the RAC see any possibility of expediting a final IOM product so that we can begin to provide better care to our Gulf War—or compensation to our veterans in the Gulf War? And is there anything your group can do to assist them?

Mr. BINNS. Again, to go back to what the statute provides. The law gives the Secretary the option to use other evidence. He is not required to follow only the IOM reports. He could look at, for example, VA's own recent large survey of Gulf War veterans' health, which found that 25 percent of Gulf War veterans have chronic multi-symptom illness, and that is the largest problem, and conclude on the basis of that that you have more than an equal possibility that this is associated with the war and create a presumption. So he doesn't have to wait for the IOM.

And I don't think that this process that is going on now with the IOM committee is going to clarify this whatsoever, because the IOM committee has a rather narrow charge, and it will do that charge very well as Dr. Goldman has said, but it will not clarify whether on these larger issues who is right.

Mr. HALL. Dr. Steele, why do you think that the IOM considered a narrower scope of evidence than RAC? And what do we do to rectify this? Or in the future perhaps should we do to rectify this?

Dr. STEELE. You know, a lot of people believe there are different motivations from different sectors that are driving this. I actually have no idea about any of that.

All I can say is that Gulf War Illness is very complicated as Dr. Roe indicated. And the evidence that has now accumulated over 18 years is very complicated. And it is really—it doesn't work to just sort of cook book a little method where you look at all these studies of cancer and all these diseases that Gulf War veterans don't have and see if the human evidence indicates that Gulf War exposures leads to these diseases.

In other words, it was just the very limited scope of what they looked at in very great detail, but that this didn't really address the elephant in the room.

So they chose to do the method that they use for Agent Orange. That may have been appropriate for that, but it really was not appropriate for this more complex situation.

Mr. HALL. Is this the biggest population that you are aware of that is been given PB pills?

Dr. STEELE. By far. By far. Nothing even close.

Mr. HALL. Is PB currently being prescribed for anything or given to humans?

Dr. STEELE. It is. As we talked about it is prescribed for a specific disease, myasthenia gravis, it compensates for a chemical deficiency in myasthenia gravis. In healthy people, in soldiers it is still approved for use in the war theater for one specific nerve agent, but it has not been used for that purpose since the Gulf War.

Mr. HALL. To your knowledge do people who are receiving PB to restore their nerve transmitter normalcy, are they exhibiting any of the same symptoms?

Dr. STEELE. On a short-term basis, yes. If they go off the PB they are terribly ill. I am not sure you would notice Gulf War syndrome kinds of problems long term in people who took PB for 2 weeks and then went off of it. So it is not apples and apples, it is apples and oranges.

Dr. GOLDMAN. In the way that is the crux of the challenge that all of these committees have had when they look at these substances. Because you can look at what PB does to people who are chronically on PB because they have myasthenia gravis, which is a chronic disease. You don't have a bunch of people who were on PB and then off of it, and then a couple of years later develop or didn't develop a chronic disease.

Dr. STEELE. You have one group like that.

Dr. GOLDMAN. So, you can find a few studies like that, but it is difficult to find a lot of evidence like that for almost anything.

Dr. STEELE. Except if you look at Gulf War veterans who are the study group.

Dr. GOLDMAN. Right. So you have the veterans themselves for whom we know that around 25,000 people were given the pills. But then in the studies not everybody given the pill takes the pill. It is very complicated. Some take one or two pills, some take the whole pack, some don't take any pills at all. So when you start taking the studies apart, if that is all you have and then you get back to the problem with the exposure information I agree with you.

Dr. STEELE. Absolutely, it is very complicated. But you are right, if that is all you had you probably wouldn't think that it was causally associated. But since we have so much more that all point in the same direction we feel that high hurdle of causality was met.

Mr. HALL. Dr. Steele, and Dr. Goldman also, did your studies show depleted uranium (DU) as a factor at all?

Dr. STEELE. No. Depleted uranium, along with several other exposures during the Gulf—there was very little evidence to support any connection between depleted uranium and Gulf War multisymptom illness. We don't know if it may be associated with other things. There haven't been a lot of studies in populations that have looked over the long term after an initial exposure.

Mr. HALL. Well it hasn't been long enough for some of the diseases you would be looking for.

Dr. STEELE. In theory, if there were to be cancers for example resulting from this, some would have been showing up by now, but no one has been looking at that.

Mr. HALL. Thank you.

Dr. GOLDMAN. And this means it depends on the type of cancers; different types have various latency periods. There are ongoing studies of the depleted uranium, and I think that those are important, because this is also probably the first time there has been a large enough group of people with documented DU exposures to be able to carry out those studies. Some cancers kept very long latency periods, some shorter, and I think it is worthwhile to look for that.

Mr. HALL. To keep an eye on it.

Dr. GOLDMAN. Yes.

Mr. HALL. Okay. Thank you very much. Thank you, Mr. Chairman.

Mr. MITCHELL. Thank you. And I want to thank this panel for the work that you are doing. It is very valuable, and I think as we get into the rest of the testimony with the rest of the panels we will find that there is not much more we can debate about what your two charges are; it is now going to be up to the VA to make a decision.

So I want to thank all of you for the research and the dedication you have put in to helping our veterans. Thank you.

Dr. GOLDMAN. Thank you very much.

Dr. STEELE. Thank you.

Mr. BINNS. Thank you

Mr. MITCHELL. I would like to welcome panel number 2 to the witness table. For our second panel we will hear from Dr. Robert Haley, Professor of Internal Medicine at the University of Texas Southwestern Medical Center; Dr. Roberta White, Professor and Chair of the Department of Environmental Health and Associate Dean of Research at the Boston University School of Public Health; and Anthony Hardie, a Gulf War veteran from Madison, Wisconsin.

Again, if you would please keep your comments to 5 minutes, and after that I want you to also know that your complete statement will be in the record. I would like to recognize first Dr. Haley, then Dr. White, and then Mr. Hardie up to 5 minutes.

STATEMENTS OF ROBERT W. HALEY, M.D., FACE, FACP, PROFESSOR OF INTERNAL MEDICINE—EPIDEMIOLOGY, DEPARTMENT OF INTERNAL MEDICINE, UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER AT DALLAS, TX; ROBERTA F. WHITE, PH.D., PROFESSOR AND CHAIR, DEPARTMENT OF ENVIRONMENTAL HEALTH, AND ASSOCIATE DEAN FOR RESEARCH, BOSTON UNIVERSITY SCHOOL OF PUBLIC HEALTH, BOSTON, MA; AND ANTHONY HARDIE, MADISON, WI, (GULF WAR VETERAN MEMBER, RESEARCH ADVISORY COMMITTEE ON GULF WAR VETERANS' ILLNESSES)

STATEMENT OF ROBERT W. HALEY, M.D., FACE, FACP

Dr. HALEY. Mr. Chairman, Ranking Member Dr. Roe, other Members of the Committee, I am a professor of internal medicine, epidemiology, and clinical science at University of Texas Southwestern Medical Center. I spent 10 years at the Centers for Dis-

ease Control and Prevention doing research, epidemiology research, and I have been on the faculty for 25 years at Southwestern doing clinical research.

The purpose of this morning is to describe our research program. We have been working on this for 15 years, and we now have a large group of researchers from eight different universities around the country collaborating. And our goal is really to move beyond what caused this and try to find out what do we do about it.

So we really have three goals for our research program. One, to understand the medical reasons for this multi-symptom illness. What is causing those symptoms?

Second, to develop an objective diagnostic test. Because what we need in the VA is for every VA Medical Center to be able to perform some objective tests to say who has this illness and who doesn't, both for service-connected purposes, as well as for our diagnosis and triaging people to the appropriate treatments.

And third, to actually develop the scientific basis for developing new treatments, because we are pretty optimistic that there perhaps will be treatments for this that will make these people feel better.

The program really has three major components, and I will just sort of discuss those from the big picture all the way down to the brain cell research.

The three components are first a national survey in a random sample of 8,000 Gulf War veterans selected randomly from the entire population. The purpose of that is to take a look at the illness, manifestations, 19 years, 18 years after the war. We have a component in this looking at the longitudinal effects. Has this improved, got better, gotten worse, or what? We are also collecting blood samples from all of the sick veterans and a random sub-sample of the well veterans, about 2,000 in all, to get DNA and do a, we hope eventually, a genome-wide association study to see if we can look at the genetic basis of this illness. So that is the national survey.

The second part is a series of brain imaging studies, sequentially repeating a set of brain imaging studies in one group after another to try to hone in on what are the right tests to do to understand these symptoms; what is causing those symptoms. And then to use that to develop a diagnostic test and also to bear on treatments.

To date we have studied one major group of veterans, and we are getting ready to now study a sample from our National survey, so that the results of that—we are going to try to replicate what we found in our first series of studies in a group that is nationally representative so that it would be even stronger evidence. So that is the neuroimaging phase.

And the third phase is a basis science studies looking at what do those chemicals, pesticides, pyridostigmine bromide, PB, and Sarin nerve agent, what do these do to brain cells? Because if we can figure out what these chemicals—assuming that these were the cause, and we don't know that for sure—but if they are, what do they do to brain cells, and if we know that, we may be able to reverse engineer this and come up with an antidote that actually reverses the symptoms. On the model of Parkinson's disease, when they figured out that dopamine problems were causing Parkinson's, we came up with El dopa and other medications.

Now our findings to date, in our National survey, we have reconfirmed again that there is a unique Gulf War syndrome. It has three variants, which are important to know because they had different brain imaging findings, and we think they actually are different components of illness. We have also looked at the time course and shown that Gulf War veterans are not getting better.

Now in the brain imaging studies we have looked at each of the symptoms of Gulf War Illness. Memory problems, thought process is slowed, constant body pain, chronic fatigue. These are the major symptoms that cripple these veterans. And our brain imaging studies can show what the brain is doing when they are having these symptoms. We can illicit these in the brain scanner and show exactly what is happening to the brain. And we now are coming up with what the mechanisms are of this multi-symptom illness in the brain. And so we think from this we will develop diagnostic tests that we would be able to then hand off at the VA Medical Centers around the country to diagnose Gulf War Illness just the way you would diagnose thyroid disease or whatever.

And finally our studies in animals. We developed a mouse model in which we can give low doses of pesticides, PB, and Sarin nerve agent in collaboration with the U.S. Army at Aberdeen Proving Ground, and we can reproductively now produce a behavioral disturbance in mice, which interestingly, just like in Gulf War veterans, doesn't come on immediately; it takes about 6 weeks or so for this behavioral disturbance to occur, which would be just what we saw in the Gulf War with Gulf War veterans. And we now have ten different laboratories around our university and in some other places looking at mouse models to see what is happening 3 months later after this exposure. What has changed in the brain in the ones exposed to the chemicals compared to the ones that were not exposed? And the idea is, if we can get down to the molecular mechanism of what is changed, we may then be able to reverse engineer that to a medication or some other rehabilitation treatment that would actually reduce the symptoms or eliminate the symptoms of this illness and return veterans back to a normal life.

Now, I must say, having talked with hundreds of Gulf War veterans who are my patients through the last 15 years, I have not found one veteran that wants to be service-connected and get disability. They all say, doctor, I want somebody to make me well so I can go back to work. I would like to go back in the military is what they say.

And so our goal is to use brain imaging, understand the brain mechanisms of these symptoms, develop a diagnostic test from that, correlate that with the animal models and see if we can then develop a treatment for it.

[The prepared statement of Dr. Haley appears on p. 62.]

Mr. MITCHELL. Thank you. Dr. White.

STATEMENT OF ROBERTA F. WHITE, PH.D.

Dr. WHITE. Good morning, Mr. Mitchell, Dr. Roe, and Members of the Committee.

This morning I want to talk about my experience with Gulf War veterans over the last 16 years and their health problems. I will speak from a research perspective on the epidemiologic investiga-

tions in which I have participated. These studies have examined health outcomes related to chemical exposures in Gulf War veterans. I will also talk about my clinical experience in working with veterans as a neuropsychologist at the VA and in university medical center settings. My aim is to integrate these two sources of experience in order to better provide an understanding of the challenges involved in understanding and treating Gulf War Illness.

As mentioned in my prior testimony in May, our research efforts in Boston over the last 16 years have focused on relationships between exposures experienced in the Gulf War and health outcomes. We have carefully controlled for stress symptoms, diagnosis of posttraumatic stress disorder (PTSD), psychiatric diagnoses, and other variables that affect performance on our outcomes like neuropsychological test performance, questionnaire answers, and neuroimaging results. These are the confounders that Dr. Goldman talked about.

These studies have led to the five conclusions that I am going to summarize this morning. First, pesticide exposures in Gulf War veterans are associated with increased health symptoms, especially those involving the central nervous system.

In addition, such exposures are associated with poorer neuropsychological test outcomes and with chronic multi-symptom illness.

Second, exposure to pyridostigmine bromide is also associated with neuropsychological test outcomes and increased health symptoms.

Third, mixed exposure to high levels of pesticides and PB is associated with more severe effects, including elevated health symptom complaints, poorer neuropsychological test outcomes, and chronic multi-symptom illness.

Fourth, exposure to nerve gas agents in Khamisyah is associated with poorer neuropsychological test performance and smaller white matter volumes in the brain in a dose-dependent manner. That is, higher exposure predicts greater pathology.

Fifth, Gulf War veterans with higher numbers of symptom complaints have smaller white matter volumes on brain imaging than those with low numbers of symptoms.

It is important to note that the above findings were seen in veterans who were not diagnosed with clinical illness by physicians. They did not have diagnosed brain damage nor were their neuropsychological or brain imaging results considered to be in the abnormal range. Most of the study participants were working at the time of their participation.

The epidemiological study results suggest that there are subtle changes in brain structure and function associated with chemical exposure in Gulf War veterans. Such changes are often referred to as "sub-clinical" central nervous system effects of exposure. The research results suggest that these exposures are also associated with significant experiences of poor health and dysfunction in daily life.

How do such findings relate to the clinical examination of individuals with exposure to pesticides and other neurotoxic chemicals? When patients are seen clinically, neuropsychological test results and brain imaging can vary. They can be abnormal, but they can

also be interpreted as being normal, even among patients who experience significant health symptoms and functional problems in daily life. This reflects the insensitivity of the diagnostic tests available as well as other factors.

Gulf War veterans often show this picture, and it can be perplexing to clinicians when they observe poor health and multisymptom complaints in individual patients. This may lead to confusion about diagnosis, treatment options available for patients, and even whether to accept the patient's complaints at face value.

The clinical and research evidence suggest that health symptom complaints in Gulf War veterans should be taken seriously, especially if the veteran has known exposure to neurotoxicants in theater. These include pesticides, PB and Sarin and Cyclosarin gas exposure. Diagnosis of post-traumatic stress disorder is made and compensated based on self-report of psychological symptoms in the context of a significant stressor. Self-reported physical symptoms and dysfunction in daily life deserve to be taken just as seriously.

[The prepared statement of Dr. White appears on p. 68.]

Mr. MITCHELL. Thank you. Mr. Hardie.

STATEMENT OF ANTHONY HARDIE

Mr. HARDIE. Thank you Chairman Mitchell and Ranking Member Dr. Roe and Members of the Subcommittee. I would also like to thank my fellow Gulf War veteran, Matt Letterman, who drove here on his tractor across the country to be here and it is really an honor to have other Gulf War veterans here as well.

Thank you for the invitation to testify today regarding implications of U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research. By limited I take that to mean it hasn't been focused on treatments to help improve our lives.

I am honored to fulfill the Subcommittee's request to testify today as a Gulf War veteran regarding my own personal experiences, observations, and recommendations on these issues, most of which is contained in my written submission due to the time constraints. My experiences are far from unique, and I am sharing them in the hope that it will help to better inform the Subcommittee and the VA and to help assist countless thousands of my fellow Gulf War veterans who like me have been injured and ill for nearly two decades following the war without effective treatment.

In mid January 1991, my team was directed to begin taking the PB pills that we had all been issued. We were told they were experimental, not FDA approved, that we had no choice in consenting, we were ordered to take them, and that we would probably experience symptoms similar to mild nerve agent poisoning; which was the case.

Like tens of thousands of my fellow Gulf War veterans, I experienced significant side effects including watery eyes, runny nose, confusion, dizziness, muscle twitching, diarrhea, weight loss, and a host of other symptoms, including feeling generally ill.

Because of the technological advances of the 1991 Gulf War displayed around the clock on CNN, it was easy to understand why there was and seems to be a persistent belief in the U.S. that for the first time in history, there was no fog of war during this war.

On the ground it was most definitely a different story as in every war before.

We were told that the Iraqis has not used or even forward-deployed their chemical weapons and the alarms must have been sand or other false alarms. We now know today that wasn't true.

We received communication at one point that a nearby unit at R'as al-Mishab had been hit with chemicals, a chemical warfare agent, and we later received communication that the chemicals had been confirmed. If I remember correctly by the British. Later, it was discounted as simply a false alarm, despite the second confirmation. This story is far from unique, with Gulf War veterans having echoed similar stories in previous public testimony.

When we launched into southeastern Kuwait with coalition forces, we found a sand-table map covered with chemical warfare and other symbols. That was the object of great interest to the Untied States Central Command officers who flew in the following day before the facility was closed off permanently thereafter.

In one bunker complex north of the Kuwait Bay, a handful of us went through, I was captivated by the lovely fragrance that smelled just like the red flowers that filled my grandmother's garden back home, and it pervaded all of those Iraqi bunkers that I went through that were so hastily evacuated that plates of half-eaten food and loads of personal gear had been left everywhere. In fact, for anyone who has ever been in the military to leave half-eaten food is the most unusual thing you could ever imagine. No one is going to leave food behind.

Years later I was horrified to learn that what I smelled, along with the pervasive smell of wet onions, was the characteristic odors of Lewisite and Mustard, a classic mixture used heavily by the Iraqis during the Iran-Iraq war. Even still, I discounted my own severe respiratory illness as having been from that, simply because I didn't know until just a couple of years ago that while the damage is immediate, symptoms don't necessarily evolve until as long as even 24 to 48 hours after exposure.

I have now heard enough first-hand accounts from Gulf War ground troops about coming across chemical mines and all sorts of other chemicals that I now firmly believe that the Central Intelligence Agency and the DoD had and have no basis for their long-held statements that Iraqi ground commanders never possessed or used chemical weapons during the war. The extent and impact of intelligence failures were widely discussed on and off the battlefield as part of that fog of war.

Sadly for most of my fellow Gulf War veterans who are ill, the VA's limited scope of Gulf War Illness research on treatments has not even begun to yet address the health outcomes associated with these widespread chemical warfare agent exposures, exposures to pyridostigmine bromide, and all the other agents that were—and exposures that were listed in the Persian Gulf War Veterans Act of 1998 by Congress more than a decade ago. We know what caused Gulf War Illness, we just simply need to work on treatments.

I have had difficulties and experiences with my VA, including most recently I had—my cough for example has never subsided since 1991. This spring after 18 years, I was finally able to get a

brochoscopy looking into my lungs, and its results were yet one more bittersweet revelation, like the revelation from the Research Advisory Committee in Gulf War Veterans' Illnesses that finally acknowledged that Gulf War Illness is real and that what has been going on with this is real. The revelation was my lungs were red, irritated, and angry looking with mucus and a diagnosis of a form of chronic obstructive pulmonary disease. For me this was no surprise.

Due to VA's limited scope of Gulf War Illness research not focused on treatments or effective diagnosis, I found this bittersweet victory on my own with private health care, not at a VA facility.

As I have often said, if it weren't for the military I wouldn't have been able to keep on struggling to stay in the workforce, but then again if it weren't for the military well, I guess I wouldn't have had to.

Submitted with my written testimony is a statement written by my mother more than a decade ago in support of my VA claim, which has been challenging like most other Gulf War veterans. It could frankly have been written by any Gulf War veteran's mother describing what she saw in her son, all the symptoms, all the changes for the worse.

Clinicians at local VA hospitals, still after 18 years, seem to have no idea what to make of or to do for Gulf War veterans than simply to put band-aids on our symptoms. Because of VA's research inadequacy it is not focused on treatments for Gulf War veterans, clinicians at VA facilities have not known what to tell Gulf War veterans, what to do that might even help to improve our health or lives, and as well have not been known for what to tell us to avoid or be careful of.

VA and other doctors have not known to tell ill Gulf War veterans to avoid at all cost any additional exposure to pesticides, paint primers, and related chemicals. I have had to find that out on my own, like so many other Gulf War veterans.

A friend like Joel, a career soldier and now lives in Iowa, I believe he is truly a hero. He is now totally disabled, despite being a decorated multi-combat tour veteran. This is not right.

And finally, like many Gulf War veterans, I have beliefs in how we got to this point when more than 18 years later we have almost nothing to show for all of it, with the exception of the most recently funded promising ongoing DoD Congressional Directed Medical Research Program research and the University of Texas Southwestern efforts. There are no treatments, no advisements, no adequate assistance to give ill Gulf War veterans, and the benefits process is grossly broken.

Later in this hearing you will hear from others more eloquent than me about how VA's fundamentally flawed contracts with—or earlier reliance on reports have led to today's stark failure regarding Gulf War veterans' illnesses. The greatest failure is one of the outcomes. More than 18 years after the war, VA has essentially nothing to show for or to provide to Gulf War veterans for all of its quote "efforts," and little or nothing to offer the one-fourth to one-third of all Gulf War veterans who like me remain ill, disabled, at home, and with no effective treatments.

I am happy to answer any questions, and again thank you for this opportunity.

[The prepared statement of Mr. Hardie appears on p. 70.]

Mr. MITCHELL. Thank you very much. Dr. Haley, a couple things. What are your thoughts regarding the differences presented here today between the RAC and the IOM in their findings?

Dr. HALEY. Yeah, that is a bit far a field from what we are doing. Basically I think it comes down to how you ask the question, and if you ask the question differently you get different answers. I think that is basically my take on it.

Mr. MITCHELL. One other question. With all the missing links of DoD documentation of what veterans were exposed to, do you believe that science will ever be able to answer why Gulf War veterans continue to suffer these undiagnosed symptoms? Is there any hope for veterans through science?

Dr. HALEY. Yes, I think so, and that is where we are focused. And you know, the question is, what help are you talking about? If we are talking about proving what caused this we will—with further and further epidemiologic and clinical research, we can get closer and closer to that. We will never be able to say that perfectly, but that is not what the veterans are looking for. The veterans want to know how do I get better? And what they need is a diagnostic test, an objective test that they can go to their VA and the doctor can say, oh you have Gulf War Illness, well let us send you over here to go through the test battery. And the results come back from the doctor and he says, oh you have type one Gulf War Illness or type two Gulf War Illness. Well, we know here is the treatment for that, and we will then send you over to the clinic and give you the medication or the rehab strategy or whatever. That is what they want. And there has been very little research done in that way, and that is our total focus is to do what a group of scientists—and we have done this, sit down and agree with scientists—how would you get to a diagnostic test and how would you get to a treatment? And the idea is the plan that we have here. And we are fairly far along.

In our second study that we just finished we now believe we can see what is going wrong in the brain when they are having problems with memory, or when their thought process is slow, when they are having constant body pain.

We can see parts of the brain that are now functioning. And we are getting ready to try to replicate this now in a random sample of the population to be absolutely certain of this. And then we think from this we will be able to develop—within the next year or so—we will have a diagnostic test that we can hand off to VA Medical Centers so that Anthony and other veterans like him can go to a VA and get a real diagnosis with objective tests that has a high degree of certainty to it. And then another couple of years, 2 or 3 years down the line, we hope our studies in animals will then lead to clues about what kind of drug or what kind of rehab strategy we will need to cure that. I think that is really what the veterans are looking for.

Mr. MITCHELL. Thank you. Dr. White, based on both your clinical experiences with Gulf War veterans and your scientific research, do

you believe the IOM's report draws significant conclusions and findings?

Dr. WHITE. Well, I am not exactly sure how to answer that question. We heard today that they believe that Gulf War Illness exists, which is something that is a little difficult to find out of the report. I believe that the scientists at IOM, and I do work for IOM myself as a volunteer, I am on a committee right now, work in good faith and try to do what they are supposed to do.

I think they looked at different data, looked at it in different ways than the RAC did, and that really what needs to be done is that all the sources of evidence and summary reports that have been produced need to be considered by VA.

Mr. MITCHELL. Thank you. And Mr. Hardie, as a well-informed Gulf War veteran who is a member of the RAC, are your perceptions of the VA's interest in Gulf War research in caring for the—or what are your perceptions of the VA's interest in Gulf War research and caring for our ill Gulf War veterans?

Mr. HARDIE. Well first I would like to say that I think that their intentions are honorable. I think that they have a very difficult job. I think that the difficult job, they are sorting through the directions given to them by law from Congress, they are sorting through all the scientific recommendations, the recommendations being given to them by veterans, and many of them are not medical doctors as well so it makes it even more challenging.

At the end of the day I guess I am not so interested in where we were or how we got to where we are today, I am deeply frustrated. It is heart breaking when I find my veteran friends on Facebook and so many are ill, so many are totally disabled. This affects women veterans as well.

I think the focus has got to be on—Dr. Haley clearly has been working with Gulf War vets like me. He said it again today, and that is that we need to be focused on helping Gulf War veterans to get better, and that is really what this has got to all be about.

Mr. MITCHELL. One last question as my time is up. If you could sit down with Secretary Shinseki as a Gulf War veteran, what recommendations for the way ahead would you give to him?

Mr. HARDIE. I would say that programs like the Prosthetic Research Program have been profoundly effective, and model programs after the prosthetic—VA has done wonderful work on prosthetic research making a huge impact for those who have lost their limbs. I would say to follow the National Center for PTSD with their ways of informing people and clinicians with clinician guides. And I would say to follow other effective models that have worked. Traumatic brain injuries (TBI)—I have been evaluated now and gone through that program and have talked with folks there. Have folks go through the TBI Program. Give people memory aids. Give them like we do for TBI troops coming back from Iraq and Afghanistan, give them a Palm Pilot if that is going to help them to remember their appointments and so on.

But all the things that are working now, focus on those kind of things and focus on doing the kind of tests like lung tests for those of us who have lung injuries, whether they be biopsies or whatever might be the case, I think they will find there are things that can be treated as well.

Mr. MITCHELL. Thank you, my time is up. Dr. Roe.

Mr. ROE. Thanks, Mr. Chairman. And just to give you an idea about how absolutely complicated this is, and I think one of the reasons when the war was first over and the veterans came home, I think one of the things that had delayed this were the very low number of casualties. I think that threw everybody off a little bit. There were no casualties, so for a long time no one looked for anything because we—I mean for one it is too many, but for the number and the number of troops that were sent—I was raised in Clarksville, Tennessee where the 101st Airborne is, and I think they came back without a single fatality from that war, which is astonishing when you think about it. But I think where we dropped the ball was we didn't think there could have been some other casualties.

The other thing that made this difficult, just to give you an example, 17 percent of the population have headaches. If you look at depression, that is where I think we got thrown off, a certain percentage of it. So when you combine, especially Dr. Haley in your phase one, I read your study last night, and I think that is what threw people off to begin with was because here you had something that has a prevalence and an incidence in the population in general, and was there a cause and effect. And I think that is where we got thrown off.

I think Mr. Hardie that is what happened. And not to apologize for anybody, but I can see how it happened. And I think now you are absolutely right, that is all behind us, let us do something to fix it.

The question I have, Dr. Haley, for you is have these studies of the brain been reproducible, and when you compare them to someone who is let us say depressed or has chronic headaches, do you see similarities in the findings? Just for clinical.

Dr. HALEY. Yeah, that is the key question. And we actually did these studies—a subset of these studies we are doing now we did 10 years ago on the same group that we just brought back to do 10 years later, and we find that the ones that showed abnormalities 10 years ago are right on target again. That is, for example, there is a chemical test, an MR spectroscopy, NMR of the brain, and you can study chemical changes. Ten years ago we reported a finding where basal ganglia, these deep brain structures down in the middle of the brain and the brain stem had a chemical imbalance, actually a reduction in a chemical. It was a definable chemical difference that has been shown in many studies to indicate damage to neurons. And then 10 years later, we brought these same guys back and they have the very same thing, the same side of the brain, the right side of the basal ganglia is worse than the left just the way it was 10 years ago.

Similarly, we have done a spec study where we give them a medication that simulates a Sarin exposure or a pesticide exposure. It is a benign medicine that doesn't hurt you, but it stimulates the same parts of the brain. Ten years ago we showed that sick Gulf War veterans respond just the opposite to normals to this drug. That is, something through those parts of the brain so that the response is exactly 180 degrees from normal, and we just replicated that and found the very same thing is occurring 10 years later, and

now we are getting ready to do this in a totally new group. It is a random sample of the population to see if it replicates out in the total sample of Gulf War veterans.

Mr. ROE. How many have been studies? I know there have been—I think PB—Mr. Hardie, I may have heard this wrong, a quarter of a million troops, and is that accurate from the RAC study?

Mr. HARDIE. It was stated on the earlier panel, but I believe it was—250,000 was the number I heard.

Dr. HALEY. In our current study we have 60 veterans, about 15 in each group. We have three syndromes, syndrome one, two, and three, they are clinically different, and then a control group. In a neuroimaging study typically you have between 10 and 20 per group, and we have 10 to 15 in each group. What we are going to be doing when we bring in the national sample, we are going to have 20 per group to give us even more power than we need.

Mr. ROE. And Dr. White, just out of curiosity, I was raised on a farm and fooling around with a lot of pesticides. Do you have anything in the farm community where—I mean, I have seen crop dusters fly out and as a kid that was a great thing to go watch, I mean you got dusted.

Dr. WHITE. Well the pesticides of greatest importance that were used in the Gulf War in terms of the health effects are organophosphates and carbamates, both of which are neurotoxic. There is a huge occupational literature on farmers, migrant workers, lots of different occupational groups, and you see the same kinds of patterns in those groups where they have symptoms, sometimes even depressive or behavioral changes after long-term exposure. So what we are seeing in the Gulf War veterans in terms of pesticide effects is very consistent with what you see in farmers.

Mr. ROE. Just in conclusion. Mr. Hardie thanks for your service to your country, and we will try to get this right.

Mr. HARDIE. Thank you, sir.

Mr. MITCHELL. Thank you. Mr. Walz.

Mr. WALZ. Thank you, Mr. Chairman. I would echo the Ranking Member's sentiment, thank you so much for your service and also for you to know Mr. Hardie that we appreciate your continuous service to your comrades in arms to get this right and to know that our responsibility is to make sure it is not just thanks, but in a tangible way this Nation thanks you and that is by making sure our care is right. So I am really pleased that both these panels have been focusing on how we take this to the next level of providing care.

I do think it is important to note in this that our majority counsel is a Gulf War veteran, was at Khamisyah, and those things matter. Because the Chairman and the Ranking Member are very, very cognizant of this issue.

And I would also note, I saw Mr. Hardie you are from Wisconsin, so I know both of us are glad Bret Farve is retired. I am from Minnesota so get that straight.

There was a statement in here in your statement Mr. Hardie that I think really sums up where we are at, and I have to be honest with you, it is very touching, but also incredibly frustrating for me. Here is what it says, "Thousands of other young men in their

twenties and thirties suffer in silence not wanting to complain. Someone needs to speak out for them. If the Government waits until all the studies are done before they act, it will be years and then it will be too late." That was written by your mother on March 27th, 1998.

Mr. HARDIE. Yes, that is right.

Mr. WALZ. And here we sat listening to some studies, listening to where it is at. I will have to say though, Dr. Haley, your comments about us getting much closer to the idea and then listening to what we just heard in the last panel, we can get to the point, we can get a diagnostic test, we have met the threshold of benefit of the doubt for the veterans, we can get that done and we can move forward.

And Mr. Hardie, I would ask you, I am with you on this, I am the biggest advocate of the VA. These are people that want to do right. But because of that I am also their biggest critic.

What would happen today for someone who was a Gulf War veteran, they walked into a VA hospital and said, I got body aches, just can't rid of this, what would happen to them?

Mr. HARDIE. Well, I think that it varies depending on the location. I think that at this point my experiences are different than some others.

I have heard as recently as this spring that a Gulf War veteran walked into a VA Medical Center in—I will get the State wrong, I thought it was Oklahoma—but was told that there was nothing wrong with him and he was complaining and seeking help from others that he was just simply getting sent to mental health.

In my case being sent to mental health was the best thing that ever happened to me because they referred me back to primary care and to specialty care because they said that it wasn't associated with any known psychological condition. So I would hope that that is what would ultimately happen with that veteran as well.

At this point, I think that the VA doctors are very compassionate, they are very talented, they are caring, they are a wonderful bunch by and large. I couldn't say that 15 years ago with a couple of bad experiences, but I would say that today unequivocally. And I think that they will do their best to try and treat symptoms. But again, I think the problems—I have always believed this—the problems lie here in Washington and the problems lie here because the VA docs will do the best they can to treat symptoms, but they don't know what to do for folks. If you have a chronic cough, how often do you see Mustard Lewisite veterans anyplace? How often do you see folks who have Sarin brain damage anyplace? And so we need to find answers to what to do to make people's lives better.

And the benefit system is broken, just to add that in there. That is a whole separate topic, you could have countless hearings on that. The benefits system for Gulf War veterans is not okay. The benefit system is terribly broken for service-connection, which is the gateway to getting health care.

Mr. WALZ. Well, I agree with you as I said, and just like your mother said, okay, we have studies, that was 11 years ago now.

I think Dr. White said it, I think it was pretty unequivocal today, and I haven't heard it a lot, that yes, it is an absolute connection, that we agree that there is a connection there. We don't know the

actual causality and all of this, but if you are deployed to the Gulf War, you are going to come back with something wrong with you, you know, in more cases than not. Is that true, Dr. White, is that kind of what you heard?

Dr. WHITE. Well, I mean I have heard that, that a substantial portion of people who come back from the Gulf War have this. Probably 25 to 33 percent.

I will say that the VA knew Gulf War veterans were coming back with symptoms very early, because they started calling me about it within a year of the war, they were paying attention to it at that time.

I would also like to say that I think we really need to pay attention in terms of diagnosis, compensation, and triaging people for treatment of symptom complaints. I don't think there has to be a physical diagnostic test. And that if we wait for a physical diagnostic test we are going to hold up paying attention to empirical and mechanism-based treatments that we can be starting right now.

So really when I said we need to believe what Gulf War veterans say about their symptoms, we know what the core set of symptoms is, I meant that. We do that for PTSD, and we should do it for Gulf War Illness.

Mr. WALZ. Well, I think the time has come. My biggest fear is, and I can tell you that the Gulf War veterans and there are some here and obviously you, Mr. Hardie would say, take down their words and we will come back in 11 years from now on this hearing and still be following it. And they would say that not out of cynicism, but out of experience. I hope our pledge is that that is not the case, that we break this. I think we are at a breakthrough point and maybe we will get there. So I yield back.

Mr. MITCHELL. Thank you. Mr. Alder.

Mr. ADLER. Thank you, Mr. Chairman.

First, Mr. Hardie, thank you for a couple things. I join my colleagues here in thanking you for your great service to our country. I also thank you however for your conversation with Mr. Walz regarding the quality of physicians and other medical providers you have encountered at the VA.

We have had a couple experiences in the last few months on this Subcommittee. We have had to look at some situations where VA hadn't quite met the standard we would seek for all of our veterans everywhere across the country, and so I think it is very gratifying for all of us in the Subcommittee to hear a positive testimony on behalf of the men and women that work in the VA system and try to do the best they can.

But as I heard Dr. White's comments just now about 25 to 30 percent of our Gulf War veterans presenting with symptoms and multi-symptoms, if you can't somehow put it into a box and say what the disease is, it is still a disease. These people need help.

I guess I am wondering from your panel what any of you could recommend we could do to expedite either a correct diagnosis through better research, or a better education of our VA physicians and other providers so we don't have Mr. Walz' nightmare scenario of 11 years from now reading back Mr. Hardie's mom's words in frustration again. Maybe one of you could give us some suggestions

of what we can do to move the ball forward quickly and effectively for our vets.

Mr. HARDIE. I am going to defer to my scientist colleagues, but I would just like to say just briefly, that you know, if Dr. Roe were treating a patient and the patient presented with a condition that he had never seen or heard of before and it was called amyotrophic lateral sclerosis (ALS), it would be very difficult to figure out what to do with that patient. And I know we still don't have treatments for all the Gulf War vets that have ALS and multiple sclerosis (MS), the same kind of a situation. A condition like acquired immune deficiency syndrome presents lots of conditions in lots of different ways. I think there are underlying mechanisms and I will defer to my scientist friends here to perhaps elucidate that better.

Dr. HALEY. Yeah. You know, if you look back in the history of developing treatments for diseases there are really basically two ways that you do it. One is you just happen upon a treatment by trying to treat people, you know, digitalis and some of the famous drugs, nobody ever did studies of those, they just happened upon it.

And the other way is to do very detailed research, understand the mechanisms of the disease, and engineer a treatment, that is called the rational approach as opposed to the serendipitous approach. We ought to be doing both.

And I think Bobbie said it right. I think it would be good for the VA right now to declare a real effort to educate the physicians. You know there was an education program like what 15 years ago that said basically this is psychological and you don't really need to do anything about it, and that has never been changed as far as I know, that is the record. And so it would be very productive to rethink that and say when people come in with symptoms here are a bunch of things we can try and just see if we get lucky and hit on something that will work. Because there is a lot of literature about how you treat chronic fatigue syndrome and fibromyalgia and some of these other diseases that look a little bit like this. So there are a lot of things they could try, and if they had a systematic approach they might be able to really come up with a breakthrough just by luck.

On the other hand, what our program is doing is trying to go step by step to slug out this hard science and get to the bottom, get to the mechanisms both of what is going on in the brain and then what do these chemicals do to the inside, to the machinery of brain cells just like in Parkinson's disease, then see if we can engineer a treatment, but that is going to be a longer effort.

And so in the meantime we ought to be aggressively triaging these people based on their symptoms and then having a program to try to try different treatments for them. You think, Bobbie?

Dr. WHITE. Well, I do have two suggestions. One would be to continue some of the funding started by CDMRP and other agencies focused on treatment trials; those can be empirically based or mechanistically based. We do have some theories about the mechanisms underlying Gulf War Illness that are amenable to treatment approaches. So that is one research way we could go about this, that is to systematically look at treatment possibilities.

My second suggestion would be clinically based in terms of educating VA physicians again with probably a new program. And secondly, developing a set of experts to which Gulf War veterans could be referred for specific work-up. So people who are experts in the effects of chemicals on health, people who are experts in the pulmonary consequences of different kind of exposures, people who do neurological evaluations of people with multi-symptom illnesses.

So I think there needs to be a well-thought-out research approach and a well-thought-out clinical approach in order to deal with the problem. And I think there are things that could be done right now. We need more science, but we also need to just move.

Mr. HARDIE. And may I add to that? Add as well of advisements on what to avoid. Avoid DEET. I mean, it makes me ill, it makes my fellow Gulf War veterans ill. Avoid KILZ when you are covering the paint on your wall and you want to put on the new primer, avoid that.

VA has done a wonderful job of updating its Web site here recently for Gulf War Illness in the last week or so, and they have a new structure. The clinician's guide unfortunately is still outdated, and I know that there is a new VA official I was just sitting next to who is coming into a big job and it would be great if VA would take on that task of fixing the clinician resource. I sure wouldn't want one of my buddies walking in the VA hospital now and being seen by a doctor whose only experience was that outdated clinician's guide.

Mr. ADLER. I thank you for that comment. One more question, is that all right?

Mr. Hardie, this is just to you. What are you presently service-connected for? And do you think that is the right category?

Mr. HARDIE. Sure, I am service-connected for a list of things. I had a non-combat related issue for which I was at Walter Reed for more than a year with my lower leg. That was purely a muscular and venous issue and so I am okay with that. But I am also service-connected for post-traumatic stress disorder at 30 percent, which is similar for—most of the guys I served with in Somalia have a similar diagnosis. I am service-connected for fibromyalgia, chronic fatigue syndrome and irritable bowel syndrome. I would like to highlight that for VA you can only be service-connected for fibromyalgia, or chronic fatigue syndrome, they are both at 40 percent together, but the fact that even though my fibromyalgia and chronic fatigue are so debilitating that I am no longer able to work, I was an executive at the Wisconsin State Department of Veterans Affairs, an agency of about 1,200 up until just a few months ago, the maximum as I understand is 40 percent, irritable bowel at 10 percent. I am service-connected for asthma. I don't have asthma. I appreciate the fact that some VA clerk somewhere service-connected me for asthma because I had a misdiagnosis of asthma of 10 percent back in the military. I have never had asthma. They called it post-exertional asthma since they didn't know what to do with it. I filed repeatedly, I have stated in my VA claims paperwork I don't have asthma. I have an undiagnosed lung condition, which was finally diagnosed this March. The irony of that diagnosis of COPD, chronic obstructive pulmonary disease, is that now I am no longer able to get service-connected under the undiagnosed

illness provision. So I guess I am service-connected for asthma and that is where it is going to be.

Mr. ADLER. I thank you for that.

Mr. HARDIE. I may have forgotten some as well. There are a couple smaller ones in there somewhere.

Mr. ADLER. I think we made our point together. Thank you, sir.

Mr. HARDIE. Thank you.

Mr. ADLER. I yield back.

Mr. MITCHELL. Thank you very much. And again, I would like to express the gratitude of this Committee and our country for the work you are doing and researching and trying to get to this. And Mr. Hardie, thank you for your service. Thank you.

Mr. HARDIE. Thank you.

Mr. MITCHELL. I would now like to welcome panel 3. For our third panel we will hear from Doug Dembling, Associate Chief Officer for Program Coordination, Office of Public Health and Environmental Hazards for the Veterans Health Administration, U.S. Department of Veterans Affairs. Mr. Dembling is accompanied by Dr. Victoria Cassano, Acting Chief Consultant for the Environmental Health Strategic Health Care Group, Veterans Health Administration; Dr. Joel Kupersmith, Chief Research and Development Officer, Office of Research and Development, Veterans Health Administration; and David Barrans, Deputy Assistant General Counsel, U.S. Department of Veterans Affairs.

And if we will, we will begin with Mr. Dembling and you will have 5 minutes. Thank you.

STATEMENTS OF DOUGLAS E. DEMBLING, ASSOCIATE CHIEF OFFICER FOR PROGRAM COORDINATION, OFFICE OF PUBLIC HEALTH AND ENVIRONMENTAL HAZARDS, VETERANS HEALTH ADMINISTRATION, U.S. DEPARTMENT OF VETERANS AFFAIRS; ACCOMPANIED BY VICTORIA ANNE CASSANO, M.D., MPH, ACTING CHIEF CONSULTANT, ENVIRONMENTAL HEALTH STRATEGIC HEALTHCARE GROUP, OFFICE OF PUBLIC HEALTH AND ENVIRONMENTAL HAZARDS, VETERANS HEALTH ADMINISTRATION, U.S. DEPARTMENT OF VETERANS AFFAIRS; JOEL KUPERSMITH, M.D., CHIEF RESEARCH AND DEVELOPMENT OFFICER, OFFICE OF RESEARCH AND DEVELOPMENT, VETERANS HEALTH ADMINISTRATION, U.S. DEPARTMENT OF VETERANS AFFAIRS; AND DAVID BARRANS, DEPUTY ASSISTANT GENERAL COUNSEL, OFFICE OF GENERAL COUNSEL, U.S. DEPARTMENT OF VETERANS AFFAIRS

Mr. DEMBLING. Good morning, Mr. Chairman. Thank you for this opportunity to discuss VA's work in studying the illnesses of Gulf War veterans. I am accompanied today, as you pointed out, by Dr. Joel Kupersmith, Dr. Victoria Cassano, and Mr. David Barrans.

My written statement, which I submitted for the record, provides background information on Gulf War veterans, explains VA's relationship with the Institute of Medicine, discusses VA and IOM agreements with regard to animal studies, describes the range of services and benefits available to Gulf War veterans, and outlines Federally sponsored research related to Gulf War veterans.

In the few minutes that I have, I would like to make several points. In following the laws Congress passed, VA has utilized the

National Academy of Sciences, Institute of Medicine, for almost two decades to evaluate potential associations between environmental hazards encountered during military deployment and specific health effects.

Congress directed us to work with IOM initially regarding Agent Orange and urbacide exposures of Vietnam veterans, and later regarding the various exposures experienced by Gulf War veterans.

IOM's work has allowed VA to recognize approximately a dozen diseases as presumed to be service-connected allowing veterans who where in theater during the relevant period to be compensated for these conditions without having to prove their connection to service.

Since Congress directed VA to enter into an agreement with IOM to review and evaluate the available scientific evidence related to Gulf War veterans, nine IOM committees have generated comprehensive reports on Gulf War veterans health issues. This work has allowed VA to presume service-connection for conditions includes ALS, and under forthcoming regulations nine infectious diseases.

Current law already provides presumptive service-connection for Gulf War veterans, undiagnosed illnesses, or unexplained chronic multi-symptom illness regardless of whether the condition can be causal linked to a specific exposure in the line of duty.

IOM is an independent world-class organization. They put their analysis through rigorous internal and external review. VA relies on their determinations and has confidence the methods they used to conduct their assessments. When VA contracts with IOM we defer to their professional opinions concerning methodology so they maintain that independence.

IOM reports consider the available research, including both human and animal studies to guide their findings about whether there is evidence of an association between exposure to a substance or hazard and the occurrence of an illness, and whether there is a plausible biological mechanism or other evidence to support that connection.

There have been some concerns expressed that VA may have instructed IOM to disregard animal studies in their scientific assessments; this is a misperception. In reviewing all of the contracts for the nine IOM studies, there is no language in the contracts, including the statements of work, that either requires or requests IOM to disregard animal studies. VA has provided this Subcommittee with the statements of work for both the Gulf War and Agent Orange IOM studies.

The standard procedure for all VA contracted IOM committee studies is to leave each independent committee completely in charge of deciding what research to include and how to interpret it.

VA takes the illnesses of Gulf War veterans very seriously and has established a robust research program to study these illnesses. VA had spent over $20 million in support of research on Gulf War veterans' illnesses in both fiscal years 2007 and 2008. Research is an important element of our support for veterans, and by turning information into action, VA directly improves the care of America's veterans. VA trains its providers to respond to the specific health

care needs of all veterans, including Gulf War veterans with difficult to diagnose illnesses.

Moreover, every VA Medical Center is required to have an environmental health clinician available to discuss any concerns veterans or providers may have regarding combat theater exposures.

VA distributes similar information to providers through newsletters, brochures, conference calls, and the war-related illness and injury study centers to educate providers to the unique needs to combat veterans.

In conclusion, Mr. Chairman, Congress has directed VA to utilize IOM's independent evaluations of research when making determinations about Gulf War veterans' illnesses. IOM is a nationally recognized authority in analyzing clinical research, and we rely on their ability to provide sound assessments.

At the same time Secretary Shinseki recognizes that this well-established process takes time. He has asked VA staff to review this approach and determine if there are additional ways to more rapidly uncover the data necessary to determine a connection between exposures and military service and specific health outcomes.

Thank you for the opportunity to testify. My colleagues and I are prepared to address any questions you or any of the other Committee Members might have.

[The prepared statement of Mr. Dembling appears on p. 79.]

Mr. MITCHELL. Thank you. Dr. Kupersmith?

Dr. KUPERSMITH. Yes, I do not have an opening statement. I was a late entry in this as a witness, and we agreed to have to statement in within the next few days.

[The prepared statement of Dr. Kupersmith appears on p. 83.]

Mr. MITCHELL. Thank you. A couple questions. First of all to Mr. Dembling. You heard from all three panels. First of all that there was an agreement on the first panel, the RAC and the IOM, that there is a multi-symptom case which they all agree called Gulf War Syndrome. I got that nod from both of them. So there is such a thing as a multi-symptom Gulf War Illness.

And you heard from the second panel that what these veterans are after, they are not after disability, they are after a cure. They want to get back to a normal life. And you heard from Mr. Hardie that it has taken 18 years and he is still trying to get the services he needs.

In your statement you are really going back and defending—that is fine—IOM and so on.

Let me tell you, from what I have gathered here, and I want to quote the statute that Mr. Binns was referring to. It says, and this is under section 1602, the presumption of service-connection. It says, "This section is to warrant a presumption of service-connection by reason of having a positive association with exposure to a biological chemical or toxic agent." And then it goes on to say, and it talks about the exposure of human or animals to a biological chemical and so on. "The Secretary shall take into account reports submitted by "—all the groups that we have talked about—" and other sound medical and scientific information and analysis available to the Secretary. An association between the occurrence of an illness in humans or animals and exposure to an agent, hazard, or medicine or vaccine shall be considered to be a positive for pur-

poses of this subsection if the credible evidence for the association is equal to or outweighs the evidence against the association." And as Mr. Binns said, if it is about equal deference should be given to the veteran.

We are hearing, you know, that they are still having trouble in the VA of trying to get the services they need for these particular illnesses.

Now my question is, how does the VA plan to mediate the differences between these two different reports and how it will affect veterans? How do you plan on mediating these differences? You just can't fall back and say we are only going to take one or the other. Both of these groups were authorized by Congress. And the question is what are you going to do about it?

Mr. DEMBLING. That is a good question, Mr. Chairman. And Congress has directed us, as you know, to work with the Institute of Medicine and getting updates on a periodic basic and use those updates to make determinations about presumptions of service-connection, which we have done. Going back to the years where we were doing these studies using Agent Orange. And it is our expectation, and I think as you heard from Dr. Goldman, that there will be a discussion of the underlying scientific research. We don't anticipate that IOM will review the review of previous scientific——

Mr. MITCHELL. They are not doing that.

Mr. DEMBLING. They are not doing that. They will be reviewing the scientific literature.

Mr. MITCHELL. So you are only saying that you are going to look at the IOM. What about the RAC? That is also established. They have some credibility.

Mr. DEMBLING. Right.

Mr. MITCHELL. So what are you going to do with them?

Mr. DEMBLING. Well let me yield to Dr. Kupersmith, he handles the research portfolio for us. It is a Research Advisory Committee. Their views and recommendations have been taken into consideration by VA over the years.

I think with regards to this specific issue of whether there is a causal relationship—a cause for the unexplained illnesses of veterans or not, we want to see the next report from the Institute of Medicine, which will consider any scientific evidence that wasn't considered in their previous reports that VA's Research Advisory Committee might have used in coming to their determinations. And they will be reporting to use in early 2010, and we expect that they will consider all the research that was conducted up to that point.

Mr. MITCHELL. In the meantime what happens to people like Mr. Hardie? You know, he had to go out on his own to find out that he had a bronchial problem, and now he can't get any kind of service for that. He has been there over 18 years. How many more studies? You know, you really haven't answered. What are you going to do with the RAC report?

Mr. DEMBLING. Dr. Cassano is a physician, she is heading up our Environmental Health Program.

Mr. MITCHELL. Yes, but you are the one in charge of the VA, right?

Mr. DEMBLING. You are specifically asking about health care and what can be provided to veterans for health care. Let me see what Dr. Cassano can say about that.

Dr. CASSANO. As Mr. Dembling had previously mentioned, there are two different focuses. What we do with the IOM has been demonstrated here in the first Committee. The RAC is supposed to advise Dr. Kupersmith's group regarding the direction of future VA research.

I think the best way to resolve these issues, as we have already initiated a dialog between both IOM and the RAC, to discuss how they came up with different conclusions. The RAC report did review more current literature than the IOM did. That may be part of the problem, and we recognize that. However, once we get this report in February, we will review that report and see if there are still differences and we will have to decide at that point which evidence—what evidence we are going to use, but that involves a process. It is the same process. Whenever we get a report, either if it is Agent Orange or Gulf War, there is a process that VA goes through to analyze the results of those reports.

Mr. DEMBLING. And at the time——

Mr. MITCHELL. Did you hear Dr. Haley's comment about research, how you happen to get to it and the people he is dealing with, that these are real symptoms, and Mr. Hardie went through the same thing? And you are just going to sit and rely strictly on what the IOM says?

Mr. DEMBLING [continuing]. Just because there may be a lack of understanding about the cause of certain illnesses or diseases doesn't mean we can't treat them and provide services and health care to veterans, and that is what we are doing at our VA Medical Centers every day.

Mr. MITCHELL. Okay. But let me tell you, there is a perception among far too many Gulf War veterans that when they go in to the VA that they just keep—who is supposed to help them improve their health, that they are just getting procedural excuses, and they just keep getting put off. That is the perception.

Mr. DEMBLING. Okay.

Mr. MITCHELL. Now if it is not true, VA has a lot of work to do to overcome this and that is your job.

Mr. DEMBLING. Absolutely. And there may be cases where veterans did not get the services that they should be getting and we want to know about them. If there are specific examples of veterans not getting services we can follow up on that.

One of the things that we have set up——

Mr. MITCHELL. One at a time. Two hundred and fifty thousand people and you are going to do one at a time.

Mr. DEMBLING [continuing]. Well one of the things that we have done that was established shortly after the Gulf War hostilities were over was to establish referral centers for veterans that had difficult to diagnose illnesses. That has been expanded. We now have three War-Related Illness and Injury Study Centers that provide comprehensive physical examination and work ups to veterans that may have conditions that are difficult to diagnose and understand. And that is an exhaustive process that tracks these veterans

and follows up for their care and then makes recommendations back to their primary care physicians.

So we are trying to provide the services that we can to those veterans even in the absence of information that tells us specifically what might have caused their illnesses.

Mr. MITCHELL. But as I said, the perception of many Gulf War veterans is that they are just getting procedural excuses and not getting the service that they need.

Mr. DEMBLING. And I think what we need to do is a better job of education for our health care providers and our clinicians. And one of the things that I think Mr. Hardie mentioned has to do with the Veterans Health Initiative (VHI), the clinical guides that we use, and those are going to be updated. We are working with our Employee Education System to get those VHIs updated as quickly as we can and we are working on that as well.

Mr. MITCHELL. And this may be to Dr. Kupersmith. In the 2008 annual report to Congress it states that it was obligated to the VA for Gulf War Illness research a total of $21.6 million. Of this $21.6 million, $15 million of it has been allocated to Dr. Haley's study specifically, and that leaves $6.6 million for all the other ongoing Gulf War research. Is that enough?

Dr. KUPERSMITH. Well let me just first say, I think as you referred to the report, we are in agreement with the reports recommendations concerning our research direction and how we should be doing it. And also, I——

Mr. MITCHELL. In agreement with who?

Dr. KUPERSMITH. The report, the RAC report that you just quoted.

Mr. MITCHELL. The RAC.

Dr. KUPERSMITH. Yes.

Mr. MITCHELL. Okay.

Dr. KUPERSMITH. This includes research into sophisticated imaging techniques such as what Dr. Haley has talked about. He is doing it, it is being done in centers also. Genomic studies we think are very important because one of the—you know, over the years there had been tremendous frustration in research results, but one of the things that may be true is that certain individuals had genetic predispositions to these exposures. That will also help us with what might be the mechanism or way that these exposures exert the effects that they do. So we are in general agreement with one point after another.

I think the recommendation was that we spend approximately $20 million, which we are, as you said. We have new initiatives now. New initiatives in the treatment of Gulf War disease. New initiatives in other areas. So we are evaluating our budget for next year.

Mr. MITCHELL. Well let me ask, do you feel that the $6.6 million is adequate for the rest of the research?

Dr. KUPERSMITH. Well that has been our analysis up to now, but we will be seeing what research we can do within our system, and if it requires more funding we will certainly give it.

Mr. MITCHELL. One last question before I turn to Dr. Roe. The VA's three largest Gulf War research projects that are ongoing—there are three I understand—could you give us the status of each

and the dollar amounts that have been spent and let us know what it is the VA gets out of this?

Dr. KUPERSMITH. Well let me say, I think, you know, we have examined over these last 18 years what research has been done. The research agenda has in general been set by the deployment health working group, which is a group of experts from the Department of Defense and the VA. That was soon after the Gulf War that began. It is clear, as everybody has said here, that it has not accomplished the goals of finding what we might call a silver bullet for the treatment of Gulf War veterans' illness, and for determining the many other aspects of it. So we are undertaking new areas.

And all of us are very much in agreement with Dr. Haley with what he said, with what Dr. White said, what Mr. Binns said concerning the need for approaching these in new ways. So we are undertaking sophisticated imaging studies as we said. The state-of-the-art imaging correlations with tests of brain function. Genomic studies, we feel, may be very important to solving some of the issues related to what is susceptible and indicating who had an adverse outcome from this. Studies to determine biomarkers, which are diagnostic tests that may show us who had the disease. Because it is clear, as has been testified to in the previous hearing, that it will be very difficult to analyze the exposures now 18 or 19 years later.

Those are just some of the areas that we are getting into. And this represents the use of new technology, some of which has been developed in the VA to try to address these problems.

Mr. MITCHELL. In terms of research dollars, could you tell me how much has been allocated to TBI and PTSD compared to Gulf War research?

Dr. KUPERSMITH. I think they were submitted. And I apologize, I do not have the exact numbers with me. I can give you those, and I would rather——

Mr. MITCHELL. Can you give me ballpark figures?

Dr. KUPERSMITH. You know, I would rather not say, because you know, I will be quoted. I apologize for that. I could get these very quickly for you, I just don't have them in my head. I know they were submitted.

Mr. MITCHELL. All right, I would like to see those.

Dr. KUPERSMITH. We will certainly do that.

[The information is provided in Question 4 of the Post-Hearing Questions and Responses for the Record, which appears on p. 121.]

Mr. MITCHELL. Thank you.

Dr. KUPERSMITH. I apologize for not being able to quote them from memory.

Mr. MITCHELL. Dr. Roe.

Mr. ROE. I apologize for having to step out for a moment, but I guess the conclusion I am coming to in listening to this, and obviously as I said last night I couldn't read that volume of information. But I guess in the VA system now, how are Gulf War veterans with this presumed illness being treated? When they come in, I mean, is there a clinic or an expert? We have a VA facility in my hometown, Mountain Home VA in Johnson City, Tennessee, and I haven't asked them that. Is there a standard methodology of treatment?

For instance, we talked a lot about electronic medical records and evidence-based medicine. Well we are gathering evidence now about this and ongoing research and millions of dollars have been spent. And I guess what I worry about is if we spend millions and millions and millions of dollars and don't have any more conclusions than we have now and maybe we are denying veterans care by spending the money, that is my concern. I have watched that happen over and over.

And I know from doing clinical research, Dr. Haley had mentioned this a minute ago, you know, sometime we just stumble on a treatment and it works and then sometimes you do animal studies—I mean, from level one all the way through and spend a billion dollars with a new drug and find out it doesn't work.

So do we have any treatment guidelines in the VA right now that if I went back to the clinic at home and put my stethoscope on again, there's a methodology I can use to treat a veteran that comes in with these symptoms?

Dr. KUPERSMITH. You know, I deal with the research part of it.

Dr. CASSANO. Dr. Roe, let me step a back a little bit and discuss the progression. Before there was ever an IOM report on Gulf War, we had asked Congress for special authority to service-connect undiagnosed illnesses, which now includes 13 different sets of symptoms, as well as fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome, which are considered the unexplained chronic multi-symptom illnesses. Since that time, we have gotten IOM confirmation of the three unexplained illnesses, fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome associated with Gulf War service, to further suggest service-connection.

At about the same time, however, we realized that we needed to find a way to care for these veterans. There were several initiatives started.

First of all the VHI, which was the training program for veterans, does need to be updated, but that is out there for clinicians who take care of veterans from the Gulf War to look at. We have about 15 VHIs. There is one specifically for Gulf War.

In addition, the environmental health clinician is specifically in the clinic to be able to take care of those post-deployment related issues whether it is Gulf War or Agent Orange or some of the issues from the current conflict. They are in every VA Medical Center. They actually are used on the front line along with the primary care doctor to look at various symptoms and various illnesses and see what proper treatments are necessary.

In addition, we started the War-Related Illness and Injury Study Centers which are the referral centers Mr. Dembling spoke of. They are more than just a referral center. They are really the subject matter experts on unexplained and undiagnosed illness. So they act not only as a referral clinic, but also as a subject matter expert with the primary care docs and the environmental health clinicians so that their expertise is utilized on the front lines when somebody comes in with a possible illness or symptom related to the Gulf War.

In addition, all of our conferences—we have a new conference coming up—the Evolving Paradigms conference in September that will deal with these issues specifically so that we continue to train

our clinicians that we are not just taking care of a patient in a veterans health care system, but we are taking care of veterans in a veteran specific, veteran centric health care system.

Mr. ROE. I know one of my pet peeves when I practiced medicine and I saw someone that came in, if we don't know what was wrong with you, we either said you had a virus or it is between your ears, when we didn't know. And as several have pointed out, MS is a perfect example of people you see that have a symptom and it may take 10 years to diagnose that patient because of evolving symptomology, and that is one of the things I said at the last meeting, was that we need to continue to follow this to gather this evidence over a lifetime.

But also I think what we need to do is now get as concise as we can the set of symptoms, educate our clinicians and our practitioners, and get this care to veterans. And also continue the research.

The biggest problem we have in disease, if we don't have an etiology, it is very hard to treat something. I know a lot of non-clinical people don't understand that. But if I know you have pneumococcal pneumonia I can treat that. The problem is when you have a symptom over here, and a symptom over here is trying to, number one, get an etiology, and then get an effective treatment program.

So I would suggest that we deal with the knowledge that we have, and in 10 years we may look back if we continue to gather this information and say, how in the world did we ever draw that conclusion? I have done that before. I've looked back and thought that treatment was totally wrong. But I think that is what needs to be done from what I have heard now and put together.

And I think our third meeting, Mr. Chairman, I think we need to push in that direction. I yield back.

Mr. DEMBLING. We agree with you completely, Dr. Roe, that is why we have the vigorous research program under way, we have education programs under way for our providers, and as Dr. Cassano mentioned, a massive conference—the Evolving Paradigms conference—it will be held in September that will educate over a thousand providers and health care folks from around the country as to the new experiences of combat veterans. And at the same time providing health care to the maximum extent possible that we can in our Medical Centers with the knowledge that we have and that we have learned over the past few years.

Mr. ROE. Yeah, understanding that it is imperfect. I think as I have had a chance to think, and I will think more about this, I believe this is a bell-shaped curve and you have some people out here who don't have Gulf War Syndrome who will exhibit some symptoms. I believe that, and you are going to include some of those in payment, so be it. We can't get everything right with something that is hard to diagnose as this. But I truly do believe we have to get this particular group of veterans that probably do have something, whatever it is, and try to do something for them.

And again, I went through this at the end of Vietnam, I am a two-ID guy from Korea and I watched this happen to a group of veterans. It doesn't need to happen again. And I think good people are trying, I really do. I don't think they are ignoring it. And I

think Mr. Hardie, I think his problem is that, it is been almost 100 years since we have had people breathe Mustard Gas or inhale it.

So I hope we do that, and I hope we are able to, Mr. Chairman, come to a conclusion here after our next hearing and give some real solid recommendations so that we can get this information in the clinical room, in the treatment room for the patient.

Thank you all very much and I yield back.

Mr. MITCHELL. One thing I would just like to finish with. I don't doubt at all the research and the methodologies that Dr. Goldman and Dr. Steele were going through. And you know, sometimes we are arguing over how many angles dance on the head of a pin instead of getting down to what really matters, and that is treating the veteran, those who have Gulf War Symptoms.

And as I mentioned earlier, the perception of far too many Gulf War veterans is that the VA has nothing new to offer except procedural excuses.

And I just want to quote one last thing out of the statute. And I know, Dr. Cassano, you are talking about relying on IOM and so on, and this is where I think sometimes people talk about the excuses and putting things off. It is been a long time since we have had that war. And I just want to quote this one section. It says, "Under section 1603 of the Persian Gulf War Veterans Act 1998, the Secretary shall determine whether or not a presumption of service-connection is warranted for each illness."

They can do it. You can do this. You don't need an Act of Congress. It is up to you. And I really feel bad when we take a look and see how some veterans perceive the lack of service and we hide behind again all of the little details when they are out there being disabled and can't work and can't function properly. And I think that the VA has got to take—and I really appreciate the research that Dr. Haley and others are doing, because this goes far beyond—you know, the research that has developed here and the results, far beyond the veterans, it goes to the whole humanity, and that is what is important. And don't get hung up on that. We have soldiers out there, veterans who need help.

I would like to thank all of our witnesses for testifying here today. And it is evident from our last hearing and from this hearing that this is still an issue of utmost importance to all of our veterans.

In our first hearing we looked at the history. Today we looked at the science. And now it is time to move forward and provide answers for those that sacrificed for our country over 18 years ago.

Our next hearing will focus on benefits and the lessons we have learned from both Agent Orange and Gulf War research. These are lessons we need to apply not only to our Gulf War veterans suffering here today, but also to the brave men and women fighting in Iraq and Afghanistan today.

It is essential that we get this right so that 20 years from now down the road we are not having these same discussions again.

And again, I want to thank all of our witnesses for joining us today. Dr. Roe.

Mr. ROE. And just one final comment. Mr. Chairman, thank you for having this very important hearing and hopefully we will have some recommendations in the very near future. And once again,

thank you for having this and I thank all the witnesses too for being here.

Mr. MITCHELL. Thank you, this hearing is adjourned.

[Whereupon, at 12:24 p.m., the Subcommittee was adjourned.]

APPENDIX

Prepared Statement of Hon. Harry E. Mitchell, Chairman, Subcommittee on Oversight and Investigations

Thank you to everyone for attending today's Oversight and Investigations Subcommittee hearing entitled, *the Implications of U.S. Department of Veterans Affair's Limited Scope of Gulf War Illness Research*.

It has been upwards of 19 years since the United States deployed nearly 700,000 service Members to the Gulf in support of Operations Desert Shield and Desert Storm. When these troops returned home, some reported symptoms that were believed to be related to their service and possible exposure to toxins, agents, and chemicals. However, the amount and combination of these chemicals used during this period is unknown and conflicting research has created a real challenge for being able to prove a veteran's symptom resulted from service connection.

As a result, there are many veterans with undiagnosed illnesses and multi-symptom illnesses relating to their service in the Gulf War who are still suffering from chemical agent exposure, and are finding themselves fighting the VA to have Gulf War Illness recognized as service connection and compensation.

As many of you know, in May of this year, this Subcommittee held its first of a series of hearings to address this issue. During that hearing we examined the impact of toxins and pesticides used during the Vietnam and Gulf Wars. And with a growing chorus of concern over the accuracy of existing research, I believe it is time for us to take an in depth look at the scientific research surrounding Gulf War Illness Research.

Today's hearing will focus on how the current research is progressing, including taking a closer look at the reports offered from the Institute of Medicine (IOM) and the Research Advisory Committee (RAC). In addition, the hearing will examine the VA's role in treating Gulf War Illness.

There are few things that I would specifically like to examine today. First, did VA and IOM meet congressional mandates and the essence of Public Laws 105–277 and 105–368 to include animal and human studies, along with evaluating diagnosed and undiagnosed illnesses? Second, were methodologies used by IOM equivalent in both Agent Orange and Gulf War studies? And third, I would like to examine the methodologies utilized in production of the RAC report.

We have learned and will continue to learn that Gulf War Illness Research is a challenge, but a missing link appears to be a lack of documentation of exposure and compounds that exposed our veterans. Additionally, we are waiting for science to bridge the gap between self reported illnesses and diagnostic evidence, just as we did with Agent Orange veterans.

Our last hearing on this issue shed light on the fact that we aren't doing enough for our Gulf War Veterans and that they continue to fight for what they deserve. Today, I am hopeful that we will all examine this issue with open minds and get one step closer to a consensus amongst Congress, VA, scientific bodies, and most importantly, our veterans.

For today's hearing, we have brought experts from all fields to discuss this important issue. I am hopeful our panelists here today will discuss the merits of the RAC report in comparison with IOM methodologies and the results of both, as well as discuss the best course to ensure that this important research will benefit veterans. I'm anxious to hear from the VA what actions they have taken in response to the RAC report, and more importantly, how the questions surrounding Gulf War research affect our veterans and how the VA plan to move forward.

While I praise all of our panelists here today for the research work they are doing on behalf of our Gulf War veterans, we must find a way to give these veterans the answers they have been looking for since returning home from theater almost 20 years ago.

Prepared Statement of Hon. David P. Roe, Ranking Republican Member, Subcommittee on Oversight and Investigations

Mr. Chairman, thank you for yielding me time.

As you indicated in your opening statement, this is the 2nd of a 3-part hearing series on Gulf War Illness Research. The focus and title of this 2nd hearing is the "Implications of VA's Limited Scope of Gulf War Illness Research." While I'm not sure that VA has had limited scope in the area of Gulf War illness research, I appreciate you calling this hearing to further evaluate the research that has been completed and reviewed, not just by the Research Advisory Committee on Gulf War Veterans' Illnesses, but also by the National Academy of Sciences, Institute of Medicine. I understand that both organizations are represented here today as witnesses.

As a follow up to our first hearing, we have received responses to questions for the record from Dr. Roberta White, from Boston University, Dr. Lea Steele from Kansas State University, Paul Sullivan of Veterans for Common Sense, as well as the VA. I appreciate that we received their responses prior to today's hearing. Their input from the last hearing is important information to have as we proceed today.

On Tuesday afternoon, the Committee also received the Secretary's "Annual Report to Congress on Federally Sponsored Research on Gulf War Veterans' Illnesses for 2008." This report is also important for us to review, as it reflects the large body of work that is continuing on this matter. From FY 1992 through FY 2008, the VA, the Department of Defense, and Health and Human Services funded 347 distinct projects relating to health problems affecting Gulf War veterans. As of September 30, 2008, 288 of these projects were completed, and 59 projects were either new or ongoing. I am pleased we received this report prior to today's hearing.

I am looking forward to a lively discussion today, as we have representatives here from several different scientific backgrounds, representing different studies on Gulf War Illness, and the possible causes. I am pleased, Mr. Chairman that you have decided to include in this hearing the Institute of Medicine representatives, who have compiled large volumes of material on Gulf War Illness, possible causes, and comorbid diseases which may or may not have come from exposures during the first Gulf War. I am interested in learning whether these same exposures were also present during the current conflict and what we can expect, as the authorizing Committee, as to new presumptions for exposures in both conflicts.

I would like to remind my colleagues as we proceed that we must throughout this series of hearings keep an open mind as to the reports and studies being presented to us, and the way ahead for us as the authorizing Committee for benefits and services provided to our Nation's veterans.

Again, Mr. Chairman, I appreciate your diligence in pursuing these hearings and yield back my time.

Prepared Statement of Hon. John J. Hall

Thank you for yielding Mr. Chairman, and thank you to the witnesses who have taken the time to come here today to discuss a very important issue to our Nation's veterans.

We are here today because of an issue that we can all agree deserves our utmost attention. Gulf War Illness has had a crippling effect on approximately 200,000 veterans of the 1991 Gulf War. Since 1998, the VA has funded independent studies by the Institute of Medicine in order to find out how best to address the health problems that Gulf War veterans are suffering from.

Unfortunately, there has been disagreement between the IOM and the VA's Research Advisory Committee on how to approach this research. In particular, the RAC feels that the IOM studies were too narrow, not satisfying the requirements set out by Congress. The IOM's emphasis on human studies versus animal studies and not focusing on undiagnosed illnesses are some of the issues delaying a final report.

I am very concerned about these disagreements, and the impact they are having on providing adequate care and compensation to our veterans. Many veterans are being turned away from VA hospitals, and being denied treatment, because there is no way to properly diagnose their illness. An uncertain method of diagnosing Gulf War Illness also complicates the compensation process. Compensation is critical when it comes to caring for our veterans, and making sure they are able to live their lives to the fullest.

I understand that these disagreements are important to resolve. A scientific consensus will allow the VA to better treat those who suffer from Gulf War Illness and related injuries. My worry, however, is that in the meantime, while the VA and the

IOM seek to reach that consensus, veterans are suffering. I hope that we will hear today that at the very least the RAC and the IOM can agree that there is no time to waste. I look forward to the solutions that I hope this hearing will provide.

Prepared Statement of Lynn Goldman, M.D., MPH, Professor, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, and Member, Committee on Gulf War and Health, Institute of Medicine, The National Academies

Good morning Mr. Chairman and Members of the Subcommittee. Thanks to Congressman Mitchell and Members of the Subcommittee on Oversight and Investigations, House Committee on Veterans' Affairs for your concern about veteran's health.

My name is Lynn Goldman. I am a professor of environmental health sciences and epidemiology at the Bloomberg School of Public Health at Johns Hopkins University in Baltimore and chair of our program in applied public health. Prior to joining Hopkins in 1999 I served for 6 years at the U.S. Environmental Protection Agency (EPA) as Assistant Administrator for the Office of Prevention, Pesticides and Toxic Substances. My primary training is in pediatrics and epidemiology. I also have served as Chair of two Institute of Medicine (IOM) Gulf War and Health Committees: the Committee that worked on the report *Gulf War and Health: Review of the Medical Literature Relative to Gulf War Veterans Health*, and the Committee that produced the report *Gulf War and Health: Fuels, Combustion Products, and Propellants*. Additionally, I was a Member of the Committee that produced *Gulf War and Health: Insecticides and Solvents*. I am here before you today because of my experience as a volunteer serving on those IOM Committees and as an elected Member of the Institute of Medicine.

I will focus on four main points in my testimony. First I will discuss the overall study process, including the review process, for the Gulf War series of reports and how that process compares to the study process for the IOM Agent Orange reports, including the report review process. Second I will discuss the categories of association used by the Gulf War & Health Committees to classify the likelihood that exposure to a given agent is related to a given health effect, and how those categories compare to those used by the Agent Orange Committees. Third, I will discuss how scientific studies are used by the Gulf War and the Agent Orange Committees, with a focus on animal studies. Finally, I will discuss what is known about exposures during the Gulf War and how that affects the Committees' work.

Let me begin with the IOM study process. The IOM is a division of The National Academies, a non-governmental institution originally chartered by President Lincoln to provide independent scientific advice to the Nation. That scientific advice is usually in the form of consensus reports produced by expert, unpaid Committees. In the case of the Gulf War and Health and the Agent Orange studies, the Committees usually comprised ten to twenty Members with expertise in epidemiology, toxicology, exposure assessment and relevant areas of clinical medicine. The Members are usually from universities, nonprofit organizations, and consulting firms. The reports are developed through an established study process designed to ensure Committees and the reports they produce are free from actual or potential conflicts of interests, are balanced for any biases, and are independent of oversight from the sponsoring agency. At no time during a Committee's deliberations or during the preparation and review of an IOM report is the sponsor allowed to participate in the process or have access to any part of the report. In cases where a Committee asks the sponsor for information, any such information is made public.

Committees review relevant literature, hear from experts, and deliberate. Once the Committee has reached its consensus, but prior to the report being released, the draft report is subjected to a formal, peer-review process. External reviewers are nominated by a broad range of individuals including IOM and National Academy of Sciences (NAS) Members, Committee Members and other interested parties. The list of reviewers' is approved by a review oversight body, the National Academies Report Review Committee, which ensures the reviewers have the necessary expertise. The reviewers read the draft report and individually provide comments on: 1) whether the Committee has addressed its charge; 2) the strength of the evidence for and the validity of the Committee's conclusions; and 3) the technical aspects, clarity and flow of the report. Comments of the reviewers are provided anonymously so that Committee Members and the study staff do not know the source of the review comments when they receive them. In the case of the Gulf War and Health and the Agent Orange studies, 10 to 15 experts in various scientific fields reviewed

the reports. The Committee must respond to each comment from each reviewer and indicate what revisions were made to the report to address the comment or provide a detailed explanation why the suggested revision was not made. After all the comments have been addressed, each study Committee Member must "sign off" on the revised report. The report is then sent to the Review Monitor, who is a Member of the National Academies Report Review Committee, and a Review Coordinator, who is assigned by the IOM executive office. Those two individuals assess the Committee's response to reviewers' comments and ensure that the Committee has adequately addressed every comment. Only when they are satisfied is the final report released to the public on their recommendation. A courtesy copy of the final report is sent to the sponsor immediately prior to public release. The sponsor is not provided an opportunity to review the report or any portions of the report, or to suggest changes to the IOM report prior to its release. This stringent and established process was followed for both the Gulf War & Health and the Agent Orange reports.

In addition to those general procedures that are required by The National Academies, each Committee also has procedures it follows in reviewing the data and drawing its conclusions. Each Committee begins its deliberations by discussing and developing an approach to the Committee's statement of work. This statement of work has been approved by The National Academies governing body and has been included in the contract between the IOM and the study sponsor. However, in general these statements of work do not detail the specific approach to be used to complete the work, allowing the Committee to use its expertise to identify the best approach. For the Gulf War & Health and Agent Orange reports Committees needed to consider not only the statements of work but also the requirements of the legislation mandating the studies in developing approaches to how the Committee would gather, review and evaluate the information it collects.

I can tell you from personal experience that the Members of the IOM Committees take their responsibility to assess the scientific data in a fair and unbiased manner very seriously. For each Gulf War and Agent Orange report, the expert Committee Members reviewed, evaluated and interpreted literally thousands of scientific publications that were identified through comprehensive searches of electronic databases such as those of the National Library of Medicine. On the basis of their analyses and deliberations, the Committees reached consensus conclusions. Each Committee prepared a consensus report outlining its findings which includes descriptions of the methods it used, the scientific information it reviewed, and the rationale for its conclusions.

By direction of the U.S. Congress, most IOM Gulf War studies have looked at chemical or biological agents or other possible deployment exposures and have drawn conclusions about what adverse health outcomes could be associated with or caused by those exposures. Similarly, the Veterans and Agent Orange studies look at specific chemical agents (Agent Orange and other herbicides) used during the Vietnam War and draw conclusions about what adverse health outcomes could be associated with or caused by those exposures. The conclusions are based on categories of evidence. In both cases, the legislation requests that the IOM Committees make conclusions on the strength of the evidence for an association between exposure to certain agents and potential health outcomes. Successive Gulf War Committees have decided to use the following five categories of association to describe the weight of the evidence and to make conclusions:

- sufficient evidence of a causal relationship between an exposure and a health outcome,
- sufficient evidence of an association between an exposure and a health outcome,
- limited/suggestive evidence of an association,
- inadequate/insufficient evidence to determine whether an association exists, and
- limited/suggestive evidence of no association.

Those categories evolved from the categories used by the Agent Orange Committees, which in turn were adapted from established categories of evidence used by the International Agency for Research on Cancer when it ranks evidence for chemicals that may cause cancer. The Agent Orange categories have gained wide acceptance over more than a decade by Congress, government agencies, researchers, and veterans groups.

The major difference between the categories used by the Gulf War Committees and the ones used by the Agent Orange Committees is the addition of the category of *sufficient evidence of a causal relationship* for all but one of the Gulf War Committees. The additional category makes causation explicit and includes evidence beyond that found just in epidemiologic studies. Although *association* and *causation*

are often used interchangeably they have different meanings scientifically. To demonstrate an *association*, the evidence simply must indicate that as exposure to an agent increases, the occurrence of an adverse outcome also increases. That an association is not the same as causality can be understood using the following example: fire trucks are associated with fires but they do not cause fires. For causation, the evidence must demonstrate that the exposure *leads* to the health outcome. For example, the influenza virus causes a person to get influenza. Therefore, the categories of evidence used by the first and subsequent Gulf War committees explicitly distinguish between *causation* and *association*.

One other change the Gulf War committees made was to clarify the definitions of *Limited/Suggestive Evidence of an Association and Sufficient Evidence of an Association*. The Committee added the phrase "in human studies" to those definitions where they discuss "chance and bias, including confounding". Chance, bias and confounding are much more significant problems in human epidemiology studies than in animal studies (which are more controlled). The addition of the statement about human studies simply clarifies that point. Although this phrase has been read to mean that the IOM studies have only addressed human studies, in reality both the Agent Orange studies and the Gulf War studies evaluate animal studies. This is quite evident when you read the reports and review the references that have been cited. At the same time, the IOM has put more weight on the human studies than on the animal studies. The Gulf War and Health volumes simply clarified that point, but conduct their studies in the same manner as the Agent Orange studies.

This leads me to address the issue of how animal data have been used by the Gulf War and the Agent Orange committees and why human studies have been given more weight. First, as might be expected, the published studies that are potentially relevant to the exposures evaluated by the Gulf War committees include studies that are conducted in animals. The committees looked at all relevant animal studies, including published reviews of the animal studies. However, many of the chemicals reviewed by the Gulf War committees have been tested in animals for decades in hundreds of studies and have well-established effects in animals that are described in basic toxicology text books. In such cases, committees have sometimes determined that it was not necessary to review all the individual animal studies that support those established effects but instead to cite reviews that summarize these specific well-established effects. Even in those instances where the health effects of an agent are well known, however, the committee still reviewed and described in their reports all of the animal studies that are critical to the committee's conclusions.

Animal studies have been relevant and important but, there are limitations when drawing conclusions in humans on the basis of data in animals, which is why those studies were given less weight than human studies. Animal studies sometimes provide very different information than studies in humans. For example, vinyl chloride causes cancer in different organs in animals than in human; arsenic is a known human carcinogen but animals do not show similar tumors; and saccharine causes bladder tumors in male rats but not in humans. Using animals to look at human health effects is especially problematic for symptoms for which there are no diagnostic tests. A person can tell you that he or she has a headache, is tired, or just doesn't feel very well, but a rat or mouse can not; by definition, such symptoms only can be seen in human studies. Therefore, the Gulf War committees have relied more on human studies, including epidemiologic and clinical studies, to reach conclusions regarding the association between an exposure to an agent and a health outcome. Animal data, when available, provide support for those conclusions.

Next I would like to briefly discuss what we know about the exposures in the Gulf War, and how that has affected the work of committees. The legislation that led to the Gulf War and Health studies lists a number of chemical and biological agents that the IOM was asked to consider. The number and diversity of those agents precluded all of the agents being reviewed by a single Committee in a single report. The IOM held an open meeting with veterans and veteran service organizations to help identify the agents the veterans were most concerned about. On the basis of that meeting, the agents were prioritized for review.

All of the Gulf War committees have grappled with the issue of exposure and the lack of information, not only on how much of a chemical a person was exposed to, but even the specific chemicals a person might have been exposed to. For example, the committee could not find any information on which vaccines or medications, or the amount of a medication, that a specific person took during deployment. The committee members heard from veterans about being given a vaccination, for example en route to the combat arena, but they did not know what the vaccination was for, and the Committee was told by the DoD that there are no records of who received what vaccinations. In other cases, when asked, veterans reported being ex-

posed to a multitude of agents such as pesticides, pyridostigmine bromide, kerosene heaters, and oil well fire smoke during their deployment, but the levels of exposure to specific agents have not been determined and possibly never will be. This lack of information on exposure makes it very difficult to link a given health effect in veterans to a specific exposure.

Although most of the Gulf War committees looked at the health effects of the potential exposures, one of the committees was charged, as directed by the attached legislation, with evaluating Gulf War veterans' health. This Committee reviewed the published studies conducted on the Gulf War veterans themselves and made conclusions on the prevalence of health outcomes in the veterans. Because of the lack of exposure information, however, that report does not link health outcomes to specific exposures. An updated review of the literature on Gulf War veterans published since the preparation of that report is currently underway.

With that, I would once again like to thank you for inviting me to testify before this Subcommittee. I appreciate the work of this Subcommittee on Oversight and Investigations of the House Committee on Veterans' Affairs. On behalf of all IOM Gulf War committee members past and present I thank you for your trust in our ability to assist you with this important work for our Nation's veterans. I know from my service on these committees that the Nation's scientists are happy to serve, and look to you for guidance on how we can be of most assistance to you and the VA in assessing health impacts of Gulf War deployment. I look forward to answering any questions you might have.

Prepared Statement of James H. Binns, Chairman, Research Advisory Committee on Gulf War Veterans' Illnesses

Chairman Mitchell, Ranking Member Roe, Members of the Committee, the Research Advisory Committee on Gulf War Veterans Illnesses is a public advisory body of scientists and veterans mandated by Congress and appointed by the Secretary of Veterans Affairs. The Committee's statutory mission is to review research studies and plans related to the illnesses suffered by veterans of the 1991 Gulf War.

In a moment you will hear from Dr. Steele how the Committee's approach to reviewing the science has differed from that used in the Institute of Medicine reports. I will discuss the legal background of the reports.

It is important to understand is that neither the Research Advisory Committee report, nor the IOM Gulf War reports, are original scientific research. They are intended to be summaries of what others have found.

The reason the IOM is involved in this subject is because, in the same law that established the Research Advisory Committee, Congress directed VA to contract with the IOM to prepare reports to guide the Secretary of Veterans Affairs in determining Gulf War veterans' benefits. Congress was very specific about how it wanted these reports done.

Congress directed VA to have IOM review the scientific literature for thirty-three hazardous substances to which troops were exposed in the war to see if any of those substances have been associated with an increased risk of illness. If there was sufficient evidence of such an association, the Secretary was directed to prescribe a presumption of service connection for Gulf War veterans' health and disability benefits. Because most studies of hazardous substances are done in animals, the law required that both human and animal studies be considered. Because veterans were often exposed to combinations of substances, the law required that the reports should consider combinations of exposures. And because Gulf War veterans' illnesses often do not fit conventional diagnoses, the law required that undiagnosed illnesses should also be considered.

Yet, as the IOM reports themselves state, only evidence from human studies was considered, combinations of exposures were not considered, and undiagnosed illnesses were not considered. The result is that the committees of scientists who worked on the IOM reports were attempting to put together a puzzle that was missing half the pieces.

Virtually all of these scientists, who are volunteers who spend most of their time reviewing the literature that IOM staff sends them, had no idea they were not following the law, I'm sure. They were undoubtedly told that they were following standard IOM methodology. The Gulf War reports state that the methodology comes from earlier IOM reports ordered by Congress related to Agent Orange exposure in Vietnam. As a Vietnam veteran, I well remember that for twenty years after that war, the government denied there was any connection between Agent Orange and

the health problems of Vietnam veterans until Congress ordered the IOM to do this kind of report.

However, a close examination shows that the Agent Orange methodology was subtly changed in the Gulf War reports. One word, the word "human," was inserted in the definition of whether there is sufficient evidence that a substance is associated with an increased risk of illness. That definition determines the conclusion of the report. It is what the Secretary is directed to rely upon in deciding if there should be a presumption of service connection for veterans' benefits. The effect of this change is that animal studies were not considered in the conclusion of the reports, even though the law specifically required them to be considered in the conclusion by both the IOM and the Secretary. Whether they were considered elsewhere is of no consequence.

In short, the IOM Gulf War reports do not follow the requirements of the law that ordered them, nor do they follow the established methodology of the IOM itself. As a result, there have been no significant presumptions of service connection made on the basis of the IOM reports.

As to how this could have occurred, I would refer you to my written testimony, which includes correspondence between VA and IOM staff prior to the start of one of the reports. The documents show that discussions between VA and IOM staff led to an agreement that placed conditions on the report that predetermined its outcome before the IOM committee to prepare it was ever appointed.

Today I am pleased to report that the VA official involved in those discussions has recently left the VA. I am also encouraged that the new Secretary of Veterans Affairs is manifestly committed to transforming the culture at VA headquarters to better serve veterans. So I hope that change is on the way and look forward to the testimony of the Department of Veterans Affairs this morning.

Change is sorely needed. I have worked for three previous Secretaries of Veterans Affairs, who were all honorable men, but have sadly seen VA staff continue to minimize the serious health problems of Gulf War veterans, including the misuse of the Institute of Medicine. Benefits continue to be denied. And because of the stature of the IOM, its reports have misled researchers, physicians, Congress, veterans' families and veterans themselves. In December, VA ordered a new IOM report to review the report of the Research Advisory Committee, rather than act on its recommendations. IOM has a Committee working on this new report, although IOM says it will not review the RAC report.

What is clear is that the VA/IOM relationship is in urgent need of reform. I am distressed that these two great institutions cannot candidly acknowledge these problems and address them. The Institute of Medicine is the high court of American medical science. Manipulation of its processes by the government is a serious breech of public trust with implications far beyond this topic.

In view of the gravity of these issues, I will describe them in detail and provide the original documents to the Subcommittee staff showing precisely what has occurred. Page references are to the document package provided to staff.

Has VA complied with the statute requiring the IOM reports, and has the IOM followed the statute and its own established methodology?

In the same 1998 laws that established the Research Advisory Committee, PL 105–277 and PL 105–368, Congress directed the Department of Veterans Affairs to contract with the National Academy of Sciences (NAS, the parent organization of the Institute of Medicine), to review the scientific literature regarding substances to which troops were exposed in the Gulf to determine if these substances are associated with an increased risk of illness. These reports were to be used by the Secretary of Veterans Affairs in determining whether the illness should be presumed service-connected for the purpose of veterans' benefits.

The law directed the NAS to identify the "biological, chemical, or other toxic agents, environmental or wartime hazards, or preventive medicines or vaccines" to which members of the Armed Forces may have been exposed during the war. 38 USC Sec. 1117, note Sec. 1603 (c). [documents p. 2] The law listed thirty-three specific "toxic agents, environmental or wartime hazards, or preventive medicines or vaccines associated with Gulf War service" to be considered, including various pesticides; pyridostigmine bromide, a drug used as a nerve agent prophylaxis; low-level nerve agents; other chemicals, metals, sources of radiation; and infectious diseases. 38 USC Sec. 1117, note Sec. 1603 (a), (d). [documents, pp. 3–4] The law further required the NAS to identify illnesses, "including diagnosed illnesses and undiagnosed illnesses," experienced by Armed Forces members who served in the war. 38 USC Sec. 1117, note Sec. 1603 (c) [documents, p. 4]

"For each agent, hazard, or medicine or vaccine and illness identified," the law provided that:

"The National Academy of Sciences shall determine . . .

(A) whether a statistical association exists between exposure to the agent . . . and the illness . . .
(B) the increased risk of the illness *among human or animal populations* exposed to the agent . . . and
(C) whether a plausible biological mechanism or other evidence of a causal relationship exists . . .''

38 USC Sec. 1117, note Sec. 1603 (e) [documents, p. 4, emphasis added]

The statute went on to provide that the Secretary of Veterans Affairs should consider both human and animal studies in determining whether a presumption of service connection is warranted. He was to consider ''the exposure *in humans or animals*'' to an agent and ''the occurrence of a diagnosed or undiagnosed illness *in humans or animals*.''

38 USC Sec. 1118 (b)(1)(B) [documents, p. 9, emphasis added]

Congress thus expressly required consideration of animal as well as human studies by both the National Academy of Sciences (the Institute of Medicine) and the Secretary of Veterans Affairs. This statutory requirement reflects the fact that most studies on the biological effects of hazardous substances are done in animals, for ethical reasons. Consider, for example, the twenty-three studies on the long-term effects of low level sarin exposure, or the eighteen studies evaluating the combined effects of pyridostigmine bromide, pesticides and insect repellant listed on pages 160–161 and 170–171 of the Research Advisory Committee report, all of which were done in animals.

When the first IOM report was conducted under the law, however, animal studies were omitted from the standard for determining whether an association exists between an exposure and a health effect. The report states:

''For its evaluation and categorization of the degree of association between each exposure and a human health effect, however, the [IOM] Committee only used evidence from human studies.''

Gulf War and Health, Volume 1, p. 72 [documents, p. 11]

Considering only human studies and not the substantial relevant literature on animal studies, and disregarding other statutory requirements described below, the IOM Committee rarely found sufficient evidence of an association for the exposures considered, and none directly applicable to the exposures and illnesses experienced by Gulf War veterans. Following the guidance of the IOM, the Secretary of Veterans Affairs made no determinations of service-connection for veterans' benefits. This pattern has been followed in all IOM Gulf War reports to date.

The failure to consider animal studies contravened clear and repeated statutory requirements. IOM's Gulf War reports have also been deficient with respect to other statutory requirements, as described in the Research Advisory Committee report at pages 54–55. The IOM reports were required by law to consider not only diagnosed illnesses but also undiagnosed illnesses, but they have not. The second IOM Gulf War report, for example, acknowledged that the IOM Committee was not charged with addressing ''nonspecific illnesses that lack defined diagnoses . . .'' Gulf War and Health Volume 2, p. 13. [documents, p. 12] As a result, IOM Committees have preoccupied themselves with diagnosed illnesses that have not be found to date in elevated rates in Gulf War veterans, while ignoring the multisymptom condition known as ''Gulf War illness'' that afflicts one in four.

The law also defines toxic agents to include combinations of exposures (''whether through exposure singularly or in combination.'') 38 USC Sec. 1117, note Sec. 1605(1) [documents, p. 8] The Research Advisory Committee report lists several pages of scientific studies that have been done on combinations of agents to which veterans were exposed in the Gulf War. [Report, pp. 168, 170–171, 175] Yet, the second IOM report also acknowledged that ''exposure to multiple agents'' was not within the Committee's charge. Gulf War and Health Volume 2, p. 13 [documents, p. 14]

These findings alone would be sufficient to require that the erroneous IOM Gulf War reports to date be redone in accordance with the law, as recommended by the Research Advisory Committee report at page 57.

However, a close examination of what occurred makes clear that the problem is worse and that the exclusion of animal studies cannot have been an oversight. It was deliberate.

To express conclusions as to whether an association between an exposure and an illness exists, the first IOM Gulf report defined five ''Categories of Association.'' Gulf War and Health, Vol. 1, pp. 83–84. [documents, p. 13–14] The same categories have been used in all subsequent IOM Gulf War exposure reports:

- Sufficient Evidence of a Causal Relationship
- Sufficient Evidence of an Association
- Limited/Suggestive Evidence of an Association

- Inadequate/Insufficient Evidence to Determine Whether an Association Does or Does Not Exist
- Limited/Suggestive Evidence of No Association.

Each substance was ranked according to these categories. How a substance is ranked becomes the all-important conclusion of the report as to whether an association exists between an exposure and illness.

Where did these categories come from? The report explained: "The Committee used the established categories of association from previous IOM studies, because they have gained wide acceptance for more than a decade by Congress, government agencies, researchers, and veteran groups." Gulf War and Health, Volume 1, p. 83. [documents, p. 15] "The categories closely resemble those used by several IOM Committees that evaluated ... herbicides used in Vietnam ... " Gulf War and Health, Volume I, p. 83. [documents, p. 15]

IOM Gulf War reports have repeatedly stressed over the years that their methodology is based on the IOM Agent Orange reports. However, it is revealing to compare a category of association used in the Agent Orange reports with the same category used in the Gulf War reports.

Agent Orange:

"Sufficient Evidence of an Association. Evidence is sufficient to conclude that there is a positive association. That is, a positive association has been observed between herbicides and the outcome *in studies* in which chance, bias, and confounding could be ruled out ... "

Veterans and Agent Orange: 1996 Update, p. 97 [documents, p. 15, emphasis added]

Gulf War:

"Sufficient Evidence of an Association. Evidence is sufficient to conclude that there is a positive association. That is, a positive association has been observed between an exposure to a specific agent and a health outcome *in human studies* in which chance, bias, and confounding could be ruled out ..."

Gulf War and Health: Volume I, p. 83 [documents, p. 13, emphasis added]

The Gulf War category does indeed "closely resemble" the Agent Orange category—with a conspicuous exception. The word "human" has been inserted in the Gulf War category.

This addition obviously did not occur by accident. It was deliberate, as was the misleading language that these were the "established categories of association from previous IOM reports."

Thus, not only have the IOM Gulf War studies been conducted in violation of the direction Congress provided in the statute; this violation has been deliberate, with intent to conceal.

As to why it was done, one can speculate based on the knowledge that the Agent Orange language, just a few years earlier, had produced an IOM report that found that Agent Orange exposure was associated with cancer (after two decades of government denial of any health consequence). This finding led to a presumption of service connection for thousands of Vietnam veterans with cancer.

It should be noted that the IOM Gulf War reports state that animal studies were considered for purposes of "biological plausibility": "For its evaluation and categorization of the degree of association between each exposure and a human health effect, ... the Committee only used evidence from human studies. Nevertheless, the Committee did use nonhuman studies as the basis for judgments about biological plausibility, which is one of the criteria for establishing causation." Gulf War and Health, Volume 1, p. 72 [documents, p. 16]

The terms of the Gulf War categories of association make clear, however, that biological plausibility and causation only relate to the highest category of evidence, "sufficient evidence of a causal relationship," and are not considered unless there has been a previous finding of "sufficient evidence of association":

"*Sufficient Evidence of a Causal Relationship*. Evidence is sufficient to conclude that a causal relationship exists between the exposure to a specific agent and a health outcome in humans. *The evidence fills the criteria for sufficient evidence of association (below) and satisfies several of the criteria used to assess causality*: strength of association, dose-response relationship, consistency of association, temporal relationship, specificity of association, and *biological plausibility*.

Sufficient Evidence of an Association. Evidence is sufficient to conclude that there is a positive association. That is, *a positive association has been observed* between an exposure to a specific agent and a health outcome *in human studies* in which

chance, bias, and confounding could be ruled out with reasonable confidence." Gulf War and Health, Volume 1, p. 83. [documents, p. 13, emphasis added]

Thus, only if there has already been a finding of "sufficient evidence of association" do the issues of causality and biological plausibility arise, and a finding of "sufficient evidence of association" depends solely on human studies. Unless an association is found based on human studies, biological plausibility—and animal studies—are not considered.

It is notable that the statute does not require evidence of a "casual relationship" to trigger a presumption of service connection. It only requires evidence of a "positive association":

"[T]he Secretary shall prescribe regulations providing that a presumption of service connection is warranted [if the Secretary makes a] determination based on sound medical and scientific evidence that a *positive association* exists between—

> (i) the exposure of humans or animals to a biological, chemical, or other toxic agent, environmental or wartime hazard, or preventive medicine or vaccine known or presumed to be associated with service in the Southwest Asia theater of operations during the Persian Gulf War; and
> (ii) the occurrence of a diagnosed or undiagnosed illness in humans or animals."

38 USC Sec. 1118 (b)(1) [emphasis added, documents pp. 8–9]

In short, in direct contravention of the statute, the methodology established for the IOM Gulf War reports deliberately excluded animal studies from consideration as to whether an association exists between an exposure and an illness, the only question that matters in the determination of benefits.

As to how this was done, the history of one of the IOM Gulf War reports provides an indication. The 2004 IOM Updated Literature Review of Sarin is the most egregious example of the distortion of science produced by excluding animal studies from the evidence considered in report conclusions. In late 2002, a number of new studies on sarin nerve gas, sponsored by the Department of Defense, revealed that contrary to previous belief, low level exposures (below the level required to produce symptoms at the time of exposure) produced long-term effects on the nervous and immune systems. Naturally, these studies were done in animals.

A previous IOM report on sarin in 2000 had found insufficient evidence of an association between low-level sarin and long-term health effects based on scientific knowledge as of that date. On January 24, 2003, then-VA Secretary Principi wrote the Institute of Medicine: "Recently, a number of new studies have been published on the effects of Sarin on laboratory animals." He asked the IOM to report back "on whether this new research affects earlier conclusions of IOM . . . about possible long-term health consequences of exposure to low levels of Sarin." [documents, p. 17]

In 2004, the IOM delivered its report. The Updated Literature Review of Sarin discussed the new animal studies in its text. However, true to form, the report did not consider animal studies in the all-important categories of association, even though the new animal studies were the only reason for doing the report."

"As with previous Committees, this Committee used animal data for making assessments of biological plausibility . . . rather than as part of the weight of evidence to determine the likelihood that an exposure to a specific agent might cause a long-term outcome." Updated Literature Review of Sarin (2004), p. 20 [documents, p. 18] Accordingly it found insufficient evidence of an association.

To understand how such a bizarre outcome was even possible, it is necessary to understand the process through which IOM reports are prepared. After the IOM is requested to do a report, a proposal is prepared by the IOM which becomes the basis for a contract between the IOM and the requesting organization (in this case VA). Then IOM staff recruit a Committee of scientists to carry out the assignment. As described by an IOM staff Member, she looks for scientists with expertise in fields relevant to the subject of the report, but who have no particular knowledge of that subject. IOM staff then staffs the preparation of the report by the Committee.

The proposal for the sarin update was sent to VA on March 11, 2003, with a cover letter from Susanne Stoiber, executive director of the IOM, to Dr. Mark Brown, director of the VA Environmental Agents Service. The cover letter stated: "This proposal follows a request from Secretary Anthony J. Principi and discussions with yourself requesting an update of the health effects of the chemical warfare agent sarin." [documents, p. 19]

The proposal contained the following "Statement of Task": [documents, p. 22]

"The Committee will conduct a review of the peer-reviewed literature published since earlier IOM reports on health effects associated with exposure to sarin and related compounds. Relevant epidemiologic studies will be considered. With regard to the toxicological literature, the Committee will generally use review articles to

present a broad overview of the toxicology of sarin and to make assessments of biologic plausibility regarding the compound of study and health effects; individual toxicology research papers will be evaluated as warranted.

The Committee will make determinations on the strength of the evidence for associations between sarin and human health effects. If published peer-reviewed information is available on the dose of sarin exposure in Gulf War veterans, the Committee may address the potential health risks posed to the veterans . . .''

In other words, the Statement of Task established that the update report would use the same ''categories of association'' as the earlier Gulf War reports. The ''determinations on the strength of the evidence'' would be made on the basis of the ''associations between sarin and human health effects.'' ''With regard to the toxicological literature'' (which included the new animal studies), its use would be confined to the assessment of ''biological plausibility'' to which animal studies had previously been relegated. Thus, the update report would exclude animal studies from its key conclusions, even though animal studies were the only reason for doing the report.

Moreover, the Statement of Task set up another fundamental constraint for the report. The IOM Committee would be permitted to address the potential health risks posed to the veterans ''[i]f published peer-reviewed information is available on the dose of sarin exposure in Gulf War veterans.'' As anyone familiar with Gulf War research would know, including Dr. Brown and his IOM counterparts, there is no published peer-reviewed information available on the dose of sarin exposure in Gulf War veterans, for the reason that no such information was collected during the war. As noted in the previous 2000 IOM report on sarin, ''as discussed throughout this report, there is a paucity of data regarding the actual agents and doses to which individual veterans were exposed.'' Gulf War and Health, Volume 1, p. 84. [documents, p. 14] In order for the IOM Committee to address the health risks posed to veterans, it had to meet a condition that was impossible to meet.

These constraints in the Statement of Task were not contained in the letter from Secretary Principi requesting the report. (To the contrary, they appear to contradict it.) Thus, they must have come from the ''conversations with yourself'' referred to in Ms. Stoiber's letter to Dr. Brown.

Thus, conversations between Dr. Brown and IOM staff determined the outcome of the report before the IOM Committee to prepare the report was ever appointed.

In conclusion, VA staff has not complied with the law requiring the IOM Gulf War reports, and IOM has not followed the law or its own established methodology, restricting the scientific evidence required to be considered. This action has been deliberate. Conversations between VA and IOM staff have shaped the methodology of the reports so as to predetermine their outcome.

The practices described in this testimony demonstrate that the relationship between VA and the IOM should be thoroughly investigated and reformed at both the government and Institute ends. Past IOM Gulf War reports should then be re-done in accordance with the law, as recommended by the Research Advisory Committee report. Alternatively, VA should make a determination of a presumption of service connection on the basis of the scientific evidence contained in the 2008 Research Advisory Committee report and the large VA study published in April 2009, ''Health of U.S. Veterans 1991 Gulf War: A Follow-up Survey in 10 Years,'' which shows that multisymptom illness is the most prevalent health problem of Gulf War veterans, afflicting one in four.

Prepared Statement of Lea Steele, Ph.D., Adjunct Associate Professor, Kansas State University School of Human Ecology, Manhattan, KS, and Former Scientific Director, Research Advisory Committee on Gulf War Veterans' Illnesses

Good morning Mr. Chairman and Members of the Subcommittee. I'm Dr. Lea Steele. I've been asked to testify this morning on why and how scientific findings of the Institute of Medicine (IOM)'s *Gulf War and Health* reports differ from those of the Research Advisory Committee on Gulf War Veterans' Illnesses. As you may recall from my appearance before the Subcommittee last May, I am an epidemiologist, and first conducted research on the health of Gulf War veterans for the State of Kansas in 1997. More recently, I preceded Dr. White as Scientific Director of the Congressionally mandated Research Advisory Committee on Gulf War Veterans' Illnesses, or RAC. In that position, I had primary responsibility for overseeing the RAC's review of research and preparation of a comprehensive report, *Gulf War Illness and the Health of Gulf War Veterans*, released in November, 2008.

Issues surrounding health problems affecting veterans of the 1991 Gulf War are exceedingly complex. An enormous amount of research studies and government investigations have been done to determine what happened during the Gulf War and why so many veterans developed Gulf War illness. This is the term most often used for the pattern of symptoms consistently found at high rates in Gulf War veterans, but not explained by established medical or psychiatric diagnoses. The 2008 RAC report provided a detailed review and synthesis of evidence provided by nearly 2,000 scientific studies and government reports and documents. The report concluded that this evidence clearly indicates that Gulf War illness is real and continues to be widespread, affecting at least one in four of the nearly 700,000 U.S. veterans of the 1991 Gulf War. Further, multiple sources of evidence point most consistently to two primary causes: (1) the small white pyridostigmine bromide pills, or PB, given to protect troops from the deadly effects of nerve agents, and widely used only in the 1991 Gulf War, and (2) pesticides, used excessively during the 1991 Gulf War to protect troops from disease-causing insects in the region. Both PB and some pesticides overused in the Gulf War affect the brain and nervous system by altering levels of an essential nerve signaling chemical, the neurotransmitter acetylcholine. The evidence from multiple studies also consistently shows that Gulf War illness was not caused by serving in combat or psychological stress and that posttraumatic stress disorder (PTSD) affects relatively few veterans of the brief 1991 Gulf War, compared to veterans of other conflicts.

Many of the 2008 RAC Report's major conclusions differ fundamentally from those of the IOM's *Gulf War and Health* reports. The IOM reports were prepared under contract with the Department of Veterans Affairs (VA) in response to a Congressional directive. As described by Mr. Binns, VA was directed to commission IOM to perform a comprehensive scientific review to determine what the evidence showed about health problems affecting Gulf War veterans and their associations with exposures during the Gulf War. As part of the RAC's work, we reviewed all the IOM *Gulf War and Health* reports. Our Committee was sufficiently troubled by how IOM reviewed the evidence on Gulf War health issues that our report details a number of far-ranging problems, raising fundamental questions about both the process used by IOM and their resulting findings. We recommended that the IOM reports be redone to adhere to the requirements set forth by Congress.

I want to be clear that Members of the RAC have great respect for the IOM, generally, and were not anxious to criticize IOM's Gulf War reports. Our Committee includes an honored Member of the National Academy of Sciences and the Institute of Medicine, and several scientists who have served on IOM panels over the years. We felt it necessary to raise these concerns, however, because of the wide expectation that the IOM reports would provide definitive information on the health of Gulf War veterans, and because of the complexity and importance of Gulf War health issues. VA relies on the IOM *Gulf War and Health* reports to assist the Secretary in making decisions about veterans' disability compensation. And, as you heard at last May's Subcommittee hearing on Gulf War illness, both VA and Department of Defense (DoD) officials cite these reports as being authoritative. We did not take lightly our decision to raise such serious questions about the IOM Gulf War reports, but believed there was an obligation to do so.

Table 1. Types of Evidence Used to Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report

Categories of Research EvidenceRelevant to the Health of Gulf War Veterans	*Was This Type of Evidence Considered in Report Findings?*	
	IOM Gulf War and Health Reports	*2008 RAC Report*
Results of Peer-reviewed and Published Scientific Studies		
Studies of Gulf War veterans		
1. Studies that assessed prevalence of diagnosed medical and psychiatric conditions in Gulf War veterans.	**YES**	**YES**
2. Studies that assessed prevalence of undiagnosed multisymptom illness in Gulf War veterans.	(Limited)	**YES**

Table 1. Types of Evidence Used to Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report—Continued

Categories of Research EvidenceRelevant to the Health of Gulf War Veterans	*Was This Type of Evidence Considered in Report Findings?*	
	IOM Gulf War and Health Reports	*2008 RAC Report*
3. Studies that assessed associations between Gulf War exposures and diagnosed conditions in Gulf War veterans.	(Limited)	**YES**
4. Studies that assessed associations between Gulf War exposures and undiagnosed multisymptom illness in Gulf War veterans.	No	**YES**
Studies of chemical exposures in other human populations		
5. Studies that assessed association of exposures with diagnosed diseases.	**YES**	**YES**
6. Studies that assessed association of exposures with undiagnosed symptomatic illness.	No	**YES**
Studies of effects of chemical exposures in animal models		
7. Studies of biological and behavioral effects of exposures in animals.	No	**YES**
8. Studies of effects of combinations of exposures ...	No	**YES**
Results of Other Federally-sponsored Gulf War Scientific Studies		
9. Findings provided in project reports from DoD-funded studies.	No	**YES**
10. Findings presented at scientific conferences, RAC meetings.	No	**YES**
Investigations, Reports on Exposures During the Gulf War		
11. Reports from Federal agencies (e.g. DoD, CIA) that documented or modeled types, levels, and patterns of Gulf War exposures (e.g. pesticides, oil fire smoke, nerve agents, depleted uranium).	No	**YES**
12. Reports from nongovernmental sources (e.g. RAND, Battelle) that investigated and/or modeled Gulf War exposures.	No	**YES**

So, why are the IOM reports' findings so different from those of the RAC Report? There are two overarching reasons: (1) the primary questions addressed by the IOM and RAC reports differed fundamentally, and (2) the RAC considered a much broader scope of evidence to arrive at its findings. The differences between the RAC and IOM reports are not subtle, and are not explained by minor variations in the review methods used or how individual study results were interpreted or weighed. Rather, they are the result of major differences in the scope of questions addressed by the two reports, and the scope of the evidence used to answer those questions.

There are many sources and types of research that provide credible information on the health of Gulf War veterans and exposures during the Gulf War. Twelve general categories of research that directly relate to Congress's directives for the IOM Gulf War reports are listed in Table 1. Each category includes multiple individual investigations—sometimes hundreds of studies. All categories of evidence in the table were found to be informative and useful by the RAC, and were considered, in detail, to arrive at the findings and recommendations in the 2008 RAC report. IOM's *Gulf War and Health* reports relied, in large part, on just two categories of evidence: (1) studies that assessed rates of diagnosed medical and psychiatric conditions in Gulf War veterans, and (5) studies that assessed diagnosed diseases in

other human populations exposed to chemicals. Most of the hundreds of findings in the IOM *Gulf War and Health* reports were based exclusively on studies of diagnosed diseases in these other populations, for example studies of a type of cancer in workers exposed to a specific chemical in the workplace. Although this was a detailed effort, the long list of IOM findings almost all pertain to diagnosed diseases that have never been associated with service in the Gulf War. A very limited number of the IOM's findings relate specifically to health problems found in Gulf War veterans.

Major categories of evidence were not considered by IOM, or were considered only in a very limited way. As described by Mr. Binns, the many animal studies conducted to identify biological and behavioral effects of Gulf War exposures and combinations of exposures were not considered by IOM in assessing levels of evidence. IOM findings also made little use of the hundreds of government investigations on types and patterns of exposures during the Gulf War, which provided important insights in a broad range of areas. These include modeled estimates of low-level exposures to nerve agents in theater, detailed investigations into PB use among Gulf War veterans, and in-depth reports on the types and patterns of use of over 60 different pesticide products, which indicated that thousands of troops were overexposed during deployment. In addition, the hundreds of detailed Gulf War epidemiologic findings on associations between Gulf War illness and Gulf War exposures were scarcely considered by IOM.

Limitations in the evidence considered had profound effects on the IOM *Gulf War and Health* reports and underlie the major differences between RAC's findings and IOM's findings. There are numerous examples of specific differences, many of which are somewhat technical to describe. One straightforward example relates to the magnitude of the Gulf War illness problem. Both the IOM and the RAC reports indicate that all studies consistently identify significantly excess rates of symptoms and multisymptom illness in Gulf War veterans. But the IOM and RAC provide very different figures for how many veterans have been affected. Seven studies have provided estimates of the excess rate of multisymptom illness in Gulf War veterans, when compared to era veterans who did not deploy to the Persian Gulf theater. Six of the studies were published prior to both the IOM and the RAC Gulf War reports; findings from the seventh study were provided to the RAC prior to publication.

As shown in Table 2, six of the seven studies found that 25–32 percent of Gulf War veterans were affected by a defined pattern of multisymptom illness, in excess of background symptom levels affecting nondeployed era veterans. One study reported about half that rate, 13 percent. The RAC report presented results from all seven studies. Based on the consistency of the excess rate of illness in 6 of 7 studies, and other supporting indicators, the RAC found that between 25 and 32 percent of veterans were affected by multisymptom illness, in relation to service in the Gulf War. In contrast, the IOM report relied on a single estimate from just one study, the 13 percent estimate. Overall, different Gulf War studies have different strengths and weaknesses. But the single study on which IOM relied was not superior to the other studies, and had some important limitations. We know that a more recent and larger study from the same veteran population found an excess rate of 25 percent of Gulf War veterans with multisymptom illness. So it is unclear why the IOM finding on prevalence relied on a single study indicating an excess prevalence of 13 percent, when all other studies consistently found the rate to be about twice as high.

Table 2. Excess Prevalence of Multisymptom Illness in Gulf War Veterans, Compared to Nondeployed Veterans: Studies Considered in IOM Gulf War Reports and the 2008 RAC Report

				Was This Finding Included in Report?	
Veteran Group Studied	**Study**	**Number of Gulf War Veterans**	**Excess Prevalence in Gulf War Veterans**	**IOM Gulf War and Health Reports**	**2008 RAC Report**
U.S. Air Force veterans	*Fukuda,1998*	1,155	**30%**	No	**YES**
U.K. male veterans	*Unwin, 1999*	4,428	**26%**	No	**YES**
Kansas veterans	*Steele, 2000*	1,548	**26%**	No	**YES**
New England Army veterans	*Proctor, 2001*	180	**32%**	No	**YES**

Table 2. Excess Prevalence of Multisymptom Illness in Gulf War Veterans, Compared to Nondeployed Veterans: Studies Considered in IOM Gulf War Reports and the 2008 RAC Report

				Was This Finding Included in Report?	
Veteran Group Studied	**Study**	**Number of Gulf War Veterans**	**Excess Prevalence in Gulf War Veterans**	**IOM Gulf War and Health Reports**	**2008 RAC Report**
U.K. female veterans	*Unwin,2002*	226	**29%**	No	**YES**
U.S. national study, Phase III	*Blanchard, 2006*	1,035	**13%**	**YES**	**YES**
U.S. national longitudinal study	*Kang, 2007*	5,767	**25%**	No	**YES**

Another example of differences between the two Committee reports relates to a highly publicized finding from IOM that there is no "unique" Gulf War illness. This finding has been widely misinterpreted to indicate that there is no Gulf War illness problem at all. The RAC report examined this issue in depth. It determined that Gulf War illness is a real and definable problem, based on the consistency of the types and patterns of excess symptoms identified in studies of Gulf War veterans from different units, regions of the U.S., and Coalition countries. It also considered different interpretations of the question of how a syndrome might be considered "unique." We concluded that the "unique syndrome" question has been rather meaningless since it can be answered in a variety of ways, depending on how it is construed. In contrast, the IOM report's finding that there is no "unique syndrome" was based on the failure of a type of statistical approach to identify a "unique syndrome." Unfortunately, the IOM report did not evaluate the scientific merit of that approach, or expert opinion and research indicating that, as applied in Gulf War studies, the method is incapable of identifying a "unique syndrome."

Returning to the big picture, what are the actual implications of the differences between the RAC and IOM Gulf War reports? Are they really important? The IOM Gulf War and Health reports were intended by Congress to evaluate the evidence on diagnosed and undiagnosed health problems in Gulf War veterans, and their association with exposures during the Gulf War. At the end of the day, after government officials and others have read the IOM reports, they will know very little about the "undiagnosed," but widespread problem of Gulf War illness—its characteristics, its impact on veterans, and its causes. They will not know that this symptom complex is consistently described in study after study of Gulf War veterans. They will not know about the large number of veterans affected, or that few have recovered over time. They will not know what an extensive number of studies tells us about associations of this illness with combat stress and with exposures during the Gulf War. And they will not know if these findings are consistent with results of animal studies, research in other human populations, or what we know from government investigations about exposures during the Gulf War. This is not because the RAC and IOM reviewed the same studies, but arrived at different scientific conclusions about what the evidence tells us. It is because the IOM reports and findings, fundamentally, do not address these issues or take into account the broad types of research available to address them.

The health problems affecting veterans of the 1991 Gulf War have presented difficult and complex challenges for veterans who are ill, and also for scientists and health care providers striving to better understand these problems. In the years since the Gulf War it has become clear that selective or simplistic consideration of the research evidence related to Gulf War illness yields few answers. Meaningful progress requires that these complex problems be engaged in a complex way, and that all available pieces of the puzzle be considered. Progress in addressing Gulf War illness remains urgently important, with thousands of ill veterans still waiting for clear answers and beneficial treatments more than 18 years after Desert Storm.

Prepared Statement of Robert W. Haley, M.D., FACE, FACP, Professor of Internal Medicine-Epidemiology, Department of Internal Medicine, University of Texas Southwestern Medical Center at Dallas, TX

Good morning, Mr. Chairman and distinguished Members of the Subcommittee. I want to thank you for inviting me to describe our research program on Gulf War illness at the University of Texas Southwestern Medical Center in Dallas and our collaborating universities and research organizations across the country. To introduce myself briefly, after training in Internal Medicine, I served for 10 years at the U.S. Centers for Disease Control and Prevention (CDC) where I received a U.S. Public Health Service commendation medal for my research on controlling hospital-acquired infections. Since 1983 I have been on the faculty of the University of Texas Southwestern, doing clinical research, teaching research design to our young assistant professors, and supervising an Internal Medicine service at Parkland Hospital. During my first 10 years on the faculty, I volunteered as an attending physician at the Dallas VA Medical Center.

Initial Studies, 1994–1998

In 1994, 3 years after the first Gulf War, Ross Perot visited with our university president and me, as Director of Epidemiology. He acquainted us with the newly emerging problem of Gulf War syndrome, and asked if UT Southwestern would undertake a study of the problem with funding from the Perot Foundation. I put together a small research team and performed an epidemiologic survey and follow-up clinical study of the 24th Reserve Naval Construction Battalion (Seabees) that had served in the Gulf War. While the research world at the time was focused almost exclusively on stress and psychological explanations, our studies pointed clearly toward a physical illness. Our findings raised the following three provisional hypotheses to be explored in further research:

1. The Gulf War syndrome appeared to be a real physical brain illness—a chronic encephalopathy—with 3 subtypes, or variants.
2. The many symptoms appeared to be due to damage to cells in different deep brain structures.
3. The damage appeared to be caused by wartime exposure to combinations of neurotoxic chemicals, including low-level sarin, organophosphate (OP) pesticides and the pyridostigmine bromide (PB) anti-nerve agent medication.

These initial findings were published in January 1997 in three high profile peer-reviewed articles in the prestigious *Journal of the American Medical Association*.

The media reaction from that publication introduced me to several young Gulf War veterans dying of Lou Gehrig's disease (amyotrophic lateral sclerosis, or ALS). My subsequent investigation documented a statistically significant threefold increase in the rate of ALS in atypically young Gulf War veterans. When this was subsequently verified by a VA study, it led to service connection for all military veterans with ALS.

Second Round of Studies, 1998–2001

With leadership and staunch support from Texas Senator Kay Bailey Hutchison, the Department of Defense provided substantial research funding to follow up our findings. We began to explore new medical technologies that would probe directly for the nature and mechanisms of the hypothesized brain cell damage to give doctors a rational basis for diagnosing and treating it and give VA objective tests for determining service connection in these veterans. Here is a summary of the main findings from this work, which spanned 1998 to 2001 and was described in prominent peer-reviewed scientific publications.

1. **Chemical Evidence of Brain Cell Damage.** We performed brain scanning with an MRI-based technique called Magnetic Resonance Spectroscopy (MRS), which measures chemical concentrations in small brain regions of living subjects. We found evidence of chemical alterations in the deep brain structures of ill Gulf War veterans compared to well veterans. This type of chemical change is characteristic of physical brain cell damage and is not found in stress and psychological reactions. The group of veterans with the syndrome 2 variant ("confusion-ataxia") had evidence of more severe brain cell damage than the syndrome 1 ("impaired cognition") and 3 ("central pain") variants.

2. **Abnormal Production of Brain Dopamine.** We performed chemical assays of metabolites of the brain neurotransmitter dopamine (recall that reduced production of brain dopamine causes the symptoms of Parkinson's disease). We found evidence that the brains of ill Gulf War veterans with the syndrome 2 variant were overproducing dopamine. Other research shows that dopamine excess can cause cognitive and emotional symptoms like those described by many Gulf War veterans.
3. **Abnormality of Autonomic Nervous System.** We used special computer modeling of 24 hour electrocardiogram (EKG) recordings to test for subtle abnormalities of the autonomic nervous system, which we suspected of causing symptoms like chronic diarrhea, sexual disturbance, excessive gallbladder disease, unrefreshing sleep and body temperature dysregulation. The results were consistent with loss of the normal day-night fluctuation in parasympathetic nervous system activity, which would indicate abnormal function of the autonomic nervous system. This abnormality was equally present in all three of the syndrome variants.
4. **Locating Damaged Brain Areas.** A fascinating experiment involved performing a SPECT scan of brain blood flow before and after infusion of a drug physostigmine that safely mimics the brain effects of sarin, OP pesticides and PB. Our prediction was that if the ill veterans' brains had been damaged by these neurotoxic chemicals, their brain function would not respond like normal subjects to a repeat exposure. The findings were consistent with the prediction. In normal Gulf War veterans, the medication appeared to reduce blood flow, but it paradoxically increased blood flow in the ill Gulf War veterans with the syndrome 2 variant and showed other abnormal patterns in the syndrome 1 and 3 variants. A provisional diagnostic test modeled from these data discriminated each of the syndrome variant groups from each other and from the well veterans. Equally important, this experiment gave evidence that specific parts of the brain appeared to be damaged and not responding normally. These findings gave us a valuable starting place for designing the next round of studies probing specific brain areas found here to be abnormal.
5. **Discovery of a Susceptibility Gene PON1.** To try to explain why some Gulf War veterans developed this chronic encephalopathy while others working next to them did not, we studied the function of a susceptibility gene called PON1 that produces the blood enzyme paraoxonase that protects our brains from neurotoxic chemicals like sarin and OP pesticides. We found indeed that the ill Gulf War veterans were born with abnormally low levels of paraoxonase, making them highly susceptible to these neurotoxic chemicals; whereas, the well veterans were born with normal to high levels. We then developed a gene therapy product containing the PON1 gene, injected it into mice, and found that it protected their brains from damage caused by exposure to OP pesticides. The university has a patent application pending, and if awarded, a possible product to protect people from OP pesticide and nerve agent exposure might result.

Development of New Technology To Measure Subtle Brain Abnormalities, 2001–2006

During the second round of studies it appeared that the brain cell damage in Gulf War illness is sufficiently subtle that the approach we had been using would not be sufficient and that we would have to develop new technology, or adapt existing cutting-edge technology, to thoroughly understand the condition and develop clinically useful diagnostic tests. Therefore over the next 5 years we concentrated on an intense technological development effort. To make this possible, we enlisted some of the top brain scientists and technology experts from the North Texas region and from universities throughout the country. These included the University of Texas at Arlington, the University of Texas at Dallas, Southern Methodist University, and the Johns Hopkins University, Emory University, and University of Florida schools of medicine

Again with stalwart support from Senator Kay Bailey Hutchison, additional funding was provided through the Department of Defense to accomplish the following technological development projects.

1. **A New High Performance Brain Imaging Center Dedicated to the Problem.** UT Southwestern Medical Center dedicated space in the imaging center for the most powerful FDA-approved MRI scanner (with 3 Tesla strength), with all the peripheral equipment configured for brain imaging studies of Gulf War illness, opened in 2004.

2. **High Resolution Imaging of Small Brain Structures.** Our physicists developed new MRI techniques to obtain very high resolution images of small brain structures, such as the brain's center for memory (the hippocampus) and sensation (the individual nuclei of the thalamus) not normally visualized adequately in standard MRI scans.
3. **Rapid MRI–Based Tests to Replace SPECT.** Although the prior SPECT study was very successful and offered a possible future diagnostic test for Gulf War illness, the protocol required two full afternoons and exposed the research subjects to radiation, both characteristics that reduce its usefulness in a diagnostic clinic setting. We therefore adapted an emerging MRI-based technique called Arterial Spin Labeling (ASL) that can obtain the same information as SPECT but in a 3-hour test on 1 day without radiation exposure. After validation, a provisional patent application was filed.
4. **Functional MRI (fMRI) Tests to Probe Symptoms.** The central problem in diagnosing and treating veterans with Gulf War illness is that the veterans' complaints are all subjective symptoms with no objective signs. To provide medical understanding of the symptoms, we developed for each symptom an fMRI "probe" to demonstrate observably how the brain is functioning when a Gulf War veteran experiences a given symptom. We developed an fMRI test to probe each of the major symptoms, such as problems with fatigue, memory, attention and concentration, word-finding, rapid thinking and reaction (executive function), body pain, depressed feelings, and emotional lability.
5. **MRI and EEG Tests of Functional Connections among Brain Structures.** To assess the effects of brain cell damage on overall brain function, we adapted cutting-edge technology called Functional Connectivity to measure the amount of "electrical traffic" among brain areas. This measures how much different brain areas are "talking" with each other. Damage to a given brain area, or the "wires" between them, reduces or eliminates the electrical transmission between them and usually causes the brain to establish alternate "work around" pathways that bypass the deficit. Knowing the state of the functional connections could inform rehabilitation treatments.
6. **MRI-Based Tests of the Brain's "Wiring."** Some chemicals are known to damage the nerve bundles that connect different parts of the brain, and they can damage either the nerve bundles themselves or the insulation (myelin sheath) that covers the nerve bundles. To measure these we developed a test using the MRI-based technology Diffusion Tensor Imaging (DTI). This approach was used by Japanese researchers to demonstrate brain abnormalities in survivors of the terrorist sarin attack in the Tokyo subway, who were left with a chronic encephalopathy similar to that in Gulf War veterans.
7. **High Resolution EEG.** While MRI-based brain imaging shows spatially what is going wrong in the brain at a given point in time, we have developed a high-resolution electroencephalography (EEG) laboratory to measure the timing of sequential events in the brain pathways damaged by Gulf War chemical exposure. EEG testing is relatively quick and cheap and is likely to figure importantly in a clinical diagnostic strategy. Its high resolution implementation could also discover the order and timing of brain events amenable to rehabilitation treatment strategies.
8. **Innovative Statistical Tests to Maximize the Power of Brain Imaging Tests.** Since the cutting-edge brain imaging techniques being used are barely a decade old, few sophisticated statistical techniques have been developed for analyzing the complex data, and the relatively crude techniques available are typically not very powerful in detecting the types of subtle brain abnormalities that affect ill Gulf War veterans. We therefore developed a new body of statistical theory and applications that greatly increase the power of brain imaging tests and have incorporated them into a software package for which a patent is pending. This should have wide application beyond this program.
9. **PON Laboratory.** In the past the laboratory techniques used to measure the paraoxonase enzyme activity and the different forms of the PON1 gene that protect us from low-level nerve agents and OP pesticides have required time-consuming test tube chemistry not feasible to apply to large numbers of veterans in research studies. To overcome this we set up a special PON Laboratory headed by an expert on PON chemistry, and he has developed rapid, high throughput assays that can be used in large-scale studies.
10. **National Survey.** In the first two phases of our research, we performed our studies on Gulf War veterans from a single naval reserve Seabees Bat-

talion. To determine whether the findings in this Battalion apply to the larger population of Gulf War veterans in general, we collaborated for a number of years with the well known research organization Research Triangle Institute International (RTI) in designing a computer-assisted telephone interview survey to apply in a randomly selected sample of all Gulf War veterans. Subsamples of the ill and well veterans selected from this nationally representative sample will be studied by the new brain imaging techniques.

11. **Mouse Model of Chemical Brain Damage.** To develop effective treatments for a new disease it is often necessary to understand how the disease-producing process works at the cellular and molecular levels so that new drugs or rehabilitation strategies can be directed precisely at the offending element. To make this kind of research possible, our Neurotoxicology Laboratory has developed a mouse model in which we can administer the neurotoxic chemicals to laboratory mice by a carefully tested recipe that results in a chronic behavioral disturbance comparable to Gulf War illness in humans. The brains of these mice can be studied by neuroscientists to discover exactly if and how neurotoxic chemicals damage brain cells.

Third Round of Studies, 2007–Present

After more than a decade since the initial research results on ill Gulf War veterans and with the new testing technology for studying subtle brain damage now in hand, Senator Hutchison championed and spearheaded a substantial new Gulf War illness research program through the VA hopefully to gain a higher level of understanding of the disease, a practical diagnostic approach, and ideas for treatment to be tested in clinical trials. The research program, designed to implement the *2004 Research Recommendations of the VA Research Advisory Committee on Gulf War Veterans' Illnesses (RAC)*, has three basic components:

1. A National Survey and Serum/DNA Bank of Gulf War-Era Veterans
2. A Series of Neuroimaging and Biomarker Studies
3. Pre-Clinical Studies of the Mouse Model

These components were designed on an "industrial model" much like a defense contract program to develop a major new weapons system. All of the components were developed to interact with each other so that the findings of each would inform the progress of the others. At present we are approximately 2 years into the National Survey, 18 months into the Neuroimaging studies and 9 months into the Pre-Clinical studies. The following are summaries of progress to date.

National Survey and Serum/DNA Bank of Gulf War-Era Veterans. To date we have completed the extensive standardized telephone interview with 8,018 Gulf War-era veterans to measure the manifestations of the illness, risk factors, and family impact of the illness. By the end of August, we should have completed the field work for collecting and banking serum, plasma, RNA, and DNA from all of the ill veterans and a random sample of well veterans, comprising a total of approximately 2,100 survey participants. The following are provisional findings from the initial analysis of the survey data.

- Provisional finding: Regardless of the case definition used, chronic Gulf War illness appears to be 3- to 4-times more common in the deployed than the non-deployed Gulf War-era populations, and this difference is statistically significant in the studies thus far.
- Provisional finding: The findings support the conclusion of the 2004 and 2008 RAC reports that, from subtracting the prevalence of Gulf War multisymptom illness (CDC definition) in the non-deployed population from that in the deployed population, in 2007–2008 approximately 23 percent of the deployed force still had the chronic multisymptom illness from deployment-associated exposures.
- Provisional finding: The three clinical variants of the Gulf War illness, described in our prior studies, were identified again and appear to be strongly validated in the data from the national sample. This suggests that the chronic multisymptom illness identified in the Seabees unit by our prior studies is the same as that affecting the larger population of Gulf War veterans.
- Provisional finding: In the naval reserve Seabees Battalion surveyed first in 1995, the prevalence rate of Gulf War illness appears to have remained relatively unchanged over the intervening 12–13 years, except that the milder syndrome 1 variant initially affecting younger Gulf War veterans tended to

have evolved toward the more severe symptoms of the syndrome 2 variant as these individuals aged.
- Further analyses of the survey data are proceeding, assays of paraoxonase enzymes and PON1 genes are nearly complete, and we have selected subsamples of ill and well veterans to participate in the next phase of the Neuroimaging and Biomarker Study.

Neuroimaging and Biomarker Study. Because of the complexity of studying a new brain disease, this component was designed in at least three sequential phases: a) conducting developmental pilot studies to validate the new neuroimaging techniques in normal volunteers, b) performing the complete battery of new tests on the members of the Seabees Battalion studied previously to see whether the disease had changed in the decade since the prior studies and to confirm whether the new tests detect the targeted abnormal brain function, and c) final verification of the findings in random subsamples of the participants in the National Survey of Gulf War Veterans. Provisional findings are as follows.

- Provisional finding: Findings of the prior SPECT experiment were reproduced, and we verified that MRI-Based ASL provides comparable results as the more involved and invasive SPECT, providing a far more efficient and safer diagnostic test.
- Provisional finding: The prior MRS findings of chemical abnormalities in deep brain structures (basal ganglia) were reproduced, and the findings were extended to abnormalities in hippocampus.
- Provisional finding: DTI identified a mild abnormality of myelin in white matter in ill Gulf War veterans.
- Provisional finding: EEG found an increase in slow brain waves in ill Gulf War veterans consistent with neurotoxic brain injury.
- Provisional finding: Functional Connectivity tests identified abnormal increase in brain communication in ill Gulf War veterans, indicative of generalized brain hyperarousal.
- Provisional finding: fMRI tests identified abnormal brain patterns underlying the major symptoms in ill Gulf War veterans.
    - fMRI test of Learning and Remembering identified abnormal function in the brain's memory center (hippocampus).
    - fMRI test of Working Memory found that ill veterans do not use the normal rapid memory pathways but, instead, an inefficient slower workaround pathway.
    - fMRI test of Attention and Concentration identified abnormal function in deep brain structures that normally direct attention and concentration (basal ganglia).
    - fMRI test of Word Generation identified abnormal function in the basal ganglia.
    - fMRI test of Pain Processing found exaggerated response to pain sensation in the cerebral cortex.
    - fMRI test of Emotional Control found activation of abnormal pathways for managing emotionally evocative stimuli.
- High Resolution MRI images have identified abnormal cavities in the brain's memory center (hippocampus) in ill veterans, suggesting chronic effects of brain cell damage.

Provisional Conclusions

In our latest study of the Seabees battalion, virtually every neuroimaging test showed evidence of substantial differences between sick and well groups of Gulf War veterans. This suggests that our unique brain imaging program might explain most symptoms and provide powerful objective diagnostic tests for clinical use and determination of service-connected status. It also provides a rich mosaic of evidence to suggest mechanisms of the brain dysfunction to be further tested in our pre-clinical mechanistic studies the third component of the ongoing program).

The uniform success of the tests is due to our strategy for developing the imaging tests by targeting veterans' symptoms and the brain regions known to perform the implicated functions and the clinical classification of veterans into the three syndrome variants identified in our initial studies. Since the findings differ somewhat among these clinical variants, failing to test and analyze the groups separately would have resulted in less powerful, or even negative, findings.

As far determining which neural mechanisms are in play, we have not analyzed the data sufficiently yet to favor one mechanism over others. We can state the following general working hypotheses about mechanisms:

a. Although we find evidence of abnormalities in both deep gray matter and white matter, primacy of the deep gray matter involvement seems likely (e.g., pain is not a symptom of primary diseases of white matter).
b. Deep gray matter abnormalities identified appear bilaterally asymmetrical.
c. White matter abnormality appears to involve myelin, rather than axonal, degeneration. If correct, this is optimistic for treatment; myelin may be more amenable than axonal damage.

Besides explaining the specific deficits, the mosaic of evidence points to certain general findings:

a. Structures activating during a task in well veterans often do not activate in sick veterans, but other structures do. This abnormal activation probably indicates the brain's attempts to compensate for, or work around, damaged areas.
b. The brain in sick veterans appears to be hyper-aroused and hyper-responsive to stimuli.
    1. The brain appears to be working overtime to overcome the many deficits.
    2. Chronic fatigue may be due to the brain's exhaustion from this overwork.
    3. The emotional lability and hyper-reactivity may also be due to this overwork.

Next Steps

The symptoms of veterans suffering from Gulf War illnesses are subjective, and the causes, diagnoses, and treatments are elusive. Therefore, a guiding principle for this research program has always been that objective studies—verified by researchers at different institutions and replicated in representative and increasingly-large samples of veterans—are required to arrive at conclusions on which action can be based.

With this rigorous approach, the findings to date make us optimistic that this multi-perspective testing protocol might lead to objective diagnosis. If it continues to progress along these lines, the testing approach should prove useful for future clinical and research work in the following ways:

a. Developing an objective diagnostic testing protocol for clinical work and service connection.
b. Providing pathogenetically homogeneous groups for clinical trials so that promising treatments can be tested with far fewer participants, and thus with less time and cost.

In the next phase of the Neuroimaging and Biomarker Study beginning shortly, we are preparing to process through the successful brain imaging protocol at least 80 Gulf War veterans selected randomly from the National Survey of Gulf War-Era Veterans representing the three syndrome variants and well control veterans. The findings in this sample will examine the previously raised hypotheses about the nature of Gulf War illness in the larger population of Gulf War veterans—a vital step that is required before any of the prior findings can be considered strongly supported.

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Prepared Statement of Roberta F. White, Ph.D., Professor and Chair, Department of Environmental Health, and Associate Dean for Research, Boston University School of Public Health, Boston, MA

Good morning, Chairman Mitchell, Ranking Member Roe, and Members of the Committee.

This morning I will talk about my experience with Gulf War veterans over the last 16 years and their health problems. I will speak from a research perspective on the epidemiologic investigations in which I have participated examining health outcomes related to chemical exposures in Gulf War veterans. I will also talk about my clinical experience in working with veterans as a neuropsychologist at the VA and in university medical center settings. My aim is to integrate these two sources

of experience in order to provide a better understanding of the challenges involved in understanding and treating Gulf War Illness.

As mentioned in my prior testimony, our research efforts in Boston over the last 16 years or so have focused on relationships between exposures experienced in the Gulf War and health outcomes, carefully controlling for stress symptoms, diagnosis of post-traumatic stress disorder, psychiatric diagnoses, and other variables that affect neuropsychological test performance, questionnaire responses and neuroimaging results. These studies have led to the following conclusions:

1. Pesticide exposures in Gulf War veterans are associated with increased health symptoms, especially those involving the central nervous system. Such exposures are also associated with poorer neuropsychological test outcomes and with chronic multisymptom illness. These results are consistent with the occupational literature.
2. Exposure to pyridostigmine bromide (PB) is also associated with neuropsychological test outcomes.
3. *Mixed* exposure to high levels of pesticides and PB is associated with more severe effects, including elevated health symptom complaints, poorer neuropsychological test outcomes and chronic multisymptom illness.
4. Exposure to nerve gas agents (Sarin/Cyclosarin) in Khamisyah is associated with poorer neuropsychological test performance and smaller white matter volumes in the brain in a dose-effect manner: higher exposure predicts greater pathology. These results are consistent with those seen following Sarin exposures in Japan, and the functional findings based on neuropsychological testing are of the type that would be expected with lowered white matter volumes.
5. Gulf War veterans with higher numbers of symptom complaints have smaller white matter volumes on magnetic resonance brain imaging than those with low numbers of symptoms.

It is important to note that the above findings were seen in veterans who were not diagnosed with clinical illness by physicians. They did not have diagnosed brain damage nor were their neuropsychological or brain imaging results considered to be in the abnormal range. Most of the study participants were working at the time of their study participation. The epidemiological study results suggest that there are subtle changes in brain structure and function associated with chemical exposures. Such changes are often referred to as "subclinical" central nervous system effects of exposure. The research results suggest that these exposures are also associated with significant experience of poor health and dysfunction in daily life.

How do such findings relate to the clinical examination of individuals with exposure to pesticides and other neurotoxic chemicals? When patients are seen clinically, neuropsychological test results and brain imaging can be interpreted as being normal even among patients who experience significant health symptoms and functional problems in daily life. This reflects the insensitivity of the diagnostic tests available as well as other factors. Gulf War veterans often show this picture, and it can be perplexing to clinicians when they observe poor health and multiple symptom complaints in individual patients. This may lead to confusion about diagnosis, treatment options available for patients, and even whether to accept the patient's complaints at face value.

The clinical and research evidence suggest that health symptom complaints in Gulf War veterans should be taken seriously, especially if the veteran has known exposure to neurotoxicants in theater. These include pesticides, PB and Sarin/Cyclosarin gas exposure. Diagnosis of post-traumatic stress disorder is made and compensated based on self-report of psychological symptoms in the context of a significant stressor. Self-reported physical symptoms and dysfunction in daily life deserve to be taken just as seriously.

[The attached reports, "Quantitative Magnetic Resonance Brain Imaging in U.S. Army Veterans of the 1991 Gulf War Potentially Exposed to Sarin and Cyclosarin," by Kristin J. Heaton, Carole L. Palumbo, Susan P. Proctor, Ronald J. Killiany, Deborah A. Yurgelun-Todd, and Robert White, in NeuroToxicology 28 (2007) 761–769, dated July 19, 2006; and "Effects of Sarin and Cyclosarin Exposure During 1991 Gulf War on Neurobehavioral Functioning in U.S. Army Veterans," by Susan P. Proctor, Kristin J. Heaton, Tim Heeren, and Roberta F. White, in NeuroToxicology 27 (2006) 931–939, dated May 26, 2006, will be retained in the Committee files.]

**Prepared Statement of Anthony Hardie, Madison, WI,
Gulf War Veteran Member, Research Advisory Committee on
Gulf War Veterans' Illnesses**

Chairman Mitchell, Ranking Member Roe, and Members of the Subcommittee:

Thank you for inviting Members of the Research Advisory Committee on Gulf War Veterans' Illnesses to testify today regarding the implications of the U.S. Department of Veterans Affairs' limited scope of Gulf War Illness research. I am honored to fulfill the Subcommittee's request to testify today as a Gulf War veteran regarding my own personal experiences, observations, and recommendations on these issues.

My experiences are far from unique, and I am sharing them in the hope that it will help to better inform the Subcommittee and in turn assist the countless thousands of my fellow Gulf War veterans who, like me, have been injured and ill for nearly two decades following the war without effective treatment.

Like 175,000 to 210,000 of my fellow Gulf War veterans, I have had significant health issues that began during my deployment to the Gulf more than 18 years ago, and like them have experienced a profound negative impact due to the sharply limited scope of VA's Gulf War Illness research program. To put things into perspective, in 1991, I was a young, fit, 22-year-old special operations soldier tasked to the multi-national Coalition-led Joint Forces Command-East when the war began, and I turned age 23 while in Khafji, Saudi Arabia (near the Kuwaiti border) just days before we moved across the border into Kuwait.

PB. In mid-January, my team of about 30 men was directed to begin taking the PB (Pyridostimine Bromide) nerve agent protective pills that we had all been issued. We were told that they were experimental, not FDA-approved, that we had no choice in consenting and were ordered to take them, and that we would probably experience symptoms similar to mild nerve agent poisoning. Like tens of thousands of my fellow Gulf War veterans, I experienced significant side effects, including watery eyes, runny nose, confusion, dizziness, muscle twitching, diarrhea, weight loss, and generally feeling quite ill. For me, like so many others, the acute symptoms lasted for at least as long as I took the pills, which was for a number of weeks.

Today, science has shown that these experimental pills we took, along with the industrial-strength pesticides so many of us used and overused are implicated as causes of our lasting Gulf War Illness. Yet, despite research showing the negative impact of PB in combination with pesticides at least as early as a 1990s Duke University study funded not by VA, but by Ross Perot, VA's limited scope GWI research has yet to develop effective treatments, diagnostic tests to assess the damage, advisements on what to do or not to do, or even informational materials in order to help improve the health and lives of the one-fourth to one-third of us Gulf War veterans who have been and remain ill.

Fog of War. Because of the much vaunted technological advances of the 1991 Gulf War displayed around the clock on the nascent CNN, it is easy to understand why there seems to be a persistent belief here in U.S. that for the first time in history, there was no "fog of war" during the 1991 Gulf War. On the ground, it was a different story.

When the first SCUD missiles were fired, ground troops near the border like me were concerned about them hitting our locations because the Iraqi political-military strategy was not yet understood.

When more than 700 of Kuwait's oil wells were lit on fire, Islamic and non-Islamic forces alike quietly discussed whether the midnight-darkness at noon was some sort of cataclysm, before the unprecedented cause of the unnatural, midday inky blackness became known.

When chemical alarms sounded or silkworm missiles came in, a denial cycle between forward and theater command levels led to a widespread belief that the tens of thousands of alarms—even those double-and triple-verified as accurate—were simply faulty. During the war, my team's chemical alarms went off a number of times. Like most other Gulf War troops, we were told that the Iraqis had not used or even forward-deployed their chemical weapons and the alarms must have been sand or some other false alarm. After the war, it was publicly revealed that tens of thousands of alarms went off throughout the Gulf War theater of operations. One day in particular, I remember receiving communications that a nearby unit at R'as al-Mishab had been hit with chemicals [chemical warfare agents]. We later received communication that the chemicals had been confirmed. Later, it was discounted as a false alarm, despite the second confirmation. This story is far from unique, with Gulf War veterans having echoed similar stories in previous public testimony.

When we moved forward to the evacuated Kuwaiti border city of Khafji, a nighttime missile sounding like a train overhead killed about a dozen Senegalese troops

where we had just left. Another night, we were the target of a multi-volley Iraqi artillery raid. Given the unexplained, severe, painful skin rash all over the exposed skin on my face and hands on one of those nights, as I had slept under the only open window in the building, I have long wondered about its cause and effects.

When we launched into southeastern Kuwait with Coalition forces, unlike further to the west, we encountered no resistance. We were able to quickly move into Kuwait City, where we took over the former Iraqi command center, replete with a room-sized sand-table map of Kuwait covered with chemical warfare and other symbols that was the object of great interest to the CENTCOM officers who flew in the following day, before the facility was closed off permanently for the remaining nearly 2 months I was in a neighboring building near the Kuwaiti International Airport.

HD/L/HL. In the days that followed the informal end of the ground war, small teams from my "unit" combed through former Iraqi sites in Kuwait and Iraq, assessing them, gathering information, and even picking up the occasional souvenir.

In one bunker complex north of the Kuwait bay that a handful of us went through, I was captivated by the lovely fragrance that smelled just like the large red flowers that filled my grandmother's garden back home and pervaded Iraqi bunkers so hastily evacuated that plates of half-eaten food and loads of personal gear had been left everywhere.

Along with the lovely, captivating geranium fragrance was the pervasive odor that I thought was wet onions. I found this very odd at the time because there were no onions to be found in even the emptiest of the bunkers.

If I had been looking at a watch, I could have told you shortly thereafter what the time and date was when my severe, chronic cough began. Like many Gulf War veterans (and Iranian veterans of the Iran-Iraq War who preceded us), it has never subsided. For years, I believed that my black sputum that I coughed up for 3 months, and the never-ending cough that continued thereafter, was the result of the oil well fire smoke.

Years later, I was horrified to learn that what I smelled that day were the characteristic odors of Lewisite and Mustard, a classic mixture used heavily by the Iraqis during the Iran-Iraq war. Even still, I discounted that my severe respiratory illness that began very shortly thereafter could have been because of these blister agents, not knowing until more recently that while the damage is immediate, the symptoms of mustard agent exposure don't show for as long as even 24 to 48 hours after exposure, and that the vapors I inhaled that day—by the fact that they were strong enough to be smelled—were also strong enough to do immediate and lasting damage to my entire respiratory tract that corresponds with my symptoms at the time and since.

After talking with my doctors, the soft, blackish chunks I coughed up at the end of the Gulf War, some as wide across as a dime or larger, were almost certainly not oil well fire residue, but instead soot-tinged lung tissue being sloughed off after being blistered by these Iraqi chemical warfare agents. And notably, because there were only two or three of us in those bunkers, with me in them the longest, and because none of us were well trained enough to ever recognize these characteristic odors, they were never reported—except to my family, as ironically I searched after the war in Arab shops for the uniquely fragrant, geranium-scented perfume to buy for my mother that I was certain the retreating Iraqi troops had been using so heavily that it had left its scent behind in those bunkers.

I have heard enough firsthand accounts from other Gulf War ground troops about coming across chemical mines, being hit with isolated chemical attacks, and more that I now firmly believe that the CIA and DoD has no basis for their long-held statements that Iraqi ground commanders never possessed or used chemical weapons during the war. The extent and impact of intelligence failures were widely discussed on and off the battlefield, and if there is further interest and a proper request to do so, I would be happy to provide more information in a closed setting on this issue.

Sadly for at least 175,000 of my fellow ill Gulf War veterans, VA's limited scope of GWI research has not even begun to address the health outcomes associated with widespread chemical warfare agent exposures, let alone treatments, information, or advisements that might help improve our health and lives.

Some time following my redeployment to Ft. Bragg, I sought health care at the Troop Medical Clinic (TMC) on "Smoke Bomb Hill." After explaining during triage that my "Kuwaiti cough" was unrelenting and often led to vomiting, I overheard a discussion about me just outside the exam room, "He's another one those Gulf War veterans who 'thinks' he's sick." I vowed to myself to never seek treatment again until after I was out of the military, assuming that the VA would be able to fix me up in no time. Meanwhile, based on my cough, which was the worst in the mornings and after running, I was "diagnosed" with "post-exertional asthma" and given an

inhaler, which one of my similarly diagnosed, fellow Gulf War veterans and I nicknamed our "Kuwaiti badge of pride."

Like many of my returning fellow Gulf War veterans, I did my best to deal with the chronic cough, fatigue, abdominal pain, diarrhea, nausea, dizziness, and cognitive impairment that began before returning home and just wouldn't subside. Some of my fellow soldiers also suffered from skin rashes and a variety of other symptoms.

I only just began to realize how wrong I was about finally getting proper health care from the VA, when at one of my earliest VA appointments in Milwaukee shortly after leaving the military, I tried unsuccessfully to put words to what was wrong with me, and was told by the clerk, "Well, we're all confused." Like many of my fellow veterans from Somalia, I was diagnosed with PTSD. A few months after my discharge, I had a recurrence of malaria as well, though I could get no treatment for it from VA because I had been denied service-connection. Instead, I called a buddy back at Ft. Bragg, who gladly mailed me the pills, and I haven't had a recurrence since—no thanks to VA, which to this day has denied my service-connection for malaria as well.

A year or two later, having moved to Madison, the designated Gulf War coordinating doctor's agitated words burned forever into my memory when she told me, "There's nothing wrong with you Gulf War vets. It's all in your heads, you just need to forget about it, get on with your lives, and get past it." Even if it were "just" PTSD or TBI, which it clearly wasn't, these words still ring in my ears as one of the most commonly cited examples of VA's history toward Gulf War veterans that has yet to be fully remedied, because the answers lie here in Washington, in creating the political will to find effective treatments that doctors in Wisconsin and across the country can implement with their still-ill Gulf War patients. Like other Gulf War veterans I have spoken with, what was most effective in finally getting taken seriously was when Mental Health referred me to other medical specialties because my chronic cough and other symptoms were clearly unrelated to any known mental health condition.

However, by then, I had been in the VA system for about 3 years, and it was now about 6 years after the war. I had served my country for more than 7 years, much of it in sharply austere conditions in highly underdeveloped countries, not to mention two tours under harsh combat conditions. I found it unconscionable that they were treating my brothers—and sisters-in-arms with such flagrant, caustic disregard.

Gulf War Illness. Like some Gulf War veterans, my chronic, widespread pain and MS-like neurological symptoms have been diagnosed and service-connected as fibromyalgia. Like a few Gulf War veterans, my post-Gulf chronic, painful bowel disorder has been service-connected as irritable bowel syndrome. Like many Gulf War veterans, my debilitating chronic fatigue has been well documented. But, like nearly all other ill Gulf War veterans, I am not service-connected for Gulf War Illness or Gulf War Syndrome.

Despite special provisions in the law, Gulf War veterans have had unique and special challenges due to the currently medically undiagnosable nature of many of their health conditions. In fact, the data from VA's most recent, December 2007 quarterly Gulf War Veteran Information System (GWVIS) report—which it inexplicably discontinued thereafter—shows that of the 272,215 claims filed by the 696,842 veterans of the 1991 Gulf War (a filing rate of almost 40 percent), only 3,149 undiagnosed illness claims, equaling about 1 percent of all claims filed, have been approved. The fact that only 1 percent of all Gulf War veterans' claims filed have been approved for "undiagnosed illness" violates both the letter and the spirit of the Persian Gulf War Veterans Act 1998, which was clearly intended to help ill Gulf War veterans receive expedited service-connection for their Gulf-related chronic multi-symptom illness.

Like many Gulf War veterans, I have had chronic sinusitis and chronic cough since the Gulf. Since my discharge, I have requested again and again for VA to do a lung scope to go into my lungs to see what it looked like, but at every turn was put off, told there were other tests to do first, told there was no reason to do so. Again, my cough has *never subsided* since it began in February/March 1991. This Spring, after 18 years I was finally able to get a bronchoscopy, and its results were yet one more bittersweet revelation—"red, irritated, and angry-looking", with a diagnosis of one type of chronic obstructive pulmonary disease (COPD), chronic bronchitis. Due to VA's limited scope of GWI research, I found this bittersweet victory on my own, having gotten the test done privately after having found no support from the VA for getting this test done for my 18-year-old chronic cough, despite having firmly and repeatedly requesting it since my very first VA encounter in 1994.

A reasonable person would conclude that all of these conditions, which are anecdotally very common among Gulf War veterans, should be presumptively service-connected and treated by VA under—take your pick—"Gulf War Illness," exposure to Kuwaiti oil well fire smoke, or exposure to sarin, cyclosarin, or blister-agent vapors. Yet despite all the scientific evidence, VA has not yet made any of these and so many more presumptive conditions for the tens of thousands of ill and ailing Gulf War veterans whose struggles are at least as bad as my own, and due to VA's limited scope of GWI research, there was not and still is not help, or even an understanding of what to look for in us Gulf War veterans.

The decline. Given the prevalent "warrior" mentality that pervaded every aspect of military life, years later I would find it extremely disingenuous that one early government study showed low rates of hospital stays by Gulf War veterans, with the implication that there really wasn't a problem and appeared to be one of the earlier attempts to discount that anything was wrong with us. Like me, many of us Gulf War veterans battled health issues and struggled to stay in the workforce for years. As I have often said, if it weren't for the military, I wouldn't have been able to keep on struggling, but then again, if it weren't for the military, I wouldn't have had to.

Before the military, I was seen as a bright and promising boy, with achievement test scores nearly always in the 99th percentile, being academically recognized at an early age for reading hundreds of books each year, being selected to represent my high school in high quiz bowl, and so on. That factor, combined with my enduring warrior mentality, has meant that my cognitive losses and challenges haven't always been as visible to others who didn't know me before the Gulf War. But for me, it has been extremely painful, with great difficulties in even finishing a book, and short-term and working memory loss that is much worse than my most elderly relatives and has required major adaptation over many years and reliance on new skills, devices, and assistance.

Submitted with my written testimony is a statement written by my mother more than a decade ago in support of my VA claim. It could have been written by any Gulf War veteran's mother, describing what she saw in her son—all the symptoms, all the changes for the worse. These observations are hardly unusual—spend a little time with any of us 175,000-plus ill Gulf War veterans and you'll see much the same thing.

Things have only gotten worse since then. For a few years, I believed that my symptoms would just hold steady, and I kept working harder and harder on veterans issues in a variety of roles, always seeking to help find treatments and assistance for my fellow Gulf War veterans. As things got worse, increasing amounts of caffeine and energy drinks kept me going at about the same pace. I began to need accommodations to continue working, trying to make a difference for others. Finally, even all that didn't help, and like many other Gulf War veterans, I kept getting worse, until finally this March, after a fairly major thoracic surgery, I was simply unable to return to a normal working life, and I'm now largely at home—not a fun thing when you're only what you thought was mid-way into your career.

IOM Issues. Last November, the Research Advisory Committee issued its exhaustive, definitive scientific report. In essence, the report said in scientific terms what we ill Gulf War veterans have been saying all along – that our Gulf War exposures made us ill, and that we've been ill ever since. This final government acknowledgement was truly a bittersweet victory.

Yet, more than 18 years after the Gulf War, VA has essentially nothing to show for its efforts on behalf of ill Gulf War veterans besides acknowledging that Gulf War veterans really are ill and that it is the result of our military service. The VA has nothing new to offer our Gulf War veterans to help improve our health and lives besides procedural excuses. Like me, many of us have battled Gulf War related health issues for that entire time. Today, there are no effective treatments. It is time for this Congress and this administration to truly leave no stone unturned in helping our Nation's countless thousands of ill Gulf War veterans, who served their country, were injured in war, but have yet to be taken care of as promised.

It is true that VA has retained an open door for Gulf War veterans not yet enrolled in VA to be seen at VA medical facilities for priority health care for Gulf War related conditions. And, the VA has made great strides in reducing wait times for VA health care appointments, and should be commended for this herculean achievement. Restoring Gulf-War related ("enhanced") enrollment in VA health care under Priority 6 should be an immediate, no-brainer priority and continued in perpetuity. I wonder if I'm alone in finding it absolutely stunning that VA allowed this provision to expire. Thankfully, Congressman Glenn Nye (D–Virginia-02) has been successful in including this restoration for Gulf War and Agent Orange veterans in the

current National Defense Authorization Act (NDAA), and I request for my fellow veterans that Congress unanimously support this critically important amendment.

However, as I testified before Congress 2 years ago, being seen is not the same thing as being treated. Coordinated team care is an important VA advance. Just like for me, many Gulf War veterans have told me that their treatment has consisted of suppressing individual symptoms, but without any apparent understanding of the underlying mechanism of their chronic multi-symptom illness. Treatment based on a scientific understanding of the underlying mechanisms of Gulf War Illness and not just focused on symptom-management is of key importance, and I believe is within our reach.

Flawed Research Efforts. There are a number of important, negative outcomes that have resulted from VA's failure to adequately assess, monitor, and treat ill Gulf War veterans like me through its halting, piecemeal, seriously flawed research program.

Clinicians at local VA hospitals still, after 18 years, seem to have had no idea what to make of, or to do for Gulf War veterans. In my experience, nearly all have been competent and compassionate professionals who have sought to treat every symptom they could. I stated in my testimony before another House Veterans Affairs Subcommittee in 2007 that being seen is not the same thing as being treated. What I meant by that was that having countless VA appointments, resulting in no effective treatment for the underlying injury or illness and only limited symptom management, is really just about as good as not being seen at all. As I said then, I know of many Gulf War veterans who long ago gave up on getting effective or relevant health care from VA years ago, with some seeking alternative or experimental options and others simply struggling with their array of debilitating symptoms as best they can.

Because of VA's research inadequacies, clinicians have not known to tell us ill Gulf War veterans what to do that might help improve our health and lives. In more recent years, it became clear throughout much of the medical community that Gulf War illness is real. In my case, it became clear to my doctors that Gulf War illness was real long before its reality was acknowledged by the Federal Government or in the media, though sadly, I have heard of Gulf War veterans as recently as this Spring who are still being told that it's all in their heads.

Through recent, Federally funded research, we know that veterans with PTSD who have subsequent traumatic exposures may get even worse. And we now know that one of the most dangerous things for veterans with even mild traumatic brain injury (TBI) is another brain injury while the brain is still healing.

But, because of VA's research inadequacies, clinicians have also not known to tell us ill Gulf War veterans what to avoid or be careful of. VA and other doctors have not known to tell ill Gulf War veterans to avoid at all cost any additional exposures to pesticides, paint primers, and related chemicals. Like so many of my Gulf War veteran friends, I've had to learn that the hard way, through personal experience of the terrible effects of subsequent exposures. And, VA and other doctors haven't been able to warn us of the terrible potential effects of future injuries or illnesses involving inflammation, either. Like many of my Gulf War veteran friends, I have also had to learn that the hard way – in my case, it was a whiplash that was the straw the broke the camel's back, with chronic widespread pain.

Finding old friends. In the last several months, many of my former Army colleagues have found each other again via Facebook. While it feels like "coming home" to be reuniting like this, it is also deeply disheartening to learn how many are also continuing to suffer without relief or effective treatments. As I have found and shared some old pictures from back then, finding friends like Joel—a career soldier who now lives in Iowa. When I had the honor and privilege of serving with him, Joel was the epitome of what a special operations soldier should be—smart, physically and mentally fit, a respected and beloved leader, self-sufficient yet thrived on being part of or leading a team, always ready at an instant to improvise, adapt, and overcome. And, Joel is a multi-combat tour veteran, having at least three combat tours, if not more. He's truly a hero to so many of us, so much so that he, and others like him would never consider themselves so, saying he was just doing his job. So it was all the more heartbreaking to learn that he's now totally debilitated, disabled and at home, overcome by the chronic, widespread pain that affects so many of us, and more health issues than he can name. I can only say one thing about how VA's failures in Washington and beyond have affected a decorated, multi-tour combat veteran hero like Joel—THIS. IS. NOT. RIGHT.

These issues also affect women veterans. I was deeply saddened to hear from Trish from Ohio—a friend with whom I had lost contact before the war—that she, too, has suffered terribly since the 1991 Gulf War with her Gulf War Illness. Another friend, Michelle in Maine is another of the 175,000 who has such severe neu-

rological issues that she's now losing her eyesight, in addition to the debilitating array of chronic multi-system symptoms that affect us all.

And there's Ed, from Missouri, who can barely walk due his muscle and joint weakness and pain, and I could go on and on and on. Joel and Trish and Ed and Michelle are not alone—they are just a few of the thousands of ill Gulf War veterans that are in every state and every Congressional district.

These are real people, who volunteered to serve their country and to risk their very lives in service to our Nation. Yet, VA's limited scope of research has failed, and continues to fail, all of us.

End Results. Like many Gulf War veterans, I have beliefs on how we got to this point—where more than 18 years later, we have almost nothing to show for it all (with the exception of the most recently funded, promising, ongoing DoD and University of Texas-Southwestern efforts)—no treatments, advisements, or adequate assistance to give our ill Gulf War veterans. And, because we haven't fully learned the lessons of the Gulf War toxic soup, our force protection measures remain inadequate.

However, I won't discuss that here. And, later in this hearing you'll hear from others more eloquent than me about how VA's fundamentally flawed contracts with, and reliance on the subsequently flawed reports issued by the Institute of Medicine has led directly to today's most stark failure regarding Gulf War veterans' illnesses. The greatest failure is one of outcomes—that more than 18 years after the war, VA has essentially nothing to show for its "efforts" and little or nothing to offer the one-fourth to one-third of all Gulf War veterans who, like me, remain ill and with no effective treatments.

Recommendations. In addition to immediately directing VA to correct the serious issues related to its contracts with IOM, **here's what I believe needs to be done this year, at a minimum:**

First, the administration and Congress should take **committing to Gulf War illness research focused on treatments as seriously** as recent and ongoing efforts related to PTSD, traumatic brain injury (TBI), and prosthetics development. In recent years, Congress has forcibly appropriated large sums for these and as might be expected, the results are already promising. Scientists who have made presentation before the RAC have stated that effective treatments for Gulf War illness are within our reach, and I believe they're right, if only we commit to doing what's right for our ill Gulf War veterans.

At the present time, we have the skeleton of a research program but the government needs to put some flesh and bones on it. The VA funded program at the University of Texas-Southwestern, is focused on basic research, looking for the mechanisms that underlie the illness. It should be continued, though modified with the recommendations adopted by the RAC to make it more comprehensive. VA should also substantially expand its internal research as recommended in the RAC Report.

DoD also has a critical role to play. Historically it has provided two-thirds of Gulf War research funding, but it has zeroed out those programs since the start of the current wars. In response, Congress has created a Gulf War research program within the DoD Congressionally Directed Medical Research Program. This is a very exciting program, open to all researchers, which is focused on small pilot studies of drugs and other treatments already approved for other diseases. So the payoff could be much quicker than the basic science approach. However, the program is not budgeted by DoD, so ill veterans and their handful of advocates have to struggle to keep it alive each year in competition with earmarks. It is extremely underfunded—just $8 million in FY09 for research to find treatments for at least 175,000 ill Gulf War veterans. It should be fully funded at the $40 million level recommended by the RAC. And DoD should have a high interest in having treatments available so this doesn't happen again.

The research agenda should include the most promising potential treatments. As an example, why can't VA sponsor an initiative into stem cell research to regenerate our damaged neurological systems, comparable to VA's efforts with TBI and PTSD?

It is also unclear, and highly troubling, that VA has never **developed and implemented its own internal treatment-oriented strategic research plan focused on improving the health and lives of ill Gulf War veterans.** The two RAC reports provide a clear road map for this research direction. And, there should be a direct connection and perpetual communication between the VA research arm and treatment providers, with a sustained effort aimed at communicating treatment information and "do's and don't's" advisements to treatment providers.

Second, VA should be directed to **provide presumptive service-connection** for all the conditions known to be caused by or strongly associated with each Gulf War exposure, with or without IOM input. Above all, chronic multi-symptom illness should be a presumptive service-connection for ill Gulf War veterans. As noted ear-

lier, service-connection is not just a compensation mechanism; most importantly, service-connection is the gateway to VA health care for the service-connected conditions and veterans. VA should be directed to increase the maximum allowable percentages for the three conditions currently listed as presumptive under undiagnosed illness claims, which are fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome.

Third, VA should be directed to **provide outreach** to Gulf War veterans and their loved ones, their advocates and their health care providers about all of the Federal Government's efforts related to Gulf War veterans.

- The National Center for PTSD (NCPTSD) is an incredible international resource and an excellent example of what VA can do, and could serve as a model for a clearinghouse of Gulf War illness resources and information for scientists, health care providers, veterans, and their advocates. VA should be directed to create such a center, including developing a comprehensive, informative, perpetually updated Web site about Gulf War health issues, modeled after the NCPTSD Web site.
- VA needs to be directed to develop a one-page handout on Gulf War illness listing causes, symptoms, and do's and don'ts, modeled after VA's extraordinarily valuable pocket card on traumatic brain injury (TBI).
- VA should be directed to reestablish its now-defunct direct-mail Gulf War Review newsletter, which was VA's only direct communication to Gulf War veterans related to their Gulf War service.
- VA should be directed to develop and widely disseminate information related to all ongoing research studies related to Gulf War health issues, including studies seeking volunteer participants.
- VA should be directed to develop (or revitalize the now defunct) clinician guide for treating Gulf War veterans with Gulf War Illness, updating it regularly with new research findings, promising treatments, and clinical trials.
- VA should be directed to widely publicize the existence of the Gulf War veteran brain bank, including to Gulf War veterans, their advocates and health care providers, state DVAs and CVSOs, and the scientific community. While it is too late to benefit its donors, there is hope that knowledge gained from the scientific study of the donations of their brains and spinal cords at the time of their death will help other veterans.
- VA should be directed to reinitiate its now-defunct **Gulf War Veterans Information System** (GWVIS) data reports, which are a critical resource for veterans' service providers, including State DVAs. VA should be directed to break out approved undiagnosed illness claims to show actual numbers of claims approved for general undiagnosed illness and for each presumptive condition (of which there currently are three: fibromyalgia; chronic fatigue syndrome; and, irritable bowel syndrome).

Finally, VA needs to be directed and overseen to ensure that **Gulf War Illness is not the only Gulf War health outcome** that is addressed. For too long, it was thought that PTSD was the only negative brain outcome of war; we now know that TBI is another terrible outcome of war. And as we learn more about blast injuries, we will almost certainly determine that such blasts also affect other body systems and organs and not just the brain. For Gulf War veterans, VA must be directed to focus its attention on Gulf War Illness, which affects the largest number of ill Gulf War veterans. But, VA must not be allowed to fail to fully address increased rates of ALS, MS, and cancers, Gulf-related vaccination injuries (including in those who never deployed), oil well fire smoke inhalation, raw petroleum exposures, Depleted Uranium (DU) inhalation and ingestion, and the many more issues noted in the RAC's November 2008 scientific report.

Thank you again for allowing me to testify. I look forward to your questions and comments.

What follows is a statement by my mother written in 1998 in support of my VA claim for Gulf War illness symptoms and conditions. It could quite literally have been written by any mother of any of the 175,000–210,000 ill veterans of the 1991 Gulf War.

Statement

As a concerned mother, I am writing a brief account about my son, Anthony Hardie, who is not the same person we knew before the Gulf War in 1991.

In November of 1990, my son was due to be honorably discharged from active duty in the Army, but instead he shocked us all by re-enlisting , so he could go to the Gulf. On Christmas Day, somewhere in the desert, half a world away from loved ones, he wrote a letter to his Congressman, Steve Gundersen, to say that he was there because he wanted to be there. He was only twenty-two, a strong, patriotic young man who was dedicated to his country.

Little did we realize that when he returned home five months later, his life would never be the same. He seemed overwhelmed by the hero's homecoming, with all the yellow ribbons, flags and cheers. At first he was quiet, very tired and always cold. He had developed a terrible-sounding cough, and he complained of his lungs being sore from always coughing. He attributed the thick black discharge that we saw him coughing up to the burning oil wells in Kuwait near where he had been living, so close that he says he could feel the heat. He told us of how it was often as black as night in the middle of the day, and of how everyone was covered with black oily soot that made their eyes and throats burn. When I washed his uniforms when he finally came home, the oily black soot stains would not come out even after washing them over and over, and I could only fear what his lungs must look like.

Ever since then he has become extremely sensitive to chemicals and other odors. He has had headaches and chronic sinus infections. In one year, between 1994-95, he had over ten sinus infections, and he has had two sinus surgeries at VA hospitals for these

problems. Yet these surgeries didn't take care of everything, and he still has many problems with sinus infections, which concerns us a great deal.

We worry if he will ever get better. It is often difficult for him to function when he is chronically tired most of the time, and sick from infections and from reactions to the many medications that he has been directed to take by VA doctors over the last several years. We worry if his immune system is seriously impaired and may be permanently damaged, we don't know.

In the last few years, he has seemed to find it increasingly difficult to handle ordinary stresses and cope with everyday living. Frequently he is withdrawn, has bouts of depression, mood swings, and complains of strange feelings of unreality and spaciness. We see him having concentration difficulties and memory loss, both short and long term. Sometimes when he was driving home from work he would forget where he was going. He has difficulty sleeping at night, with disturbing episodes of anxiety. In the daytime he has chronic fatigue, requiring long naps, and he is difficult to awaken in the morning, or even afternoon. Frequently he has complained of joint and muscle pain in various parts of his body. Often he has gastro-intestinal problems, with cramps, diarrhea. Right after he came back from the Gulf, and for several years after he often complained of nausea, though not as often anymore. He is quite thin.

The VA has been treating him, and doing some testing but it seems like they keep putting him on hold. Everything they do takes so long. He doesn't even know what blood tests they have done when we ask him. Their evaluations are very incomplete.

In 1993, my son was honorably discharged from the Army and as a mom, I am proud of him and his accomplishments. He is a well-decorated vet, having earned a

number of medals, including the Bronze Star. He has enough recognition awards that it covers a wall. He gave up the best years of his life for his country, but the battle is not over. He continues the fight to regain his health. Through it all he has maintained a remarkably positive attitude. Most people do not realize the burden that he is carrying. We wonder what the future holds for him, and of course we worry.

The account you are now reading is not unusual. Thousands of other young men in their twenties and thirties suffer in silence, not wanting to complain. Someone needs to speak out for them. If the government waits until all the studies are done before they act, it will take years and by then it will be too late.

Something needs to be done immediately. It has already been seven years since the Gulf War, yet the battle goes on for those who are sick. The Gulf War illness that affects my son is very complex with multiple symptoms and probably multiple causes. Yet it is as disabling as having been shot. More comprehensive testing needs to be done and complete evaluations of all who are ill, including my son.

Lois Hardie March 27, 1998

Lois Hardie

3

Prepared Statement of Douglas E. Dembling, Associate Chief Officer for Program Coordination, Office of Public Health and Environmental Hazards, Veterans Health Administration, U.S. Department of Veterans Affairs

Good morning, Mr. Chairman, Ranking Member and Committee Members. Thank you for this opportunity to discuss the work of the Department of Veterans Affairs (VA) in studying the illnesses of Gulf War Veterans. I am accompanied today by Victoria Anne Cassano, MD, MPH, Acting Chief Consultant, Environmental Health Strategic Heathcare Group, Office of Public Health and Environmental Hazards, and David Barrans, Deputy Assistant General Counsel.

You have asked us to comment on VA's statements of work with the National Academy of Sciences' (NAS) Institute of Medicine (IOM) concerning Gulf War Veterans health issues and research. Specifically, you asked us to address issues raised about the utilization and consideration of animal studies by VA's Research Advisory Committee (RAC) on Gulf War Veterans' Illnesses. My testimony will provide background information about Gulf War Veterans, identify VA and IOM's research findings and our actions based upon this information, review VA and IOM agreements with regard to animal studies, describe VA's range of services and benefits for Gulf War Veterans, and outline Federally sponsored research related to Gulf War Veterans.

Background

The United States deployed nearly 700,000 military personnel to the Kuwaiti Theater of Operations (KTO) during Operations Desert Shield and Desert Storm (August 2, 1990, through July 31, 1991). Within months of their return, some Gulf War Veterans reported various symptoms and illnesses they believed were related to their service. Veterans, their families, and VA subsequently became concerned about the possible adverse health effects from various environmental exposures during Operations Desert Shield and Desert Storm. In response, in 1994, VA asked Congress for special authority, granted under the "Persian Gulf War Veterans' Act," Public Law 103–446, to provide compensation benefits to Gulf War Veterans who are chronically disabled by undiagnosed illnesses. That authority was later expanded to include certain illnesses of unknown cause. In 1995, VA implemented the "Persian Gulf War Veterans' Act" by adding 38 C.F.R. §3.317, which defines qualifying Gulf War service, establishes the presumptive period for service connection, and denotes certain signs and symptoms that may be manifestations of such illnesses. These signs and symptoms include: fatigue, skin signs or symptoms including hair loss, headache, muscle pain, joint pain; as well as neurologic, respiratory and cardiac signs or symptoms, abnormal weight loss and menstrual disorders. In addition, three medically unexplained multisystem illnesses' namely, Chronic Fatigue Syndrome, Fibromyalgia and Irritable Bowel Syndrome, are currently recognized by both statute and regulation as "qualifying chronic disabilities" and thereby presumptively service connected based on Gulf War service.

Further, through the "Persian Gulf War Veterans Act 1998," Public Law 105–277, Congress authorized VA to compensate Gulf War Veterans for diagnosed or undiagnosed illnesses that are determined by VA to warrant a presumption of service connection based upon a positive association with exposure, as a result of Gulf War service, to a toxic agent, an environmental or wartime hazard, or a preventive medication or vaccine known or presumed to be associated with Gulf War service.

Of particular concern have been the illnesses that have eluded specific diagnosis. The latest VA study–Health of *U.S. Veterans 1991 Gulf War: A Follow-UP Survey in 10 Years* (published April 2009)–found that 25 percent more Gulf War Veterans reported suffering from unexplained multi-symptom illness than their Gulf War era military peers. *Although the majority of Gulf War Veterans seeking VA health care have had readily diagnosable health conditions, we remain very concerned about Veterans whose symptoms have not been diagnosed. VA continues to compensate and treat these conditions even without a clear diagnosis*.

VA and IOM Study Findings

As directed by Congress, VA has utilized IOM to evaluate potential associations between environmental hazards encountered during military deployment and specific health effects. The Agent Orange Act of 1991 (Public Law 102–4) directed VA to seek to enter into an agreement with NAS to review and summarize the scientific evidence concerning the association between exposure to herbicides used in support of military operations in Vietnam during the Vietnam Era and each disease suspected to be associated with such exposure. IOM's work has allowed VA to recognize approximately a dozen diseases as presumed to be connected to exposure to Agent Orange and other herbicides used during the Vietnam War, which allows Veterans who were in theater during the relevant period to be compensated for these conditions without having to prove their connection to service.

In response to increased health concerns among Veterans of the 1991 Gulf War, Congress passed the Persian Gulf War Veterans Act 1998 and again directed VA to enter into a similar agreement with NAS to review and evaluate the available scientific evidence regarding associations between illnesses and exposure to toxic agents, preventive medicines, vaccines, and environmental or wartime hazards associated with Gulf War service. This process has generated nine comprehensive IOM committee reports on a wide variety of Gulf War health issues including assessments of long-term health effects from vaccines, depleted uranium, nerve agent antidotes, chemical warfare agents, pesticides, solvents, fuels, oil-well smoke, infectious diseases, deployment-related stress, traumatic brain injury, and Gulf War Veteran epidemiological studies.

IOM's scientific assessments are regularly sought to address a range of health care issues. Their independent stature and collection of internationally recognized scholars, scientists, and researchers uniquely positions them to provide expert, well-informed objective findings. As Congress directed, VA contracts with IOM to obtain independent and objective professional opinions concerning available scientific evidence. When VA contracts with IOM, we defer to their professional opinions con-

cerning methodology in order to maintain this independence. Their reports consider all available research, including both human and animal studies, to guide their findings about whether there is evidence of an association between exposure to a substance or hazard and the occurrence of an illness and whether there is a plausible biological mechanism or other evidence to support that connection. IOM bases their recommendations upon formal findings and scientific evidence, and their review process requires each IOM report to be reviewed internally and externally before release to VA and the public.

At the direction of Congress, VA, in 2002 chartered the Research Advisory Committee on Gulf War Veterans' Illnesses to advise the Secretary on the overall effectiveness of Federally-funded research to answer central questions on the nature, causes, and treatments of Gulf War Veterans' illnesses. The RAC published and released reports in 2004 and again in 2008.

After the 2008 RAC report was released, VA requested that IOM explain discrepancies between the RAC's report and findings contained in nine congressionally mandated IOM committee reports on Gulf War health issues completed since 1998. On January 23, 2009, VA received a response from Dr. Harvey Fineberg, President of the IOM, who noted:

> "... that the RAC and the IOM committee that prepared *Gulf War and Health Volume 4: Health Effects of Serving in the Gulf War* agree that there is a multisymptom illness in Gulf War veterans... Thus both committees recognize increased occurrence of symptoms in Gulf War veterans."
> "... The RAC attributes Gulf War illness to pyridostigmine bromide (PB) and pesticides, whereas the IOM committee did not link multisymptom illness to specific exposures."
> "While the RAC and IOM committees both recognize increased reporting of symptoms in Gulf War veterans, the IOM committees were not able to associate specific exposures with particular reported symptoms."

In February 2009, Secretary Shinseki asked IOM to invite representatives of the RAC to describe the report and the basis of its findings to IOM to ensure that the basis for any differences between these reports are communicated and considered by the latest IOM committee. RAC members addressed the IOM committee at an open meeting on April 14, 2009, in Washington, D.C. The possibility that the RAC report reached different conclusions due to access to more recent scientific studies cannot be ruled out. This possibility should be answered in the current IOM full literature review on Gulf War Veterans' health, which will be completed in February 2010.

VA and IOM Agreements Concerning Animal Studies

The major criticism by the RAC regarding the scientific process used by the IOM committees' analyses is that IOM did not use animal studies to draw conclusions about the strength of association between outcome and exposure. Congress requires VA to contract with IOM for external scientific review of the accumulating science relevant to long-term health consequences of service in the Gulf War. IOM is an independent, world class, scientific organization that has extensive internal expertise and uses the world's leading external scientists for these efforts. IOM puts all of their analyses through rigorous internal and external review, and VA relies on their opinion and continues to have confidence in the methods they use to conduct these assessments.

The RAC also has stated that VA inappropriately required IOM to not use animal studies in its various analyses. In reviewing all of the contracts for the nine IOM studies, there is no language in the Charges to the Committee or the Statements of Work that either requires or requests IOM to disregard animal studies. At the request of the House Veterans' Affairs Oversight Committee, VA has provided all of the Statements of Work for both the Gulf War IOM studies and the Agent Orange IOM studies.

The standard procedure for all VA-contracted IOM committee studies is to leave each independent committee completely in charge of deciding what research to include and how to interpret it. VA relies fully upon the IOM committee's independent scientific and medical expertise in determining how they will use both animal and human studies in their evaluations. VA's formal charge to each IOM committee specifically requests they use all relevant data as they see fit.

In a January 24, 2003, letter, the Secretary of Veterans Affairs specifically asked IOM to review animal studies on health effects from the chemical warfare agent Sarin. This request was based on the fact that several published studies seemed to indicate a health effect of low-dose exposure to Sarin in animals. This request pro-

duced the 2004 IOM committee study, *Gulf War & Health: Updated Literature Review of Sarin*. That IOM committee reviewed human studies as well as over 100 animal studies as cited in the report, including several studies mentioned in the Secretary's letter on the topic. The resulting VA Task Force report to the Secretary on this IOM report included the following analysis on this issue:

> "The Committee also reported that the newly published data from experimental animals that had precipitated the interest in an updated study of sarin health effects [mentioned in Secretary Principi's letter to IOM] which were designed to mimic the potential exposures in the Gulf War, were an important step in 'determining whether a biologically plausible mechanism could underlie any long-term effects of low exposure to chemical nerve agents, but more work needs to be conducted to elucidate potential mechanisms and clarify how the cellular effects are related to any clinical effects that might be seen.'
>
> "The IOM committee and staff provided a briefing to VA on August 19, 2004. At that briefing, the issue was raised (by VA staff) that the IOM emphasis on human studies might overlook health concerns revealed only in laboratory animal studies. The IOM committee chair acknowledged this concern, but also stated that the Committee did thoroughly review available animal studies, and concluded that taken together they failed to show consistent biological effects that could be plausibly tied to potential clinical effects in humans. He added that future animal studies might change that."

VA's most recent charge to IOM was issued on January 27, 2009, and included this guidance: " . . . the goal of this exercise is to help us understand health issues among Veterans of the 1991 Gulf War. In carrying out your new charge, VA expects that you will make appropriate use of all the literature your Committee considers to be relevant. That is, we expect that your committee exclusively will be the sole determiner on what literature must be reviewed to carry out your charge."

VA does not select IOM committee members, and each IOM committee is completely at liberty to select the approach it will use in evaluating Gulf War Veteran health issues and the scientific literature it will use. After execution of the committee charge, VA has no contact with committee members until a report is finalized. The entire process normally takes 15 to 18 months.

VA Services and Benefits

Research is an important element of VA's support for Veterans, but by turning information into action, VA directly improves the care of America's heroes. VA trains its providers to prepare to respond to the specific health care needs of all Veterans, including Gulf War Veterans with difficult-to-diagnose illnesses. For Gulf War Veterans, VA developed a Clinical Practice Guideline on post-combat deployment health and dealing with diagnosis of unexplained pain and fatigue. Also, VA has three War Related Illness and Injury Study Centers (WRIISCs) to provide specialized health care for combat Veterans from all deployments who experience difficult to diagnose or undiagnosed but disabling illnesses. Starting in 2002, the WRIISCs began serving as referral centers for Veterans with undiagnosed or difficult to diagnose complaints. Veterans referred to the WRIISCs are provided with a complete exposure assessment, outpatient or inpatient evaluation (including advanced neurological evaluations), and a detailed treatment plan, which is provided to the Veterans' VA primary care providers. Based on lessons learned from the Gulf War, VA realizes that concerns about unexplained illnesses could also emerge after Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF) deployments, and we are building our understanding of such illnesses.

Following the Gulf War, VA developed the Veterans Health Initiative (VHI) Independent Study Guides for health care providers as one of many options to provide tailored care and support of Veterans. This Study Guide was principally designed for the clinical care of Veterans of that era, but has proven highly relevant for treating OEF/OIF Veterans since many of the hazardous deployment-related exposures are likely to be the same. VA developed other Independent Study Guides for health care providers to deliver appropriate care to returning Veterans from Iraq and Afghanistan that cover topics such as gender and health care, infectious diseases of Southwest Asia, military sexual trauma, and health effects from chemical, biological and radiological weapons. Study Guides on post-traumatic stress disorder and TBI were also developed and made available for primary care physicians to increase understanding and awareness of these conditions. VHIs are currently undergoing a comprehensive update which will both include the latest information and make them more accessible and modifiable than in the past. However, VHIs are only one

resource for providers. Every VA medical center is required to have an environmental health clinician available to discuss any concerns Veterans or providers may have regarding combat theater exposures. VA distributes similar information to providers through newsletters, brochures, conference calls and the WRIISCs to educate providers to the unique needs of combat Veterans.

Federally Sponsored Research

VA takes the illnesses of Gulf War Veterans very seriously and has established a robust research program to study these illnesses. VA has spent over $20 million in support of research on Gulf War Veterans' illnesses in both fiscal years (FY) 2007 and 2008. VA prepares an Annual Report to Congress that describes Federally sponsored research on Gulf War Veterans' Illnesses, and has done so every year since 1997. In the 2007 report, VA provided updated information on 19 research topics in five major research areas and a complete project listing by research focus area. The research areas include: brain and nervous system function, environmental toxicology, immune function, reproductive health, and symptoms and general health status. The 2007 report noted that between FY 1992 and FY 2007, VA, DoD, and the Department of Health and Human Services (HHS) funded 345 distinct projects related to health problems affecting Gulf War Veterans. Funding for this research on the health care needs of Gulf War Veterans has totaled nearly $350 million over this period of time. These projects varied from small pilot studies to large-scale epidemiological surveys. Nine projects were funded through the Gulf War Veterans' Illnesses Research Program and three were funded through the Peer Reviewed Medical Research Program. Both programs are managed by the Congressionally Directed Medical Research Program at DoD. VA funded two new projects in FY 2007, with one focused on Environmental Toxicology and the other on Symptoms and General Health.

Conclusion

VA Secretaries have made full use of IOM Committee reports in determining whether new presumptive service connections are warranted, as provided for in the statutes that underlie this process.

Mr. Chairman, Congress has directed VA to continue to utilize IOM's independent evaluations of research when making determinations about Gulf War Veterans' illnesses. IOM is a nationally recognized authority in analyzing clinical research and we rely on their ability to provide sound assessments.

Secretary Shinseki recognizes that this well established process takes time. He has therefore, asked VA staff to review this approach and determine if there are additional ways to uncover the data necessary to determine a connection between exposures in military service and specific health outcomes.

Thank you again for the opportunity to testify. My colleagues and I are prepared to address any questions you or the other Committee Members might have.

Statement of Joel Kupersmith, M.D., Chief Research and Development Officer, Office of Research and Development, Veterans Health Administration, U.S. Department of Veterans Affairs

Thank you for the invitation to discuss the Department of Veterans Affairs' (VA) research and development program, and specifically its work on Gulf War Veterans' Illness. I appreciate the opportunity to discuss the vital role VA research has in ensuring the health and well-being of our Nation's Veterans.

My testimony will provide an overview of VA's research programs, describe our process for allocating funding based on scientific merit, report on our current allocation of funds for Gulf War Veterans' Illness research, and describe some of the current challenges and considerations associated with the science involved in this field of study.

Overview of VA Research

For more than 80 years, VA's Office of Research and Development (ORD) has been improving the lives of Veterans and all Americans through health care discovery and innovation. Because more than 70 percent of VA researchers are also clinicians who provide direct patient care, VA is uniquely positioned to move scientific discovery from investigators' laboratories to patient care. In turn, VA clinician-investigators identify new research questions for the laboratory at the patient's bedside,

making the research program one of VA's most effective tools to improve the care of Veterans. Our fundamental goals are to address the needs of the entire Veteran population from the young recruit who returns from combat with injuries to the aging Veteran, and to use research findings proactively to benefit the future Veteran. Data generated by VA researchers are used not only in current projects but also form the foundation for future projects as well.

VA research is an intramural program that is also fully integrated with the larger biomedical research community through VA's academic affiliations and collaborations with other organizations. VA scientists partner with colleagues and foster dynamic collaborations with other Federal agencies, academic medical centers, nonprofit organizations and private industry nationwide, further expanding the reach and scope of VA research. This is often a channel for new and emerging technologies to be introduced into VA; as devices or equipment are approved by the Food and Drug Administration, VA researchers are among the first to bring them into the mainstream clinical environment, while teaching others how to use them.

While VA research is principally focused on benefiting current and future Veterans, it also impacts Veteran families and caregivers, VA health care providers, Veterans Service Organizations, other components of the Federal research establishment, academic health centers, and practitioners of health care across the country. VA research is a valuable investment with remarkable and lasting returns.

Merit Review Process

VA ensures the best research programs receive funding and support through its merit review process. A VA Office of Research and Development (ORD) program manager with specific subject matter expertise in the proposal's field reviews each submission and refers it to a Peer Review Committee for evaluation. This Committee is composed of highly qualified and senior scientists with extensive backgrounds without conflicts of interest with the proposals they review. Each Member critiques and scores the proposal; funding selections are made based upon this review. If a research proposal is not selected, the Committee's critique is provided to the researcher so that he or she can develop a better proposal for the future.

Additionally, VA's Cooperative Studies Program (CSP) within ORD supports research that will be ongoing for several years and involve multiple VA medical centers and patients. To apply for CSP support, study proponents develop a letter of intent; if this letter describes a proposal with strong scientific and clinical significance, the letter is then reviewed by a CSP Study planning group and the five Coordinating Centers that would participate in the research. This group and the Coordinating Centers work with the study proponent to further refine the project and address logistical and scientific issues. A separate reviewing body then considers the proposal to ensure all potential concerns are fully addressed before the study begins.

All studies funded by ORD that involve patients receive the highest level of scrutiny to ensure the safety of the patient and the most certainty that the study will contribute to better health care for Veterans.

Current Allocation of Funds for Gulf War Veterans' Illness Research

During Fiscal Year (FY) 2008, VA allocated more than $20 million for research related to Gulf War Veteran's illnesses. This research supports a range of programs and clinical areas, including research into the prevalence of brain cancer among Gulf War Veterans, the prevalence of multiple sclerosis in Gulf War Veterans, and a $15 million per year contract involving the Dallas VA Medical Center and the University of Texas Southwestern Medical Center (UTSW) to support Gulf War research. The UTSW research is investigating multi-symptom illnesses among Gulf War Veterans and the contract is renewable at VA's discretion on a year-to-year basis until September 30, 2011.

VA-funded epidemiological studies have proven instrumental in identifying the range of chronic symptoms and health problems reported by Gulf War Veterans. This research has found that these symptoms occurred at rates that exceed non-deployed era Veterans and that these symptoms persist. The most common symptoms include impaired cognition, attention, and memory; persistent headaches; diarrhea and gastrointestinal problems; skin rashes; extreme muscle weakness and fatigue; joint pain; and sleep disturbances. VA continues to monitor this population of Veterans for changes in mortality rates and incidence of cancers. In addition to these studies of unexplained symptoms, VA has funded investigations to assess the prevalence of other diseases, such as cancer, amyotrophic lateral sclerosis (ALS), and multiple sclerosis in Gulf War Veterans, since there is some evidence that these diseases may also occur at elevated rates in this population.

In October 2002, April 2004, and March 2005, VA issued a Request for Applications (RFA) to solicit new research projects focused on the long-term health effects of deployment in the Gulf War, the health effects of specific military occupational and environmental exposures, improvements in evaluation, diagnosis and treatment of Gulf War Veterans' illnesses, prevalence of neurological disorders such as ALS and multiple sclerosis in Gulf War Veterans, and changes in the autonomic nervous system or immune system that may be associated with, or involved in the persistence of, unexplained symptoms or illnesses reported by Gulf War Veterans. VA recently announced a fourth RFA in May 2009 to specifically solicit proposals to study new treatments for ill Gulf War Veterans, including testing treatments that have previously been used for chronic fatigue syndrome and fibromyalgia, two conditions in the VA and general populations with similarities to Gulf War Veterans' illnesses.

VA continues to support Gulf War Veterans research more broadly, and over the last 15 years, VA has spent almost $130 million on research directly related to Gulf War Veterans. These funds do not include the VA-funded research that may be related to health care concerns of Gulf War Veterans (i.e., ALS, multiple sclerosis, or cancer) but are not solely focused on the Gulf War Veteran population. The Departments of Defense and Health and Human Services have spent more than $235 million over the same time period, for a total of almost $365 million from the Federal Government. VA is committed to building on what we have spent and to expand the foundation of available data to find relief for current illnesses while planning for the future. For example, VA is directing research into genomic studies, using state-of-the-art imaging techniques and correlation of tests of brain function, delineation of biomarkers, treatment trials and determinations of autonomic and motor function.

Scientific Challenges and Considerations

VA recognizes there are challenges to establishing scientific bases for clinical determinations about medical conditions associated with military combat. Necessary data are sometimes unavailable, control groups can be difficult to establish, participants may not be easily identified, and the sheer number of potential factors or variables renders a definitive conclusion elusive. However, our charge is to learn as much as we possibly can about those conditions, no matter the obstacles.

Another challenge is a perception by some Veterans that research data will be used to make determinations regarding VA benefits. As an assurance to Veterans, research data from participants has not been used by VA to affect benefits and ORD supports and enforces that policy. Similarly, VA researchers must also consider protections established by law, regulation and policy concerning patient confidentiality. Patient confidentiality is of utmost importance to VA and we take extraordinary steps to protect our Veterans. The Privacy Act and the Health Insurance Portability and Accountability Act 1996 (HIPAA) restrict how research data may be used. Patients understand that information they provide to a researcher is personal and potentially identifiable, and VA researchers are required to clearly explain this to research participants.

Even very personal information, such as a research participant's genetic structure, can be protected, and Veterans are often enthusiastic about participating in this type of research. For example, VA research into genomic medicine has included questions asking participants about their feelings about this type of investigation. More than 70 percent of Veterans surveyed reported they would participate in genomic research; more than 80 percent of Veterans reported believing that participation in this research would help other Veterans; and more than 85 percent reported being curious about the influence of their genes on their health. This support for VA's research program provides VA with critical data and insight, and in turn holds great potential for supporting the care and well-being of all Veterans, including Gulf War Veterans.

Conclusion

In conclusion, VA remains committed to funding scientifically meritorious research projects that improve our understanding of Gulf War Veterans illnesses and enhance our ability to diagnose and treat ill Gulf War Veterans. Moreover, the knowledge we gain from these efforts may improve our ability to prevent and treat illnesses affecting participants of current and future deployments. Your support of VA's research programs is greatly appreciated and I look forward to your questions.

Statement of Major Denise Nichols, RN, MSN, USAFR (Ret.),
Vice Chair, National Vietnam and Gulf War Veterans Coalition

The Implication of the USDVA Limited Scope of Gulf War Illness Research:

The implication to the veterans of the Gulf War 1 (Operation Desert Storm) to limited scope of Gulf War illness has mainly been to affect us in the care and claim approval.

When research for one of many examples on Animal studies to not be accepted or ruled out to be reviewed it directly affects the veterans in their claims being approved as has occurred now for 18 years and has caused many to have died without having received the claim approval leaving their survivors without help. They have died feeling abandonment by their own government that they so proudly served. The veterans who live with the chronic deteriorating illnesses have no relief financially and have lost totally their standard of living. They have become demoralized and depressed due to those circumstances.

They struggle daily desperately holding on to their family or job even when they are significantly disabled. Job hoping has occurred in the medical people that have tried to stay employed because they want to avoid detection of not being able to perform as they should. This has occurred in many fields of employment. Those that turn to truck driving have ended up having to have a wife or companion travel with them to deal with the disorientation and potential safety hazards they are experiencing directly connected to their health changes from the war. Those that try the post office cannot handle a walking route or their autonomic nervous system dysfunction cannot handle the varying temperatures. These are just a few examples of the many I have from dealing directly with the veterans.

I will also emphasis to you the safety factor problem that can indirectly impact on loss of innocent civilians' lives due to this denial. I have examples that I could detail to you in a longer testimony.

The worse case is unemployed trying to get Social Security to barely sustain themselves much less their family. The stresses upon their spouses, children, and extended family are causing even more devastating impacts on the social economic fabric of the nation that veterans form the backbone to that strength historically.

Many have ended up homeless or finding a way to end their lives.

The health care they receive is minimal. They are being turned off as we say in medicine because the answers, diagnostic protocols, and treatment modalities are not there or have been considered fringe medicine. They are turned out to Psychology Departments that know this is not psychiatric! They get labeled psychosomatic or personality disorders in order to turf them out medically and to avoid claim approval. To limit time involvement, cost, and physicians retraining. This is a huge disservice that is leaving a huge black mark in our society and creates distrust in their government to grow within the veteran, their families, and extend generationally.

I want to emphasis this is not a cultural sensitivity issue but a lack of training in physicians. It is a lack of communication. It is a lack of utilize the research and translating it to actual practice that has been purposefully blocked by administration and institutional denial, indifference, ineffective law enforcement, oversight, and prosecution for failures.

It creates a moral and ethically dilemma for the health care providers within the VA that know this is a physical condition that they are being blocked from acknowledging to their patients. Many avoid or limit time with Desert Storm veterans because of that. I have had a primary care provider be in tears with me because she is so frustrated and then to tell me her hands are tied. I have had that same primary care provider that knows I was a highly educated and skilled nurse and that when I brought her research articles from a peer reviewed research journal with the names and contact information of the authors and ask that she read it and start testing and treatment as recommend by these doctor researchers and to start saving our lives ended up saying I am sorry I can't and would you like a referral to psychology. Total inappropriate response!

That is when I gave up on the VA, I would rather not have the stress of dealing with that manner of medicine and go without anything at all than have to do battle at that level when I am also battling for changes as I called it at the head of the snake for myself and all veterans of the Gulf War, who after all were and I feel still are my patients. I tried and still do try at lower levels of the VA but it is apparent and they have told me it is not because they want to be that way but because their hands are tied!

So I concentrate at the top as I do with you to get clear policy from the administration and the legislators to govern and change the total VA in regards to the Gulf

War veterans. I am part of the Gulf War veterans that became advocates/leaders/ the loud squealers for our fellow veterans since our return from the war. Even though many of us are ill, the indignity and inhumane denial we and all of our comrades have endured fuel us to keep going. Our care, health, and economic survival (claims) has been affected by the Restrictions/policy directives on Gulf War Illness Research placed on the IOM by the VA Department, the Secretary of the VA in the past 18 years and by the administration. We have also suffered by the lack of completely unified Senate and House VA Committee hearings in a consistent and timely manner to have through updates, status reports, oversight and investigations on Research, Claims, and Health Care for Gulf War Veterans.

That is why I have been since January advocating Joint Hearings on the Senate and House VA Committee on Gulf War Illness the information has become disjointed, unconnected, not focused. And most of all parties are not being heard, most of all the veterans both the advocates that have been here since 1992 and the veterans themselves. WE have suggestions for change, we have horrifying examples that you need to hear. WE have experts that served in key positions during the war that have still not been heard, they need protection to come forward. We have retaliation that has occurred that you need to hear and address!

WE need to have these hearings on a regular ongoing basis until all the problems are corrected. WE need new laws introduced and enacted and enforcement of all laws for the Desert Storm Veterans.

We need truth, accountability, clear policy from every level of government, we need change now it is past due. WE need a cleaning out from government of those who were involved in this denial, delay, and obstruction and interference with the truth. We need people prosecuted in order to really affect change now and in the future. That is the only way that we will overcome the historical legacy of the atomic veterans, the test veterans, the Agent Orange Veterans, and us the Desert Storm Veterans of Gulf War 1. Each generation of veterans has said NEVER AGAIN! WE have tried to make those words real and mean something but without you our elected officials on the hill and the President taking that message to heart and making it happen we are destined to repeat history errors again forever.

What the Veterans of Desert Storm Say to Have they been adequately served? The answers come fast and frequently and they include: No, the doctors at the VA don't even review the findings of physicals and tests received if we go to one of the funded research studies. No, the VA doctors still say it is stress either verbally or in non verbal means. No, the VA does not even cooperate with the Researchers that have funded studies to notify Gulf War veterans either thru posters or flyers that are being offered by the researchers. No, and in their allotted 15 minutes for an appointment they do not even have adequate time to go thru all my past problems and my current complaints, I always feel rushed.

No, the doctors do not seem to know about research findings that back up our complaints. No, I asked to be put on the Gulf War Registry and they had no idea what I was talking about. No, the doctors do not even know some of the breaking treatments in Chronic Fatigue, Irritable bowel syndrome, or fibromyalgia. No and I feel they don't like to educate their patients about their own clinical tests and findings. No, I ask them if they have had any training at all into Gulf War illness or related illnesses and they said no. They don't want to spend much time with us. No and I don't care if they are not military doctors or prior experience I just wish they would know more about the related conditions, they seem completely uninformed. No, and when I went to VA hospital I felt totally lost and there was no one to help guide me thru this mess. No and the clinic doctors told me they don't know what to do for me and want me to drive 150 miles to the VA hospital. No, all they seem to want to do is put us on pschy. drugs and not truly look into our bodies! No and I had a heart attack before Xmas and I am glad I went to a civilian hospital at least I am alive now. No and what is this about a War Related Illness Center how do I get there my doctor says he cannot help me get there!

No, the situation has not changed one bit since I went to them in 1994. No, and I still am getting denied on my claim or my claim is lost or they are stressing me out asking for more documentation I do not have. No and I got Social Security help more rapidly. No and they can't seem to find my records. No and they keep wanting to push my claim as PTSD as the priority, I guess I will take that because my family is breaking down and I am losing everything. No and it seems we should never even try to claim Gulf War illness because they refuse to adjudicate those.

That is what we get in emails, chats, phone calls every day as a Gulf War veteran and advocate! Those of us that are Gulf War veteran advocates have manned our own suicide calls from across the Nation; thank god they finally heard us with the

new OIF/OEF veterans and finally set up the hot line. Those of us who stepped forward to get answers and help not just for ourselves and others feel we are still in the war 18 years later. We wonder when the VA will ever do the right thing. Why won't the VA listen to us when we try to be constructive and help with the solutions?

What the Veterans and Advocates have asked:

Registries-Task Forces-Outside Civilian Agency Involvement—Independent Oversight

WE have asked for Death registries so that veterans, family Members, doctors, and researchers truly can see transparently what is happening. We have asked for a Diagnosed illnesses registry to serve the same purpose. WE have asked for local, state, and regional Desert Storm Veteran Illness Task Forces to involve the doctors, the veterans, and others so these issues can be addressed from the bottom up and top down. WE have asked that CDC, Cancer Association, Heart Association, and other associations be involved in getting data and evaluate if the occurrences is above the normal. WE ask for some independent oversight.

Referral Centers—Centers of Excellence—Integrative Research to Clinical Practice Centers

WE have asked for Referral centers and Centers of Excellence and Integrative Research/Clinical Practice sites be set up with major medical universities that have done some of the positive Gulf War illness research.

Training of Doctors by outside Experts in Environmental Health for VA Physicians and for the VA to Hire Environmental Health Experts or Experts in CFS or Fee Basis to Use outside Experts

We have asked for the offers made by Environmental Physicians, Physicians from the American Academy of Advancement in Medicine, Physicians that see and treat civilians with CFIDS/Fibromyalgia to train VA physicians to be accepted. We have asked that these type doctors be recruited by VA even on part time basis to be able to see us and treat us at the VA. All have been turned down.

TO HAVE GULF WAR VETERANS WHO ARE ILL AND HAVE BEEN ADVOCATES NATIONALLY TO BE INVOLVED AND HEARD FULLY

WE have asked to be involved in the process to make needed change. We have shown our willingness even if patients to take an active role in making a difference.

I myself made an extensive presentation to the National Academy of Science and IOM years ago laying out 26 specific suggestions that would help, it was all like talking to the three monkey syndrome.

I have been here every step of the way every hearing on the hill, every meeting of the PAC GWI, PSOB, many of the DoD OSI GWI townhall meeting, almost all the VA's RAC GWI meeting, many of the Gulf War Veterans Advisory Committees, NAS–IOM meetings, I worked closely with the government Oversight Subcommittee that held 3 years of hearings, I worked going door to door briefing the Members on the hill, and encouraging cosponsorship of each of the Gulf War veterans bills, I have submitted my resume for each advisory Committee that was formed, I have testified, I have brought other Gulf War veterans and their family Members forward, I have brought researchers and doctors forward, I have done outreach to not only veterans, family Members, doctors, but also researchers. I have gone to medical meetings across the country to meet doctors and researchers and interact with them. I did this not as a glory purpose but to do all I could have since I was a nurse officer and holding an MSN. I did it to try and work closely to resolve the problem but as most of us that have participated a bit or more actively we have been not welcomed. And many other Gulf War Veterans throughout the Nation have been involved the past 19 years that could be well utilized at the Dept. of Veterans Affairs.

Current Situation

Seems like it continues to be a chain of survivors holding on to each other without a lot of support. So my answer like so many of the other desert storm veterans is NO we have yet to truly pick up that stone they always said in so many testimonies that they would not leave unturned. AS I told Dr Joseph years ago during a vote break in one Committee and he got rather upset. AS I said at one of the first hear-

ings (Senator Reigle's) we the Desert Storm veterans are a family and a community we may have served different services and different locations in theater but we have had to become that family and community. We wonder where is the DoD and VA still after 18 years and where are the Commanders that are suppose to take care of their troops in all of this?

WE are frustrated and have developed PTSD because of this treatment. WE are tired of being in the studies and outside lab results to have it tossed aside and not even considered. WE are upset that some of the doctors, researchers, and officers that had information and shared it, that stood up for us have been paid in retaliation by attacks on their careers. WE took oaths as we entered the service or reenlisted and we are wondering— have others forgotten theirs? Have you forgotten to take care of your troops? Have you left us on the field of battle? WE are gathering in our bunkers and sending radio messages for evacuation and aid and it seems like the communications still are not being received.

OUTSIDE THE BOX THINKING—INNOVATIVE

Maybe we should think outside the box and call in civilian support as they do with the CRAF and mobilize civilian medical and have reactivation to recall us into our units, do a recall of who is sick, dead, triage, and start providing care to save lives. The former military nurses and doctors, and all allied medical health care providers that are ill will help in this process if given the resources, etc.

WE expect an all out Manhattan project with Combined expertise (Task forces of all related expertise) to be involved in the research effort to get answers and to make the transition fast for any findings to be deployed to the clinical setting. Any research done must have a plan to disseminate the findings, educate on the findings, means to apply it clinically in practice in an ASAP method lay out in advance of approval of funding. This isn't just for the Gulf War veterans 1990–91 but also for national security to learn how to diagnosis, test, and treat if this occurs again. It will also most probably help a large part of the civilian population that suffers from CFIDS, ME, Fibromyalgia that is costing this country greatly in economic impact in so many ways. If we can do it for weapon production we can do it in military medicine! If we don't the cost is much greater. Morally and Ethically we must.

Medicine is in a different place and different breaking research occurs faster than in the 70-1980s when we had the Agent Orange Situation. Let us reflect on the history that has been positive in advancements made in war time and in NASA advances that have benefited not just the military but civilians. One example is the rapid helicopter transport in Vietnam that is now commonplace in civilian life. The rapid treatment of shock that has transformed medicine. So many examples. I ask you here in Congress and in the administration to take the lead and make a difference, it has been 18 years! I ask VA to reexamine itself and make corrections immediately. I ask the DoD to acknowledge they handled this poorly. I ask the President to hear us and make a clear policy statement that leads us to a Yes WE CAN and YES WE WILL.

MATERIAL SUBMITTED FOR THE RECORD

Committee on Veterans' Affairs
Subcommittee on Oversight and Investigations
Washington, DC.
August 12, 2009

Lynn Goldman, M.D., MPH
Committee on Gulf War and Health
Institute of Medicine, The National Academies
500 Fifth Street, NW
Washington, DC 20001

Dear Dr. Goldman:

Thank you for your testimony at the U.S. House of Representatives Committee on Veterans' Affairs Subcommittee on Oversight and Investigations hearing that took place on July 30, 2009 on "The Implications of U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research."

Please provide answers to the following questions by Wednesday, September 16, 2009, to Todd Chambers, Legislative Assistant to the Subcommittee on Oversight and Investigations.

1. What criteria are used by the IOM in determining whether to evaluate and incorporate human or animal studies in your reports on Gulf War Illness?
2. Dr. Steele provided in her written testimony a list of categories of research evidence relevant to the health of Gulf War Veterans and indicated whether these categories were included in the IOM reports or the RAC reports. A copy of this list is provided for your review. Please explain why those categories were not included in the IOM reports?
3. Has the IOM done an evaluation on studies relating to chronic obstructive pulmonary disease (COPD), and what triggers might worsen these conditions? What type of diseases associated with service in the Persian Gulf is the IOM currently looking at, and when will the next report be issued?

Thank you again for taking the time to answer these questions. The Committee looks forward to receiving your answers. If you have any questions concerning these questions, please contact Subcommittee on Oversight and Investigations Majority Staff Director, Martin Herbert, at (202) 225–3569 or the Subcommittee Minority Staff Director, Arthur Wu, at (202) 225–3527.

Sincerely,

Harry E. Mitchell
Chairman

David P. Roe
Ranking Republican Member

MH/tc

Institute of Medicine of the National Academies
Washington, DC.
October 13, 2009

Representative Harry E. Mitchell
Representative David P. Roe
Subcommittee on Oversight and Investigations
Committee on Veterans' Affairs
One Hundred Eleventh Congress
335 Cannon House Office Building
Washington, DC 20515

Dear Representatives Mitchell and Roe,

Thank you for the opportunity to clarify the statements I made in my testimony to your Subcommittee at the hearing on July 30, 2009. I hope that my answers to your questions will finally rectify the inaccurate information that has been disseminated about the Institute of Medicine Gulf War and Health reports. The answers to the questions are below and in the attachments.

1. **What criteria are used by the IOM in determining whether to evaluate and incorporate human or animal studies in your reports on Gulf War Illness?**

First, the IOM reports are on Gulf War and Health. As mandated by Public Laws 105–369 and 105–277, these IOM committees were tasked with assessing the sci-

entific literature regarding all potential health effects that might be associated with chemical and biological agents present in the Gulf War. While these assessments encompassed undiagnosed illnesses, including illness that now is commonly called Gulf War Illness, they were not specifically focused on such conditions.

Second, the criteria used by the IOM Gulf War and Health committees in assessing the literature are spelled out in detail in each report as follows:

- In Volume 1, *Depleted Uranium, Sarin, Pyridostigmine Bromide, and Vaccines*, these criteria are explained in Chapter 3, "Methodology". This chapter describes the types of studies that the Committee considered, including animal and other nonhuman studies (pg 71), human studies (epidemiologic, pg 72; experimental studies, pg 76; and case reports and case series, pg 77). Review of animal studies relevant to the exposures was included in chapters 4 "Depleted Uranium", 5 "Sarin", and 6 "Pyridostigmine Bromide".
- In Volume 2, *Insecticides and Solvents*, these criteria are described in Chapter 2, "Identifying and Evaluating the Literature" and in Appendix C, Identifying the Literature, which describes the literatures search strategy and how the voluminous information was managed. Animal studies were used for making assessments of biologic plausibility in support of the human epidemiologic data and were reviewed in Chapters 3 "Insecticide Toxicology" and Chapter 4 "Solvent Toxicology".
- In Volume 3, *Fuels, Combustion Products and Propellants*, Chapter 2, "Considerations in Identifying and Evaluating the Literature" described the epidemiologic studies, inclusion criteria, considerations in assessing the strength of the evidence and the categories of association. Review of relevant animal studies was included in Chapter 4 "Uncombusted Fuels and Combustion Products: Background Information" and Chapter 9 "Hydrazines and nitric acid."
- Volume 4 *Health Effects of Serving in the Gulf War*, assessed human studies of the prevalence of health effects seen in Gulf War veterans, and not an assessment of health effects associated with any particular or general exposures, the criteria for studies is described in Chapter 3, Considerations in Identifying and Evaluating the Literature. The task for this Committee did not include the assessment of animal studies since the purpose of this report was specifically to assess studies of the prevalence of health outcomes in deployed and nondeployed Gulf War veterans.
- In Volume 5, *Infectious Disease*, the criteria for including animal and human studies are described in Chapter 2. "Methodology". Relevant animal studies are discussed in Chapter 5, "Levels of Association Between Select Diseases and Long-Term Adverse Health Outcomes".
- In Volume 6, *Physiologic, Psychologic, and Psychosocial Effects of Deployment-Related Stress*, criteria for inclusion of animal and human studies are given in Chapter 2, "Considerations in Identifying and Evaluating the Literature". Relevant animal studies are reviewed in Chapter 4, "The Stress Response".
- In Volume 7, *Long-Term Consequences of Traumatic Brain Injury*, the criteria for selection of human and animal studies are detailed in Chapter 4, "Considerations in Identifying and Evaluating the Literature". Animal studies are reviewed in Chapter 2, "Biology of Traumatic Brain Injury".

All documents identified from the literature searches, typically more than one thousand to tens of thousands of citations, are reviewed by the members of each committee. The literature searches are broad so that all relevant (and many nonrelevant) studies are identified. The types of literature include government reports, dissertations, published literature in peer reviewed journals, and what is commonly called the "gray literature" which includes newspaper articles, nonpeer reviewed journals and magazines, research grants, and other documents. The criteria for actually including a study in a particular Gulf War and Health report varied somewhat depending on each committee's task (for example, Volume 4 did not include animal studies), however, all the Committees used the same criteria in their consideration of human studies. Human studies fall into several categories including epidemiologic studies (cohort, cross-sectional, case reports, case series), clinical studies, occupational studies, and accidental exposures. Each of the Gulf War and Health reports separated human studies into 3 categories: primary, secondary, and other studies. For a study to be considered "primary" it needed to:

- demonstrate rigorous methods (for example, was published in a peer-reviewed journal) and include details of methods,
- have a control or reference group,
- have the statistical power to detect effects,

- include reasonable adjustments for confounders,
- include information regarding a persistent health outcome, and
- have a medical evaluation, conducted by a health professional, and use laboratory testing as appropriate.

The committee did not evaluate studies of acute trauma, rehabilitation, or transient illness (that is illness persisting for less than 6 months). Human studies reviewed by the committee that did not necessarily meet all the criteria of a primary study are considered secondary studies. Secondary studies are typically not as methodologically rigorous as primary studies and might present subclinical findings, that is, studies of altered functioning consistent with later development of a diagnosis but without clear predictive value. Other studies might be case-reports, treatment studies, etc., that contribute to the interpretation of primary and secondary studies, but which alone would not support conclusions.

As noted above in detail, animal studies were also considered in the Gulf War and Health reports (with the exception of Gulf War and Health Volume 4 as that was a study of prevalence of disease in deployed versus non-deployed forces). As stated in Volume 1 (pg 71–72):

> Studies of laboratory animals and other nonhuman systems are essential to understanding mechanisms of action, biologic plausibility, and providing information about possible health effects when experimental research in humans is not ethically or practically possible. Such studies permit a potentially toxic agent to be introduced under conditions controlled by the researcher—such as dose duration, and route of exposure—to probe health effects on many body systems. Nonhuman studies are also a valuable complement to human studies of genetic susceptibility. While nonhuman studies often focus on one agent at a time, they more easily enable the study of chemical mixtures and their potential interactions. Research on health effects of toxic substance includes animal studies that characterize absorption, distribution, metabolism, elimination, and excretion. Animal studies may examine acute (short-term) exposures or chronic (long-term) exposures. Animal research may focus on the mechanism of action (i.e., how the toxin exerts its deleterious effects at the cellular and molecular levels). Mechanism-of-action (or mechanistic) studies encompass a range of laboratory approaches with whole animals and in vitro systems using tissues or cells from humans or animals. Also, structure–activity relationships, in which comparisons are made between the molecular structure and chemical and physical properties of a potential toxin versus a known toxin, are an important source of hypotheses about mechanism of action. In carrying out its charge, the committee used animal and other nonhuman studies in several ways, particularly as a marker for health effects that might be important for humans. If an agent, for example, was absorbed and deposited in specific tissues or organs (e.g., uranium deposition in bone and kidney), the committee looked especially closely for possible abnormalities at these sites in human studies. One of the problems with animal studies, however, is the difficulty of finding animal models to study symptoms that relate to uniquely human attributes, such as cognition, purposive behavior, and the perception of pain. With the exception of fatigue, many symptoms reported by veterans (e.g., headache, muscle or joint pain) are difficult to study in standard neurotoxicological tests in animals. For its evaluation and categorization of the degree of association between each exposure and a human health effect, however, the committee only used evidence from human studies. Nevertheless, the committee did use nonhuman studies as the basis for judgments about biologic plausibility, which is one of the criteria for establishing causation.

Because of the varied nature of the numerous animal studies considered by the committee, ranging from standard toxicological studies used for government regulation of chemicals, to mechanistic studies of the action of a chemical on a particular organ or cell, the Gulf War and Health committees did not establish formal criteria for their reviews of animal studies. Nevertheless, each committee included at least one expert toxicologist (and in many cases, several toxicologists) who reviewed the animal/toxicity studies and these studies were discussed by the whole committee to determine their quality and inclusion in the reports. As with human studies, animal studies published in peer-reviewed scientific journal were preferred and given greater weight in coming to a conclusion regarding the association between an exposure and a given health effect in Gulf War veterans.

2. **Dr. Steele provided in her written testimony a list of categories of research evidence relevant to the health of Gulf War Veterans and indicated whether these categories were included in the IOM reports or the RAC reports. A copy of this list is provided for your review. Please explain why those categories were not included in the IOM reports?**

Dr. Steele appears to have misinterpreted the IOM Gulf War and Health reports. Her tables are inaccurate in the assessment of the types of evidence used by the IOM in establishing its finding with regards to the health of Gulf War veterans. It would not be possible to comprehensively correct the information that she provided to you, but on her first table (see attachment) I provide examples of the various types of evidence she lists to illustrate that such evidence is, contrary to her assertions, often cited in the IOM Gulf War and Health reports. I believe it is not only important to examine which studies were included but also the process for assessing the research in order to reach conclusions. As noted in the response to Question 1 above, the IOM committees have been careful to spell out in each report how they assessed the research evidence and how they used the evidence to reach their conclusions.

One important aspect of this process is carefully weighing the evidence. As you might expect, not all research evidence is of the same quality, even evidence published in peer-reviewed journals. Furthermore, even high quality studies many not be useful for determining an association between an exposure and a health effect; they may have been designed to answer other questions. To objectively weigh the evidence, all of the IOM Gulf War and Health committees have indicated which studies were considered to be primary, that is, which would be given the most weight based on quality and relevance. The IOM committees also have clearly identified secondary studies that may be supportive and can contribute to making judgments about the category of association for a particular exposure and health effect. Because this is an objective process, well-conducted studies that showed no association were given as much weight as well-conducted studies that did show an association. The committees also have tried to be extremely accurate in their descriptions of the studies cited in the reports as well as in the critiques of these studies. For example, when committees disagree with the conclusions reached by the study's authors, they try to carefully discuss the reasons for the different interpretations. In several cases, committee members have actually discussed studies with the authors to seek further clarification on study methods, populations, or results to assure that interpretations of studies are fair and accurate.

With regard to Dr. Steele's second table, she alleges that numerous studies were not evaluated by IOM committees which, in fact, were evaluated. I have indicated in the attachment where those studies were cited in the various Gulf War and Health reports. I should note that the IOM committees have also cited those reports for health effects other than multisymptom illness, for example, in discussions of chronic fatigue syndrome.

3. **Has the IOM done an evaluation on studies relating to chronic obstructive pulmonary disease (COPD), and what triggers might worsen these conditions? What type of diseases associated with service in the Persian Gulf is the IOM currently looking at, and when will the next report be issued?**

The IOM has not done a study that looks generally at COPD and its triggers in Gulf War veterans or in other populations. However, each of the Gulf War and Health reports has considered all health effects, including the respiratory effects, associated with exposures to the chemical and biological agents covered in that report. These effects would include COPD were such data available. Most notably, the Gulf War and Health Volume 3, Fuels, Combustion Products, and Propellants the committee examined a number of chronic respiratory conditions—asthma, chronic bronchitis, emphysema, and COPD.

Although the IOM and National Research Council reports have not carried out any other COPD specific reports, COPD has been evaluated in a number of studies, such as, the IOM Agent Orange reports, the 2004 report "Damp Indoor Spaces and Health," the 4 reports in NRC series "Research Priorities for Airborne Particulate Matter," the 1993 IOM report "Veterans at Risk: The Health Effects of Mustard Gas and Lewisite," the 2002 NRC report "Estimating the Public Health Benefits of Proposed Air Pollution Regulations," the 2000 NRC report "Waste Incineration and Public Health," the 1993 NRC report "Indoor Allergens: Assessing and Controlling Adverse Health Effects," the 2000 IOM report "Clearing the Air: Asthma and Indoor Air Exposures," and the 2008 NRC report "Estimating Mortality Risk Reduction and

Economic Benefits from Controlling Ozone Air Pollution." The IOM has also published two reports on the impact of tobacco use on respiratory health: the 2009 report "Combating Tobacco Use in Military and Veteran Populations" and "Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction." I would note that the scientific literature, including the 2004 report of the U.S. Surgeon General, indicates that approximately 80 percent of COPD is caused by smoking and most exacerbations of COPD occur as a result of a respiratory infection (Wedzicha JA and Donaldson GC. "Exacerbations of chronic obstructive pulmonary disease" Respir Care. 2003 Dec;48(12):1204–13; Soto FJ and Varkey B. "Evidence-based approach to acute exacerbations of COPD" Curr Opin Pulm Med. 2003 Mar;9(2):117–24).

The current Gulf War and Health committee: Health Effects of Serving in the Gulf War, Update 2009 will be looking at all health endpoints suggested by the literature, including multisymptom illness, chronic fatigue syndrome, cardiovascular disease, cancer, and the other health effects discussed in previous Gulf War and Health volumes. That committee's report is expected to be released in March of 2010.

Once again, thank you for the opportunity to assist the Committee on Veterans' Affairs Subcommittee on Oversight and Investigations in its efforts to provide support for the Gulf War veterans. If I can provide you with any further information, please do not hesitate to contact me or the IOM.

Sincerely,

Lynn Goldman, M.D., M.P.H.
For the Committee on Gulf War and Health

Attachment

Cc: Judith Salerno, IOM
Jim Jensen, NAS

ATTACHMENT

Table 1. Types of Evidence Used To Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report

	Was This Type of Evidence Considered in Report Findings?	
Categories of Research Evidence Relevant to the Health of Gulf War Veterans	***IOM Gulf War and Health Reports***	***2008 RAC Report***
Results of Peer-reviewed and Published Scientific Studies		
Studies of Gulf War veterans		
Studies that assessed prevalence of diagnosed medical and psychiatric conditions in Gulf War veterans	**YES**	**YES**
Studies that assessed prevalence of undiagnosed multisymptom illness in Gulf War veterans	~~(Limited)~~ **YES.** For example, in Vol 1, pgs 14, 246, 349–359 discuss the prevalence of Gulf War illness in veterans. In Vol 2, Appendix A discusses Gulf War illness and updates Vol 1. All such studies are discussed in Vol 4, Chapters 3 and 5 (pgs 202–213). These studies are also discussed in Vol 6, pages 251–254.	**YES**

Table 1. Types of Evidence Used To Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report—Continued

	Was This Type of Evidence Considered in Report Findings?	
Categories of Research Evidence Relevant to the Health of Gulf War Veterans	***IOM Gulf War and Health Reports***	***2008 RAC Report***
Studies that assessed associations between Gulf War exposures and diagnosed conditions in Gulf War veterans	~~(Limited)~~ **YES.** For example, in Vol 1, DU pgs 150, 157–158; sarin pgs 196–197; PB pgs 225–226, 245–250; vaccines pgs 285–293, 303–306. In Vol 2, associations between GW exposure and diagnosed conditions in GW vets are discussed in Chapter 4 on cancer and exposure to insecticides, Chapter 5 on cancer and exposure to solvents, Chapter 7 on neurologic effects and diseases, including peripheral neuropathy, following exposure to insecticides, and solvents; and in sections of Chapter 8 Reproductive and developmental effects and Chapter 9 additional health effects which includes aplastic anemia, cardiovascular effects, respiratory effects, hepatic effects, gastrointestinal effects, renal effects, skin conditions, and systematic rheumatic diseases. Vol 4, Chapter 4 discusses numerous specific diagnosed illnesses and what the individual study authors found with respect to possible exposures of GW veterans linked to those health effects, e.g., Nisenbaum et al. 2000, pg 75 and Haley and Kurt 1997, pg 72.	**YES**

Table 1. Types of Evidence Used To Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report—Continued

	Was This Type of Evidence Considered in Report Findings?	
Categories of Research Evidence Relevant to the Health of Gulf War Veterans	***IOM Gulf War and Health Reports***	***2008 RAC Report***
Studies that assessed associations between Gulf War exposures and undiagnosed multisymptom illness in Gulf War veterans	~~No~~ **YES.** For example, Vol 1 contains a discussion of unexplained illness in relation to specific GW exposures on pgs 13, 48, 50–51, 209, 303–306, 314, 350–359. Vol 2 discusses exposures and unexplained illness on pgs 355, 378 in a section on multisymptom illness on pgs 383–387. Vol 3 contains a section on multiple chemical sensitivity (pgs 325–331), unexplained illnesses, and possible exposures that might be responsible for this illness in GW veterans (pgs 328–329). Volume 4 discusses some of the exposures that researchers have identified as being associated with unexplained illness, e.g., Haley et al. 1997. In the sarin update, sarin exposures associated with unexplained illness are discussed on pgs 63, 65–67, 69, 78, 80, 82, 84, 86, 98, but the report does not make findings based on those associations as that was not in its statement of task.	**YES**
Studies of chemical exposures in other human populations		
Studies that assessed association of exposures with diagnosed diseases	**YES**	**YES**

Table 1. Types of Evidence Used To Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report—Continued

	Was This Type of Evidence Considered in Report Findings?	
Categories of Research Evidence Relevant to the Health of Gulf War Veterans	***IOM Gulf War and Health Reports***	***2008 RAC Report***
Studies that assessed association of exposures with undiagnosed symptomatic illness	~~No~~ **YES.** For example in Vol 1, the section on PB contains a lengthy review of studies on a variety of outcomes associated with PB based on clinical trials and epidemiologic studies in human populations other than GW vets. Many of these studies include symptoms indicative of undiagnosed symptomatic illness such as neuromuscular effects and behavior and cognitive function in elderly patients and those with myasthenia gravis. As occupational and accidental exposures to PB are unlikely there are no studies of these populations. The section on sarin reports many long term effects that are similar to undiagnosed symptomatic illness in victims of sarin poisoning events in Japan and in U.S. military volunteers prior to the GW. In Vol 2, the committee indicates on pg 515 that it was unable to identify any studies that examined the association between insecticide or solvent exposure in populations that had been exposure free for an interval and that presented long-term effects as being most likely to mimic the exposure of GW veterans. That committee was unable to identify any such studies. Vol 3 has a discussion of multiple chemical sensitivity, which is related to undiagnosed illness, in non-GW populations on pgs 329–331.	**YES**

Table 1. Types of Evidence Used To Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report—Continued

	Was This Type of Evidence Considered in Report Findings?	
Categories of Research Evidence Relevant to the Health of Gulf War Veterans	***IOM Gulf War and Health Reports***	***2008 RAC Report***
Studies of effects of chemical exposures in animal models		
Studies of biological and behavioral effects of exposures in animals	~~No.~~ **YES.** For example, animal studies are discussed in all GW&H volumes except 4, which was a prevalence study only. For example, for depleted uranium, animal studies are discussed in Vol. 1, pgs 95–106, for sarin, there is an entire section on animal studies on pgs 178–186, for pyridostigmine bromide, pgs 211–217, for vaccines, pgs 271–272, 275–280, 289–291, 296–299, and 308–309. In volume 2, there are two chapters on the toxicology, i.e., use of animal studies, of insecticides (pgs 39–69) and of solvents (pgs 82–95). In volume 3, animal studies are discussed on the following pages: 35–39, 43–49, and 351–359. Volume 6, Chapter 4 (pgs 49–66) is about the biology of the stress response including animal models.	**YES**
Studies of effects of combinations of exposures	~~No~~ **YES.** For example, in Vol 1, combinations of exposure are discussed on pgs 217–219 and 230. In Vol 2 on pgs 50, 56, 62, 69. In Vol 3, on pgs 43, 252. In Vol 4, Chapter 3 on the major cohort studies of the prevalence of health effects in GW veterans discusses all the exposure and combinations thereof that were associated with specific health outcomes.	**YES**

Table 1. Types of Evidence Used To Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report—Continued

	Was This Type of Evidence Considered in Report Findings?	
Categories of Research Evidence Relevant to the Health of Gulf War Veterans	***IOM Gulf War and Health Reports***	***2008 RAC Report***
Results of Other Federally-sponsored Gulf War Scientific Studies		
Findings provided in project reports from DoD-funded studies	~~No~~ **YES.** For example, among the DoD-funded studies cited in Vol 1 are: U.S. Army 1995 "Health and Environmental Consequences of Depleted Uranium Use in the U.S. Army"; USAEC Report UR–37 "The excretion of hexavalent uranium following intravenous administration. II. Studies on human studies." "Multiple animal studies for medical chemical defense program in soldier/patient decontamination and drug development on task 85–18: Conduct of pralidoxime chloride, atropine in citrate buffer and pyridostigmine bromide pharmacokinetic studies, and comparative evaluation of the efficacy of pyridostigmine plus atropine. Final report, June 1985–August 1988"; "Clinical Considerations in the Use of Pyridostigmine Bromide as Pretreatment for Nerve-Agent Exposure." Aberdeen Proving Ground, MD: Army Medical Research Institute of Chemical Defense. In the sarin update, examples of DoD-funded studies that are cited include: "Toxicity Studies on Agents GB and GD (Phase 2): 90–Day Subchronic Study of GB (Sarin, Type II) in CD–Rats."; "Toxicity Studies on Agents GB and GD (Phase 2): 90–Day Subchronic Study of GB (Sarin, Type I) in CD–Rats."; "Toxicity Studies on Agents GB and GD (Phase 2): Delayed Neuropathy Study of Sarin, Type II, in SPF White Leghorn Chickens." Throughout all the Gulf War and Health volumes, many DoD-funded studies that have been published in the peer-reviewed literature, particularly in the journal Military Medicine, are cited and have provided critical evidence for the committees' findings.	**YES**

Table 1. Types of Evidence Used To Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report—Continued

	Was This Type of Evidence Considered in Report Findings?	
Categories of Research Evidence Relevant to the Health of Gulf War Veterans	***IOM Gulf War and Health Reports***	***2008 RAC Report***
Findings presented at scientific conferences, RAC meetings	~~No~~ **LIMITED.** Although the Committee did review abstracts of presentations made at scientific conferences, these abstracts provided background information only and were not used in weighing the evidence on which the Committee based its conclusions. Such abstracts have not been peer-reviewed and the data they contain frequently undergo revision before being published; therefore, the committee considered such information to be preliminary only.	**YES**
Investigations, Reports on Exposures During the Gulf War		
Reports from Federal agencies (e.g. DoD, CIA) that documented or modeled types, levels, and patterns of Gulf War exposures (e.g. pesticides, oil fire smoke, nerve agents, depleted uranium)	~~No~~ **YES.** For example, in Vol 1, for depleted uranium, pgs 92–94; for sarin, pgs 172–174; for PB, pgs 208–209. In Vol 2, for insecticides, pgs 12–13, particularly the 2000 "Environmental Exposure Report-Chemical Agent Resistant Coating" and the 2001 "Environmental Exposure Report-Pesticides" from the Office of the Special Assistant for Gulf War Illnesses (OSAGWI). Volume 4, Chapter 2 is devoted to exposures in the Persian Gulf. This chapter contains an extensive review of the studies that used simulation to assess the potential magnitude of exposure to tent heaters, at the Khamisiyah demolition (including a detailed discussion of the CIA–DoD modeling), biologic monitoring for depleted uranium conducted by the VA with input from the DoD OSAGWI, and oil-well fire smoke monitoring by the Army Environmental Hygiene Agency.	**YES**

Table 1. Types of Evidence Used To Establish Findings on the Health of Gulf War Veterans: Research Considered in IOM Gulf War Reports and the 2008 RAC Report—Continued

	Was This Type of Evidence Considered in Report Findings?	
Categories of Research Evidence Relevant to the Health of Gulf War Veterans	***IOM Gulf War and Health Reports***	***2008 RAC Report***
Reports from nongovernmental sources (e.g. RAND, Battelle) that investigated and/or modeled Gulf War exposures	~~No~~ **YES.** The RAND report "Review of the Scientific Literature as it Pertains to Gulf War Illness" is cited in Vol 4 on pgs 14. The RAND report "Pesticide Use During the Gulf War: A Survey of Gulf War Veterans" is cited in Vol 2, pg 12. In Vol 1, the 1999 RAND report "Military Use of Drugs Not Yet Approved by the FDA for CW/BW Defense" is discussed on pgs 207–208, 288, the 1999 RAND report "Depleted Uranium: A Review of the Scientific Literature as It Pertains to Gulf War Illnesses" is discussed on pgs 91 and 97. The 1994 Battelle report "Dosimetry of Large-Caliber Cartridges: Updated Dose Rate Calculations" is cited on pgs 92–93, and a 1981 Battelle "Histopathologic, Morphometric, and Physiologic Investigation of Lungs of Dogs Exposed to Uranium-Ore Dust" on pgs 99–100.	**YES**

Table 2. Excess Prevalence of Multisymptom Illness in Gulf War Veterans, Compared to Nondeployed Veterans: Studies Considered in IOM Gulf War Reports and the 2008 RAC Report

				Was This Finding Included in Report?	
Veteran Group Studied	**Study**	**Number of Gulf War Veterans**	**Excess Prevalence in Gulf War Veterans**	**IOM Gulf War and Health Reports**	**2008 RAC Report**
U.S. Air Force veterans	*Fukuda, 1998*	1,155	**30%**	~~No~~ **YES.** For example, in Vol 4, pgs 74, 96, 167; Vol 6, pg 252, 254	YES
U.K. male veterans	*Unwin, 1999*	4,428	**26%**	~~No~~ **YES.** For examples, in Vol 4, pg 57, 65–67, 81, 230; Vol 6, pg 176	**YES**
Kansas veterans	*Steele, 2000*	1,548	**26%**	~~No~~ **YES.** For example in Vol 4, pg 64, 89	**YES**
New England Army veterans	*Proctor, 2001*	180	**32%**	~~No~~ **YES.** For examples, in Vol 4, pgs 89–91, 163, 229; Vol 6, pg 255	**YES**

Table 2. Excess Prevalence of Multisymptom Illness in Gulf War Veterans, Compared to Nondeployed Veterans: Studies Considered in IOM Gulf War Reports and the 2008 RAC Report

				Was This Finding Included in Report?	
Veteran Group Studied	**Study**	**Number of Gulf War Veterans**	**Excess Prevalence in Gulf War Veterans**	**IOM Gulf War and Health Reports**	**2008 RAC Report**
U.K. female veterans	*Unwin, 2002*	226	**29%**	~~No~~ **YES.** For example, in Vol 4, pg 76	**YES**
U.S. national study, Phase III	*Blanchard, 2006*	1,035	**13%**	**YES**	**YES**
U.S. national longitudinal study	*Kang, 2007*	5,767	**25%**	**No** Cannot locate a Kang 2007 reference in the published literature or in the 2008 RAC report.	**YES**

Committee on Veterans' Affairs
Subcommittee on Oversight and Investigations
Washington, DC.
August 12, 2009

James H. Binns
Chairman
Research Advisory Committee on Gulf War Veterans' Illnesses
2398 E. Camelback Road, Suite 280
Phoenix, AZ 85016

Dear Mr. Binns:

Thank you for your testimony at the U.S. House of Representatives Committee on Veterans' Affairs Subcommittee on Oversight and Investigations hearing that took place on July 30, 2009 on "The Implications of U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research."

Please provide answers to the following questions by Wednesday, September 16, 2009, to Todd Chambers, Legislative Assistant to the Subcommittee on Oversight and Investigations.

1. Please cite the exact section of the U.S. Code you believe IOM and VA are violating when they are reporting on the Gulf War studies.
2. You state in your testimony that both the RAC and IOM Committees evaluate scientific studies relating to Gulf War Veterans and report on their findings. Has the RAC cross-referenced the body of work produced by the IOM against what the RAC utilized to determine if some of the same studies have been used by both organizations, and if so, what are those reports?

Thank you again for taking the time to answer these questions. The Committee looks forward to receiving your answers. If you have any questions concerning these questions, please contact Subcommittee on Oversight and Investigations Majority Staff Director, Martin Herbert, at (202) 225–3569 or the Subcommittee Minority Staff Director, Arthur Wu, at (202) 225–3527.

Sincerely,

Harry E. Mitchell
Chairman

David P. Roe
Ranking Republican Member

MH/tc

Phoenix, AZ
December 12, 2009

Hon. Harry E. Mitchell
Chairman, Subcommittee on Oversight and Investigations
Veterans' Affairs Committee
U.S. House of Representatives

Hon. David P. Roe
Ranking Member, Subcommittee on Oversight and Investigations
Veterans' Affairs Committee
U.S. House of Representatives

Dear Chairman Mitchell and Ranking Member Roe,

I am pleased to respond to the questions in your letter regarding my testimony at the July 30, 2009 hearing.

1. Please cite the exact section of the U.S. Code you believe IOM and VA are violating when they are reporting on the Gulf War studies.

Multiple sections have been violated:
38 U.S.C. Sec. 1117, note Sec. 1603(e) requires that: "For each agent, hazard, or medicine or vaccine and illness identified . . . [t]he National Academy of Sciences [IOM] shall determine . . .

> (A) whether a statistical association exists between exposure to the agent . . . and the illness . . . [and]
> (B) the increased risk of the illness *among human or animal populations* exposed to the agent . . ." [emphasis added]

38 U.S.C. Sec. 1118(b)(1)(B) requires that the Secretary of Veterans Affairs shall consider "the exposure *in humans or animals*" to an agent and "the occurrence of a diagnosed or undiagnosed illness *in humans or animals*." [emphasis added]
Yet, as acknowledged in the first IOM Gulf War and Health report: "For its evaluation and categorization of the degree of association between each exposure and a human health effect, however, *the [IOM] Committee only used evidence from human studies*." Gulf War and Health, Volume 1, p. 72. [emphasis added] This violation of the statute has been repeated in all subsequent reports, leaving animal studies (the vast majority of studies on toxic substances) out of consideration. The result is that the IOM reports have not found "sufficient evidence of an association."
38 U.S.C. Sec. 1117, note Sec. 1603(c) requires the National Academy of Sciences [IOM] to identify illnesses, "including diagnosed illnesses and undiagnosed illnesses," experienced by Armed Forces Members who served in the war.
Yet, the second IOM Gulf War report acknowledged that the IOM Committee was not charged with addressing "nonspecific illnesses that lack defined diagnoses . . . " Gulf War and Health Volume 2, p. 13. This violation has been repeated in other reports.
38 U.S.C. Sec. 1117, note Sec. 1605(1) defines toxic agents to include combinations of exposures ("whether through exposure singularly or in combination.")
Yet, the second IOM report also acknowledged that "exposure to multiple agents" was not within the Committee's charge. Gulf War and Health Volume 2, p. 13. This violation has been repeated in other reports.

2. You state in your testimony that both the RAC and IOM Committees evaluate scientific studies relating to Gulf War veterans and report on their findings. Has the RAC cross-referenced the body of work produced by the IOM against what the RAC utilized to determine if some of the same studies have been used by both organizations, and if so, what are those reports?

There is no cross-reference index. Examples of relevant studies not cited in IOM reports are given at pages 54–55 of the 2008 Research Advisory Committee report, *Gulf War Illness and the Health of Gulf War Veterans*. An equally important problem is that the IOM reports frequently mention studies, notably animal studies, and then fail to consider them in their conclusions.
For example, the Updated Literature Review of Sarin report (2004) was requested by former VA Secretary Principi expressly because of the publication of new animal studies showing long-term health effects of low-level Sarin exposure, and the report mentions these studies in the body of the report. However, when it arrives at its all-important conclusions, the report states that the Committee did not use animal data "as part of the weight of evidence to determine the likelihood that an exposure

to a specific agent might cause a long-term outcome." Updated Literature Review of Sarin (2004), p. 20.

These issues are discussed at greater length in the attached memorandum, which I am pleased to provide as part of my response and which includes the documents cited.

Respectfully submitted,

James Binns
Chairman
Research Advisory Committee on Gulf War Veterans Illnesses

[The attached memo and additional attachments will be retained in the Committee files.]

Committee on Veterans' Affairs
Subcommittee on Oversight and Investigations
Washington, DC.
August 12, 2009

Lea Steele, Ph.D.
Adjunct Associate Professor
Kansas State University School of Human Ecology
13520 Kiowa Road
Valley Falls, KS 66088

Dear Dr. Steele:

Thank you for your testimony at the U.S. House of Representatives Committee on Veterans' Affairs Subcommittee on Oversight and Investigations hearing that took place on July 30, 2009 on "The Implications of U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research."Please provide answers to the following questions by Wednesday, September 16, 2009, to Todd Chambers, Legislative Assistant to the Subcommittee on Oversight and Investigations.

1. Who was it that asked that you testify on why and how scientific findings of the Institute of Medicine (IOM)'s Gulf War and Health reports differ from those of the Research Advisory Committee on Gulf War Veterans' Illnesses? The title of the hearing was "The Implications of U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research." Since VA is also utilizing the information provided by the RAC, I would assume that you would be coming to discuss specifically how the RAC report was formulated, and not create animosity with the IOM.
2. You mention in your testimony that the RAC Committee had several Members of the scientific community who also served on the Institute of Medicine panels over the years. Were you one of those Members? If not, shouldn't we be hearing directly from one of them as to their concerns about the IOM reports? Are you recommending that Congress to disregard the IOM reports, and start from scratch?
3. In light of Dr. Goldman's testimony, do you still believe that critical animal studies were eliminated from the IOM report, and if so, could you provide for the record a detailed list of those studies?

Thank you again for taking the time to answer these questions. The Committee looks forward to receiving your answers. If you have any questions concerning these questions, please contact Subcommittee on Oversight and Investigations Majority Staff Director, Martin Herbert, at (202) 225–3569 or the Subcommittee Minority Staff Director, Arthur Wu, at (202) 225–3527.

Sincerely,

Harry E. Mitchell
Chairman

David P. Roe
Ranking Republican Member

MH/tc

MEMO

FROM: Lea Steele, Ph.D.
Kansas State University

TO: Chairman and Ranking Member, Subcommittee on Oversight and Investigations, U.S. House of Representatives Committee on Veterans Affairs

DATE: October 12, 2009

RE: Responses to questions posed in relation to testimony for the Subcommittee's July 30, 2009, hearing on Gulf War Illness Research

Thank you for your interest in the work of the Congressionally mandated Research Advisory Committee on Gulf War Veterans' Illnesses (RAC), and for inviting my testimony related to the Committee's 2008 report on the health 1991 Gulf War veterans.[1]

My responses to questions posed in your letter received September 8, 2009, follow. If you have additional questions, please contact me by email at Lea.Steele@hughes.net, or by telephone at: 785–945–4136.

Question 1. Who was it that asked that you testify on why and how scientific findings of the Institute of Medicine (IOM)'s Gulf War and Health reports differ from those of the Research Advisory Committee on Gulf War Veterans' Illnesses? The title of the hearing was "The Implications of U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research." Since VA is also utilizing the information provided by the RAC, I would assume that you would be coming to discuss specifically how the RAC report was formulated, and not create animosity with the IOM.

Answer 1. I was asked by the staff of the Subcommittee on Oversight and Investigations to testify specifically on differences between the scientific methods and findings of the Institute of Medicine's *Gulf War and Health* reports and those of the RAC. I described those differences at the staff's request, and had no interest in creating animosity with the IOM.

I also provided some information on the formulation and findings of the RAC report in my testimony, as well as in my earlier testimony before the Subcommittee in May. Additional details concerning the formulation of the RAC report is contained in the report itself. If the Subcommittee would like additional information either on the content of the RAC report or the methods and approach used by the RAC, I would be happy to refer you to those areas of the report or to answer any additional questions you may have.

Question 2. You mention in your testimony that the RAC Committee had several Members of the scientific community who also served on the Institute of Medicine panels over the years. Were you one of those members? If not, shouldn't we be hearing directly from one of them as to their concerns about the IOM reports? Are you recommending that Congress disregard the IOM reports, and start from scratch?

Answer 2. A number of RAC Members have also served on a variety of IOM Committees over the years, although I personally have not. As stated in my testimony, the RAC, as a Committee, identified a number of fundamental shortcomings in the approach used in the IOM *Gulf War and Health* series of reports that raised concerns about the findings of those reports. Those issues were summarized in the 2008 RAC report, and specific examples were provided. My testimony was based on the consensus findings of the RAC, as reflected in the 2008 Committee report. I agree that RAC Members who have also served on IOM panels would have been in a good position to testify on these issues, but can't comment on why I was asked to testify and they were not. I believe their testimony would have been similar to mine, however, had they been asked to describe the RAC Committee's findings concerning the IOM reports.

As indicated, the 2008 RAC report found that VA did not follow the requirements set forth by Congress in the statute mandating the IOM *Gulf War and Health* reports. The RAC specifically recommended that those reports be redone, to adhere to Congressional directives.

Question 3. In light of Dr. Goldman's testimony, do you still believe that critical animal studies were eliminated from the IOM report, and if so, could you provide for the record a detailed list of those studies?

Answer 3. Neither my testimony nor the RAC report said that critical animal studies were eliminated from the IOM reports. Rather, the 2008 RAC report indicated that IOM did not consider animal research in making its determinations re: the levels of evidence relating exposures during the Gulf War to health conditions affecting Gulf War veterans. The RAC report actually concurred with Dr. Goldman's comments that some animal studies had been reviewed in the IOM reports. However, information from animal studies in the IOM reports was primarily descriptive, and did not contribute to IOM's findings on associations between exposures and health outcomes. There is an important difference between a report summarizing results from animal studies and actually using results from animal studies, along with other available research, in forming scientific conclusions. As clearly articulated by IOM [2] the *findings* of the **Gulf War and Health** reports were based entirely on results of research in human populations.

As presented in detail in the RAC Report [1] there are numerous animal studies, many conducted in recent years, demonstrating persistent biological effects of repeat, low-level exposure to neurotoxic chemicals associated with military service in the 1991 Gulf War. These include, most prominently, effects of repeat exposure to particular types of pesticides and insect repellants, the anti-nerve gas pill pyridostigmine bromide, and exposure to low levels of sarin nerve gas. Additional research in animals has demonstrated synergistic effects of combinations of these compounds, at exposure levels comparable to those experienced by Gulf War veterans.

The IOM's limited consideration of animal studies was addressed in detail in Mr. Binns' testimony. My own testimony focused more on other studies and types of research—research directly relevant to the health of Gulf War veterans, but given little or no consideration in the IOM *Gulf War and Health* reports.

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Committee on Veterans' Affairs
Subcommittee on Oversight and Investigations
Washington, DC.
August 12, 2009

Robert W. Haley, M.D., FACE, FACP
Professor of Internal Medicine
University of Texas Southwestern Medical Center
5323 Harry Hines Boulevard
Dallas, TX 75390

Dear Dr. Haley:

Thank you for your testimony at the U.S. House of Representatives Committee on Veterans' Affairs Subcommittee on Oversight and Investigations hearing that took place on July 30, 2009 on "The Implications of U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research."

Please provide answers to the following questions by Wednesday, September 16, 2009, to Todd Chambers, Legislative Assistant to the Subcommittee on Oversight and Investigations.

1. It is apparent that you have a large body of work printed in several different trade publications. However, what type of research are you currently conducting on Gulf War illnesses, and when will you be publishing a peer reviewed study to the VA on the deliverables due relating to your contract of $2.5 million for the project on Gulf War Illness Research?
2. On July 15, 2009, the VA Office of Inspector General issued a report on "Review of Contract No. VA549–P–0027 between the Department of Veterans

Affairs and The University of Texas Southwestern Medical Center at Dallas (UTSWMC) for Gulf War Illness Research." Could you please comment on what UTSWMC will be doing to rectify the deficiencies in the contract found by the VA OIG?

Thank you again for taking the time to answer these questions. The Committee looks forward to receiving your answers. If you have any questions concerning these questions, please contact Subcommittee on Oversight and Investigations Majority Staff Director, Martin Herbert, at (202) 225–3569 or the Subcommittee Minority Staff Director, Arthur Wu, at (202) 225–3527.

Sincerely,

Harry E. Mitchell
Chairman

David P. Roe
Ranking Republican Member

MH/tc

Southwestern Medical Center
Dallas, TX.
October 13, 2009

Todd Chambers
Legislative Assistant to the
Subcommittee on Oversight and Investigations

Diane Kirkland
Printing Clerk
House Committee on Veterans' Affairs

Re: Correspondence of August 12, 2009

Dear Ms. Kirkland and Mr. Chambers:

In response to the August 12, 2009, correspondence from the Chairman and Ranking Republican Member of the Subcommittee on Oversight and Investigations, I submit answers to the additional questions posed by the Subcommittee after my July 20, 2009, testimony at the U.S. House of Representatives Committee on Veterans' Subcommittee on Oversight and Investigations.

My research is focused solely on helping our veterans of the Gulf War, and is showing tremendous promise in increasing our ability to diagnose and treat Gulf War Illnesses. I appreciate the opportunity to provide the Committee additional information regarding my research as well as UT Southwestern's on-going efforts to comply with Contract No. VA549–P–0027.

Please do not hesitate to contact me should you have additional questions.

Sincerely,

Robert W. Haley, M.D., FACE, FACP

Enclosures

Question 1: What type of research are you currently conducting on Gulf War illnesses, and when will you be publishing a peer reviewed study to the VA on the deliverables due relating to your contract of $2.5 million [sic] for the project on Gulf War Illness Research?

Response: On the road to developing an objective diagnostic test and treatments for VA medical centers to use in diagnosing and treating Gulf War illness and selecting subjects for efficient clinical trials, we undertook a carefully phased approach of validating new tests and developing a scientific basis for treatment under VA contract funding that would maximize the chances of success. Our approach includes five components: 1) a 90-minute national telephone survey of 8,020 randomly selected Gulf War-era veterans to define how many of the 700,000 Gulf War veterans have the brain illness we described, followed by collection of blood and DNA from 2,096 veterans for developing treatments, 2) development of new brain MRI tests to detect the newly described brain illness in pilot studies of over 280 research subjects, 3) validation of the new MRI brain tests in studies comparing 60 ill and well veterans, 4) a formal "Neuroimaging and Biomarker Study" to test the diagnostic effectiveness of the brain illness in 90 veterans selected randomly from the national telephone survey, and 5) a series of basic brain science laboratory studies to discover how pesticides and anti-nerve agent medications given to troops damage the intracellular machinery of brain cells to cause chronic illness and thus how to coun-

teract the damage with treatment. This phased approach was designed because, developing a diagnostic test and treatment for neurotoxic brain cell damage is an extremely difficult task, fraught with pitfalls, and if everything is not done just right, the effort will have no chance of succeeding.

Even though the various research projects in our program have been funded through the contract for a relatively short time, between 9 months and 2 years, the deliverables produced for the VA have been developed into a large body of scientific publications in a very short time, and the pace of scientific publications will increase rapidly over the coming year. To date, work on the Gulf War Illness Research Program under the VA contract has resulted in 94 scientific reports, including 9 scientific papers published in leading peer-reviewed journals, 6 more submitted for journal peer review, 38 abstracts published in the proceedings of scientific meetings, and 38 papers in draft projected to be submitted to journals in the next 2–3 months. The high ratio of scientific abstracts to full length papers is due to the relatively short time the projects have been approved by the contracting process; scientific innovations are usually presented first at scientific meetings, and their abstracts published in the meeting proceedings, before being submitted to scientific journals for publication later.

I enclose a more detailed description of my research and a bibliography of related abstracts and papers.

Question 2: On July 15, 2009, the VA Office of Inspector General issued a report on 'Review of Contract No. VA549–P–0027 between the Department of Veterans Affairs and The University of Texas Southwestern Medical Center at Dallas (UTSWMC) for Gulf War Research.' Could you please comment on what UTSWMC will be doing to rectify the deficiencies in the contract found by the VA OIG?

Response: UTSWMC did not seek to perform research for the VA pursuant to a sole-source IDIQ contract and would have preferred that the VA utilize a grant mechanism to support Dr. Haley's research. Despite the significant problems caused by the use of the sole-source IDIQ contract, it always has been the intent of UTSWMC to comply with the terms of Contract No. VA549–P–0027 (the "Contract"), as amended. UTSWMC has been actively engaged in discussions and written communications with the VA regarding the issues ultimately raised by the VA OIG since April 2009, several months before the VA OIG issued its Review of Contract VA549–P–0027. Since April 10, 2009, at least 17 written communications have passed between representatives of UTSWMC and the VA regarding the VA's allegations of non-compliance on the part of UTSWMC. At least two (2) face-to-face meetings between UTSWMC and VA representatives have occurred and countless, almost daily communications between the VA and UTSWMC contracting officers have occurred regarding not only the issues that are the subject of Cure Notice but also issues pertaining to the ongoing administration of the Contract and the task orders which have now been extended via synchronization modifications through May 31, 2010. As evidenced by the quantity and quality of the communications between UTSWMC and the VA, UTSWMC and the VA continue joint efforts to correct perceived deficiencies in UTSWMC's performance of the Contract so that this most valuable research is completed and Gulf War veterans benefit from a greater understanding of the Gulf War related illnesses.

UTSWMC originally attempted to engage VA representatives in a discussion regarding contractual terms which UTSWMC believed to require UTSWMC to violate the Health Insurance Portability and Accountability Act 1996 ("HIPAA"), the Privacy Act 1974 (Public Law No. 93–579, 5 U.S.C. § 522a) ("Privacy Act"), and the Common Rule. It was UTSWMC's good faith belief and position that the VA cannot contractually require UTSWMC to perform illegal acts so UTSWMC's performance of the contractual terms should be excused under the doctrine of impossibility. The VA rejected UTSWMC's concerns regarding the illegality of many contractual terms without comment or discussion. Thereafter, UTSWMC has used its best efforts to respond in a diligent, cooperative manner with the VA to bring its performance under the Contract into compliance despite its concerns regarding the Contract's illegality. VA Secretary Eric Shinseki's letter to the Honorable Kay Bailey Hutchison, assuring her that the VA has no intention of using study information to adversely affect the service-connected status or benefits of veterans who participate in the UTSWMC studies, is beneficial in responding to concerns expressed by potential veteran study subjects.

UTSWMC and the VA have agreed on many of the disputed issues, and continue to work together to achieve total compliance with the Contract terms.

Question: What type of research are you currently conducting on Gulf War illnesses, and when will you be publishing a peer reviewed study to the VA on the

deliverables due relating to your contract of $2.5 million [sic] for the project on Gulf War Illness Research?

Response:

The research we are conducting on Gulf War illness at the present time is summarized in the attached "Roadmap" diagram; the boxes numbered 1–5 are the areas of research we have pursued with the funds received through the VA contract. Even though these research programs have been funded through the contract for a relatively short time, between 9 months and 2 years, the deliverables produced for the VA have been developed into a large body of scientific publications in a very short time, and the pace of scientific publications will increase further over the coming year. This high rate of publications is due to the important nature of the findings obtained in the VA-funded studies.

To date, work on the Gulf War Illness Research Program under the VA contract has resulted in 94 scientific reports, including 38 abstracts accepted for presentation at scientific meetings, 9 scientific papers published in leading peer-reviewed journals, 6 more submitted for journal peer review, and 38 papers in draft projected to be submitted to journals in the 2–3 months (see table below and attached bibliography). This should give you the most accurate picture of the volume and nature of the research findings we have published and will be publishing in the near future.

Scientific papers and abstracts from the Gulf War Illness Research Program under VA contract funding

	Full Length Scientific Papers			Abstracts			
Phase	Published	Submitted/in peer review	Under development	Published	Submitted/ in review	Under development	Total
1 Pilot studies to refine and validate new brain imaging tests in normal subjects	6	6	22	32			66
2 Pilot ability of brain imaging tests to detect brain differences in ill vs well Gulf War veterans			12	3		2	17
3 Neuroimaging/ Biomarker Study in national sample of Gulf War veterans							0
4 National Survey of Gulf War veterans and Serum-DNA Bank			1			1	2
5 Basic neuroscience studies of chemical damage in brain cells to develop treatments	3		3	3			9
Total	9	6	38	38	0	3	94

The high ratio of scientific abstracts to full length papers is due to the relatively short time the projects have been approved by the contracting process; scientific innovations are usually presented at scientific meetings, and their abstracts published in the meeting proceedings, before being submitted to scientific journals for publication later. The abstracts and papers, a list of which is attached, can be categorized by the phases of the research program in which they were generated (see the list of publications and the Roadmap attached).

On the road to developing an objective diagnostic test for VA medical centers to use in diagnosing Gulf War illness and selecting subjects for efficient clinical trials (see Roadmap), we undertook a carefully phased approach of validating the tests under VA contract funding that would maximize the chances of success. Our Overall Research Plan, which guided all work proposals submitted to the contract process, included two sequential VA-funded pilot studies, the first designed to tune the complex tests on normal volunteers (#1 on the Roadmap) and the second to ensure they are working in detecting subtle brain damage in a battalion studied over 12 years and thus known to have the illness (#2), before moving to the final validation study

in a population-representative sample of Gulf War veterans selected randomly from our national survey of Gulf War veterans (#3). This phased approach was designed because, developing a diagnostic test for neurotoxic brain cell damage is an extremely difficult task, fraught with pitfalls, and if everything is not done just right, the effort will have no chance to succeed.

1. Pilot Studies to refine new MRI diagnostic tests in normal volunteers (October 2007—June 2008)

After developing cutting-edge brain imaging tests to detect subtle differences in brain function over the past decade under DoD funding, with the VA contract funding we first performed a large number of short validation studies to refine the complex brain function tests and ensure that they are measuring the specific brain functions and pathways intended. Each test had a dedicated team of researchers pursuing it, and as the pilot studies were completed, they submitted scientific abstracts for the methods and findings to the leading scientific conferences, where they went through the peer review process for selecting meeting presentations. Following presentation at the scientific meetings where they receive peer review comments and criticisms from fellow scientists, the researchers compose full length scientific papers on the findings for submission to scientific journals.

This effort was incrementally funded to begin between October 2007 and June 2008. Despite the fact that it has been in operation for less than 2 years, it successfully developed and validated a new battery of brain function tests capable of detecting the subtle brain damage caused by chemical neurotoxicity. To date, work on the these developmental pilot studies under the VA contract has resulted in 66 scientific reports, including 32 abstracts accepted for presentation at scientific meetings, 6 scientific papers published in leading peer-reviewed journals, 6 more submitted for journal peer review, and 22 papers in advanced draft ready to be submitted to journals in the next couple months (see table above and attached bibliography).

2. Pilot the new MRI tests to detect brain function differences underlying symptoms in a restudy of ill vs well veterans.

Once the tuning of the cutting-edge tests in normal volunteers was completed in June 2008, we proceeded to the next phase to apply the tests to a more formal pilot study. For this study we assembled the 23 tests that passed the first pilot phase into a battery that could be administered in according to a tight daily time schedule over a 6-day period. After testing and refining the logistics of running two subjects at a time through the battery schedule, over a 12-month period we ran the battery on 57 Members of a Seabees battalion representing both ill and well Gulf War veterans first studied 10 years previously. The purpose was to see whether the tests actually detect the subtle differences in brain function between the ill and well veterans responsible for the symptoms.

This more formal pilot study, begun in late July 2008 and completed on July 3, 2009, found that all but one of the cutting-edge MRI tests successfully detected the expected subtle differences in brain function underlying the symptoms. Our teams of researchers are presently preparing abstracts for scientific meetings and manuscripts for journal publication. To date, work on the these developmental pilot studies under the VA contract has resulted in 17 scientific reports, including 3 abstracts accepted for presentation at scientific meetings, and 12 scientific papers in advanced draft ready to be submitted to journals in the next 2–3 months (see table above and attached bibliography).

3. Neuroimaging and Biomarker Study

The third phase for developing diagnostic tests of Gulf War illness involves a definitive validation of the cutting-edge MRI tests comparing ill and well Gulf War veterans selected randomly from the entire population of Gulf War veterans (#3 in the Roadmap; also see the National Survey in the next section). This phase began in August 2009, and will be completed by June 1, 2010. Consequently no abstracts or papers have yet resulted from this phase.

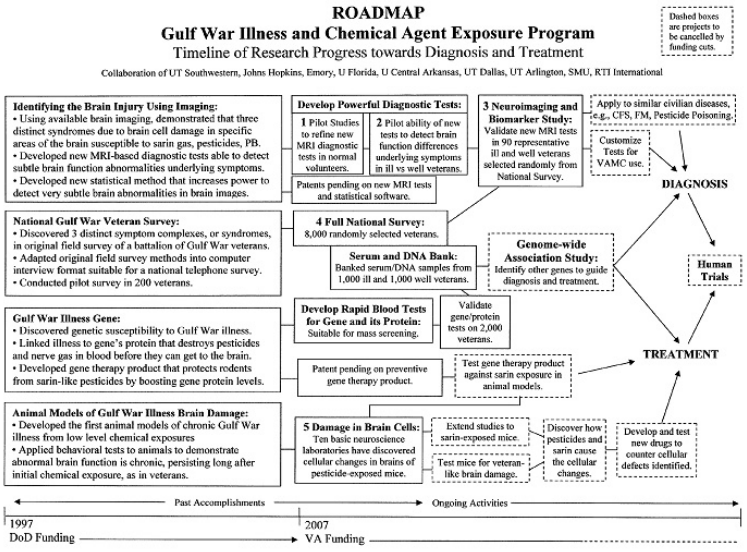
4. The Full National Survey and Serum/DNA Bank

To estimate how many Gulf War veterans have the multisymptom illness and provide the random sample for the Neuroimaging and Biomarker Study (see section 3 above), we conducted a computer-assisted telephone interview survey of 8,020 randomly selected Gulf War veterans (#4 on the Roadmap). It began in April 2007 and was completed in June 2009. During the interviews, all ill veterans and a random

sample of well veterans were asked to contribute a blood sample to a Serum and DNA Bank. The collection of 2,096 blood samples for the Serum/DNA Bank was completed at the end of August 2009. The final reports for these two phases have been completed for submission to the VA contracting office shortly, a scientific paper describing the methods of the survey has been drafted and is under review and revision internally, and the definitive tests for the Gulf War gene, discovered by our prior DoD-funded studies, will be completed by the end of November 2009. An abstract presenting the statistical innovations for the survey was accepted for presentation at a national statistical meeting.

5. Studies of Damage in Brain Cells

At present no treatment has been found to relieve the symptoms of chemical brain damage in Gulf War veterans. The road to developing treatment requires generating knowledge from basic neuroscience research to understand how the Gulf War-associated chemicals damaged the internal machinery of brain cells to produce the permanent symptoms. This is usually a many-year undertaking, so to shortcut the required time to discover such mechanisms, we have 10 basic neuroscience laboratories testing the most likely mechanisms in mice exposed to pesticides and pyridostigmine, anti-nerve agent medication given to our troops (#5 in the Roadmap). These studies comprised the last component of the program to be funded by the VA contracting process; these studies began between October and December 2008. These studies, however, have already borne considerable promising findings on the mechanisms involved in chemical damage to brain cells. To date, this work has produced 3 abstracts accepted for scientific meeting presentations, 3 full length scientific papers published in leading peer-reviewed journals, and 3 more papers under development. Additional publications will take shape as more results come out over the next 3 months.



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57. Gholipour A, Kehtarnavaz N, Gopinath K, Briggs R, Panahi I. Average Field Map Image Template for Echo-Planar Image Analysis. 20th Annual

International Conf Proc IEEE Eng Med Biol Soc. 2008;2008:94–7. ConferenceVancouver, British Columbia, Canada, August 20–24, 2008.
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2. Pilot the ability of the new tests to detect brain function differences underlying symptoms in ill vs well veterans (July 2008 to June 2009)

Papers Published in Scientific Journals

Papers Submitted or Near Submission to Scientific Journals

61. Tillman GD, Green TA, Ferree TC, Calley CS, Maguire MJ, Briggs R, Hart J Jr, Haley RW, Kraut MA. Impaired response inhibition in ill Gulf War veterans. (Manuscript to be submitted for journal peer review by September 20, 2009)
62. Calley CS, Buhl V, Tillman GD, Green TA, Hart J Jr, Haley RW, Kraut MA. Impaired word finding in ill Gulf War veterans. (Manuscript under revision, to be submitted for publication by December 2009.)
63. Gopinath K, Briggs R, Gandhi P, Goyal A, Fang Y, Jiang L, Ouyang L, Buhner D, Haley R. Quantitative sensory testing fMRI: differences between Gulf War syndrome patients and deployed controls (Manuscript to be submitted for peer review by mid-November 2009).
64. Gopinath K, Jiang L, Ouyang L, Gandhi P, Goyal A, Fang Y, Ringe W, Briggs R. Differences in functional connectivity between Gulf War veterans and deployed controls assessed with BOLD fMRI. (Manuscript to be submitted for peer review by end-November 2009.
65. Tillman GD, Green TA, Ferree TC, Calley CS, Maguire MJ, Hart J Jr., Haley RW, MA Kraut. Atypical ERP response to threatening stimuli in ill Gulf War veterans. (Manuscript under revision, to be submitted for publication by December 2009).
66. Ferree TC, Tatebe K, Bhat J, Sinton CM. Electroencephalographic differences in veterans of the 1991 Persian Gulf War. (Manuscript in preparation).
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68. Cheshkov S, Chang A, Baek H, Ganji S, Briggs R, Haley R. Persistent basal ganglia NAA/Cr ratio differences in Gulf War Syndrome. (Manuscript in development; estimated submission date November 2009).
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70. Odegard TN, Cooper CM., Farris EA, Arduengo J, Bartlett JC, Haley RW. Impaired memory in ill Gulf War veterans. (Manuscript to be submitted for journal peer review by December, 2009).
71. Odegard TN, Cooper CM, Farris EA, Arduengo J, Bartlett JC, Haley RW. Differences in brain activation during memory encoding between ill-Gulf War veterans and deployed controls. (Manuscript to be submitted for journal peer review by December, 2009).
72. Odegard TN, Cooper CM, Farris EA, Arduengo J, Bartlett JC, Haley RW. Differences in brain activation during memory retrieval between ill-Gulf War veterans and deployed controls. (Manuscript to be submitted for journal peer review by December, 2009).

Published Abstracts of Results Presented at Scientific Meetings

73. Cheshkov S, Chang A, Baek H, Briggs R, and Haley RW. Basal Ganglia NAA/Cr ratio in Gulf War Syndrome at 3T. *Proc. Intl. Soc. Mag. Reson. Med.* 17; 2009; 1126.
74. L Jiang, P Gandhi, M Qui, A Goyal, Y Fang, L Ouyang, K. Gopinath, W Ringe, R. Haley, and R. Briggs. Functional Connectivity Differences to ventral putamen of Gulf War syndrome II and control subjects. *Proc. Intl. Soc. Mag. Res. Med.* 17, abstract 1212 (2009).
75. R McColl, S Li, R Briggs, R Haley. Diffuse White matter differences between Gulf War syndrome II and control subjects revealed by diffusion tensor MRI. Human Brain Mapping 2009: abstract no. 1317.

Abstracts of Results to be Submitted to Scientific Meetings

76. Calley CS, Buhl V, Tillman GD, Green TA, Hart, J Jr., Haley RW, Kraut MA. Impaired word finding in ill Gulf War veterans. To be submitted as an abstract to the Cognitive Neuroscience Society.
77. Tillman GD, Green TA, Ferree TC, Calley CS, Maguire MJ, Hart, J Jr., Haley RW, Kraut MA. Impaired response inhibition in ill Gulf War veterans. To be submitted as an abstract to the Cognitive Neuroscience Society.

3. Neuroimaging and Biomarker Study (August 2009 to June 2010)

This phase has just begun, and so peer-reviewed abstracts and papers are approximately 9–12 months away.

4. The Full National Survey and Serum/DNA Bank (April 2007 to August 2009)

This phase just ended at the end of August 2009. The final report will be delivered to VA by the end of September. One abstract has been presented at a national meeting, and a scientific paper has been drafted and is undergoing revision.

Papers Published in Scientific Journals

Papers Submitted or Near Submission to Scientific Journals

78. Vincent G. Iannacchione, Jill A. Dever, Kathleen A. Considine, Darryl Creel, Christopher P. Carson, Heather Best, Carla M. Bann, and Robert W. Haley. The U.S. Military Health Survey: A population-based multi-disciplinary study of Gulf War syndrome. (Manuscript under revision with expected submission in November 2009).

Published Abstracts of Results Presented at Scientific Meetings

79. Vincent G. Iannacchione, Darryl Creel. Sequential modeling for contact and cooperation propensity for the United States Military Health Survey. Joint Statistical Meetings. August, 2009.

5. Studies of Chemical Damage in Brain Cells (October 2008 to December 2009)

Papers Published in Scientific Journals

80. Sidiropoulou K, Lu FM, Fowler MA, Xiao R, Phillips C, Ozkan ED, Zhu MX, White FJ, Cooper DC. Dopamine modulates an mGluR5-mediated depolarization underlying prefrontal persistent activity. *Nature Neuroscience* 2009; 12 (2): 190–199.
81. Hawasli AH, Koovakkattu D, Hayashi K, Anderson AE, Powell CM, Sinton CM, Bibb JA, Cooper DC. Regulation of hippocampal and behavioral excitability by Cyclin-dependent kinase 5. *PLOS ONE* 2009; 4(e5808): 1–13.
82. Xu J, Kurup P, Zhang Y, Goebel-Goody SM, Wu PH, Hawasli AH, Baum ML, Bibb JA, Lombro PJ. Extrasynaptic NMDA receptors couple preferentially to excitotoxicity via calpain-mediated cleavage of STEP. The Journal of Neuroscience 2009; 29(29):9330–9343.

Papers Submitted or Near Submission to Scientific Journals

83. Marvin M, Ding X, Casey B, Goldberg MS. Altered brain neurotransmitter levels and metabolism in mice exposed to chlorpyrifos and pyridostigmine bromide: Implications for Gulf War illness. (Manuscript to be submitted for journal peer review by December, 2009).
84. Wu J, Bezprozvanny I. Gulf War Illness implicated chemicals sensitize neurons to glutamate excitotoxicity. (Manuscript to be submitted for journal peer review by December 2009).
85. Mashimo T, Vemireddy V, Sirasanagandla S, Nannepaga S, Yang S, Bachoo R. Organophosphate, Diisopropylflurophosphate (DFP) exposure can transactivate oncogenic pathways, stimulate proliferation of astrocytes and stem/progenitor cells and induce diffuse gliosis in a murine model. (Manuscript to be submitted for journal peer review by December, 2009).

Published Abstracts of Results Presented at Scientific Meetings

86. Speed H, Blaiss C, Powell C. Chronic exposure of adult mice to the pesticide, chlorpyrifos, results in enhanced emotional memory and altered hippocampal synaptic transmission. Society for Neuroscience Annual Meeting. October 2009. (Abstract selected as one of the top 10 of the international meeting to be promoted to the news media.)
87. Wang Z, Vernino S. Acute and prolonged effects of pyridostigmine on autonomic ganglionic synaptic transmission in mouse. *Autonomic Neuroscience 2009*; 149: 90.
88. Puttaparthi K, Luther C, and Elliott JL. The role of AChE inhibitors in ALS. Society for Neuroscience Meeting 2009.

Committee on Veterans' Affairs
Subcommittee on Oversight and Investigations
Washington, DC.
August 12, 2009

Roberta F. White, Ph.D.
Professor and Chair, Associate Dean of Research
Department of Environmental Health
Boston University School of Public Health
Talbot Building 4W, 715 Albany Street
Boston, MA 02118

Dear Dr. White:

Thank you for your testimony at the U.S. House of Representatives Committee on Veterans' Affairs Subcommittee on Oversight and Investigations hearing that took place on July 30, 2009 on "The Implications of U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research."

Please provide answers to the following questions by Wednesday, September 16, 2009, to Todd Chambers, Legislative Assistant to the Subcommittee on Oversight and Investigations.

1. Are your studies being included in the body of work evaluated by the IOM and the RAC?
2. The research you are doing on evaluating Gulf War veterans who may have been exposed to various toxins is interesting. When do you expect to publish your results?

Thank you again for taking the time to answer these questions. The Committee looks forward to receiving your answers. If you have any questions concerning these questions, please contact Subcommittee on Oversight and Investigations Majority Staff Director, Martin Herbert, at (202) 225–3569 or the Subcommittee Minority Staff Director, Arthur Wu, at (202) 225–3527.

Sincerely,

Harry E. Mitchell
Chairman

David P. Roe
Ranking Republican Member

MH/tc

Boston University
School of Public Health
Boston, MA.
October 13, 2009

Harry E. Mitchell, Chairman
David P. Roe, Ranking Republican Member
Subcommittee on Oversight and Investigations
Committee on Veterans' Affairs
U.S. House of Representatives
335 Cannon House Office Building
Washington, D.C. 20515

Dear Congressmen Mitchell and Roe:

I am happy to address the two questions that you have sent me regarding the testimony that I prepared for the Subcommittee's meeting on Gulf war illness on July 30, 2009.

1. Are your studies being included in the body of work evaluated by the IOM and the RAC?

Most of the research was included in the RAC report that was published in November of 2008. I do not know if any of the work is being considered by the present IOM Committee.

2. The research you are doing on evaluating Gulf War veterans who may have been exposed to various toxins is interesting. When do you expect to publish your results?

The work on toxicants has been published and is included in the list of papers that I sent when I responded to the questions from my May, 2009, testimony (letter dated July 1, 2009).

Please contact me if there are any further questions, and thank you for your interest in our work.

Sincerely,

Roberta F. White, PhD, ABPP/cn
Associate Dean for Research
Professor and Chair, Department of Environmental Health

Committee on Veterans' Affairs
Subcommittee on Oversight and Investigations
Washington, DC.
August 31, 2009

Honorable Eric K. Shinseki
Secretary
U.S. Department of Veterans Affairs
810 Vermont Avenue, NW
Washington, DC 20420

Dear Secretary Shinseki:

Thank you for the testimony of Douglas E. Dembling, Associate Chief Officer for Program Coordination, Office of Public Health and Environmental Hazards, Veterans Health Administration, U.S. Department of Veterans Affairs, accompanied by Victoria Cassano, M.D., MPH, Acting Chief Consultant, Environmental Health Strategic Health Care Group, Veterans Health Administration, U.S. Department of Veterans Affairs, Joel Kupersmith, M.D., Chief Research and Development Officer, Veterans Health Administration, U.S. Department of Veterans Affairs, and David Barrans, Deputy Assistant General Counsel, Office of General Counsel, U.S. Department of Veterans Affairs at the U.S. House of Representatives Committee on Veterans' Affairs Subcommittee on Oversight and Investigations hearing that took place on July 30, 2009 on "The Implications of U.S. Department of Veterans Affairs' Limited Scope of Gulf War Illness Research."

Please provide answers to the following questions by 12:00 p.m., Wednesday, October 1, 2009, to Todd Chambers, Legislative Assistant to the Subcommittee on Oversight and Investigations.

1. Please elaborate on the differences between the RAC Report 2008 and IOMs finding. How does the VA plan to mediate the differences of the two reports and how will this affect our veterans?
2. Please elaborate on the recommendations that the Task Force made to the Secretary regarding the IOM reports from the Gulf War and the recommendations that the Task Force made regarding the RAC findings for the 2008 Report.
3. Please explain how the VA plans to alter the perceptions of Gulf War Veterans who believe that the VA provides Gulf War veterans nothing but procedural excuses when it comes to care, treatment and answers that the feel there has been little done to treat, acknowledge and explain veterans' illnesses. How are Gulf War Veterans to believe their sacrifices and service are recognized by the VA, VBA and the caregivers in the VAMCs?
4. From your response given to us, please explain how and why ORD chose to organize their budget allocating only $7 million to Gulf War Research (with the exception of the $15 million specifically earmarked to UTSW), $16.9 million to TBI and $22.9 million to PTSD. Does the VA feel that this disparity is just and that there is enough Gulf War Research on-going at this time to provide answers for how these veterans became sick and on-going studies for treatment?
5. Please explain how benefits are awarded to those with multi-symptom or undiagnosed illness from the Gulf War? Please describe at length the number of claims that are requested and awarded vs. requested and denied with Gulf War veterans. Please report the number of symptoms related to Gulf War Veterans that are granted as service connected as compared to the number of symptoms that are denied for Gulf War veterans?
6. What is the percentage of denial of claims of Gulf War veterans as compared to the population at large that applies for benefits through the VA? Are Gulf War veterans denied at a greater rate than any other war?
7. After listening to the first panel explain the differences in their reports, could you please provide a step by step process by which the VA evaluates the reports once they are received from both the IOM and the RAC, and explain any differences in the mandate for each of these reports.
8. Is the material provided to you by both the RAC and the IOM sufficient to meet the research needs of the Gulf War veterans being treated at the VA? What has VA done beyond evaluating the RAC and the IOM reports to further research on Gulf War veterans?
9. What areas of Gulf War Illnesses is VA funding research? When do you expect to see the results of these studies?
10. How much weight does VA place on IOM and RAC reports when determining presumptions for service-connected disabilities for the purposes of benefits and health care? Does VA ever make determinations of service-connection for disabilities without the use of IOM and RAC reports? Please explain.
11. How recently was the Veterans Health Initiative (VHI) Independent Study Guide for treating 1991 Gulf War veterans updated? Do you have a copy of that study guide which you can provide to the Committee?

Thank you again for taking the time to answer these questions. The Committee looks forward to receiving your answers. If you have any questions concerning these questions, please contact Subcommittee on Oversight and Investigations Majority Staff Director, Martin Herbert, at (202) 225–3569 or the Subcommittee Minority Staff Director, Arthur Wu, at (202) 225–3527.

Sincerely,

Harry E. Mitchell
Chairman

David P. Roe
Ranking Republican Member

MH/tc

Questions for the Record
Hon. Harry E. Mitchell, Chairman
Hon. David P. Roe, Ranking Member
House Committee on Veterans' Affairs
Subcommittee on Oversight and Investigations
The Implications of U.S. Department of Veterans Affairs
Limited Scope of Gulf War Illness Research
July 30, 2009

Question 1: Please elaborate on the differences between the RAC Report 2008 and IOM's finding. How does the VA plan to mediate the differences of the two reports and how will this affect our Veterans?

Response: The major difference between the Institute of Medicine's (IOM) findings and the Research Advisory Committee (RAC) report is that the RAC ascribes symptoms of unexplained illnesses to the combined effects of pyridostigmine bromide and pesticides. The IOM, based on a review of peer-reviewed literature regarding undiagnosed/unexplained illnesses, concluded that the relevant scientific literature did not lead to a conclusion of such a specific cause and effect relationship based both on biologic plausibility and epidemiology. In February 2009, the Department of Veterans Affairs (VA) asked the IOM to address the differences in the two reports. While the IOM does not intend to specifically review the RAC report (since they only review primary research and not reviews of research), in early 2010, when the next IOM update is published, we expect that they will comment on the peer-reviewed scientific literature that may be cited in the RAC report, which meets the IOM's criteria for inclusion in its reviews. Furthermore, we have requested, and received from IOM, a proposal to specifically review the literature regarding the possible relationship between the use of pyridostigmine bromide tablets and exposure to pesticides and the development of unexplained and or undiagnosed illness in Gulf War Veterans. We are planning on having this topic be the subject of the IOM's next biennial update on Gulf War Veterans health.

Question 2: Please elaborate on the recommendations that the Task Force made to the Secretary regarding the IOM reports from the Gulf War and the recommendations that the Task Force made regarding the RAC findings for the 2008 Report.

Response: VA follows the statutory process for responding to the IOM reports. The Task Force was established to enable the Secretary to meet the specific statutory requirements for responding to reports of the IOM, and has not made recommendations based on the recent RAC report. In response to the last GW Veterans' illnesses update, VA determined that it would establish presumptions of service-connection for nine infectious diseases and their long term sequelae for Veterans suffering from these sequelae.

Question 3: Please explain how the VA plans to alter the perceptions of Gulf War Veterans who believe that the VA provides Gulf War Veterans nothing but procedural excuses when it comes to care, treatment and answers that they feel there has been little done to treat, acknowledge and explain Veterans' illnesses. How are Gulf War Veterans to believe their sacrifices and service are recognized by the VA, VBA and the caregivers in the VAMCs?

Response: After the July 30, 2009 hearing, VA subject matter experts in research and development, environmental hazards, and benefits met with Members of the RAC to better ascertain the initiatives needed to improve services, care, and the perceptions about that care for GW Veterans. VA determined that meeting the basic matrix is already present to provide GW Veterans with excellent care despite the fact that their conditions remain undiagnosed. A Secretary level Work Group was formed in September 2009 to continue to forge the future directions of VA in support of these Veterans. The main focus of these efforts is treatment-oriented research, training of VA clinicians and benefits administrators regarding the conditions that are currently presumptively service-connected, and exposure related disease in general. Veterans Health Administration (VHA) has already initiated an overhaul of the Veterans Health Initiatives that are continuing medical education programs for providers.

The Work Group is focusing on:

- Defining all key areas of review (e.g., research; Veterans' access to services; treatment, claims service, policy, outreach, VA organizational and process relationships, and training of clinical staff);

- Consulting key experts and relevant stakeholders and reviewing relevant reports (e.g., the Institute of Medicine; VA advisory committees, and research experts);
- Capturing the issues, data, as well as program and performance information (e.g., complaints, claims statistics, treatment modalities, funding, and service gaps);
- Looking holistically at issues and opportunities to advocate for the Veteran (e.g., ways to deliver better and faster service and ways to expand programs); and
- Identifying, as a priority, initiatives that enhance identification and treatment of GW Veterans' unexplained and undiagnosed illnesses.

Question 4: From your response given to us, please explain how and why ORD chose to organize their budget allocating only $7 million to Gulf War Research (with the exception of the $15 million specifically earmarked to UTSW), $16.9 million to TBI and $22.9 million to PTSD. Does the VA feel that this disparity is just and that there is enough Gulf War Research on-going at this time to provide answers for how these Veterans became sick and on-going studies for treatment?

Response: Office of Research and Development (ORD) planned budget allocation in Fiscal Year (FY) 2008 was to spend an additional $7 million on Gulf War Veterans Illnesses (GWVI) above the $15 million earmarked for the contract with The University of Texas Southwestern (UTSW) for its Gulf War Research Project, for a total GWVI allocation of $22 million. The premise behind UTSW's research is that exposure to insecticide and nerve gas agents is a primary cause of GWVI, and a major focus of that research was brain imaging and blood tests designed to identify Veterans suffering from GWVI. VA supported this approach and was very hopeful that the research would provide a path forward in developing tests to help diagnose GWVI. In particular, the brain imaging studies held promise because they might show differences between afflicted and non-afflicted Veterans, no matter what the true cause or causes of GWVI might be. Accordingly, VA considered the contract studies to be a key component of its GWVI research effort. But, because most scientists studying GWVI do not believe the cause of GWVI has been solved, VA funded an additional $7 million in GWVI to look at additional possible causes as well as diverse research strategies that might provide other paths forward to developing future treatments.

Finding one or more safe and effective treatments for GWVI is critically important to suffering Veterans as well as VA. By investing an additional $7 million research funds in diverse strategies for diagnosis and treatment beyond those investigated by UTSW, VA is hoping to accelerate the research breakthroughs needed to begin the process of translating research findings into clinical support and treatment.

As such, VA never considered the UTSW contract to be a separate effort, but rather a significant component in VA's GWVI research program. The overall GWVI budget was determined with due regard to avoiding potentially wasteful duplication of the work underway as part of the UTSW contract.

VA is committed to funding research that might shed light on the cause(s) of GWVI and promising approaches to diagnosis and (eventually) treatment for Veterans suffering from GWVI. Funding for GWVI must necessarily be balanced against important studies related to other conditions faced by Veterans of the Gulf War, Veterans in other conflicts, and non-conflict related health conditions in Veterans resulting from military service. For example, Veterans who served in Vietnam and who were exposed to Agent Orange suffer from a variety of medical conditions which have been presumptively service connected, including peripheral neuropathy, leukemia, diabetes mellitus, Hodgkin disease, non-Hodgkin lymphoma, prostate cancer and respiratory cancer. Other diseases, such as osteoporosis, have been presumptively service connected for some former prisoners of war. Veterans of all eras suffer from disabling mental health issues including schizophrenia, depression, and post-traumatic stress disorder (PTSD). In addition to the somewhat narrowly defined GWVI portfolio, Gulf War Veterans may have highly prevalent mental health post-deployment disorders such as PTSD that ORD also supports at an appropriate level. At a minimum the funding for mental health research also relevant to Gulf War Veterans includes $22.9 million for PTSD; $5.9 million for mood disorders such as depression, and $12 million for addictive disorders in FY08. Current Veterans have particularly high rates of polytrauma and funding levels reflect allocation of those resources that have been provided by Congress to address this wide spectrum of conditions. These funding levels are determined largely as the result of competitive application from VA clinician-investigators who treat these conditions, and thus reflect the balance of disease being treated by VA.

Question 5: Please explain how benefits are awarded to those with multi-symptom or undiagnosed illness from Gulf War? Please describe at length the number of claims that are requested and awarded vs. requested and denied with Gulf War veterans. Please report the number of symptoms related to Gulf War Veterans that are granted as service connected as compared to the number of symptoms that are denied for Gulf War veterans?

Response: Service-connected disability benefits may be awarded on the basis of direct incurrence in service, aggravation of a pre-service disability, or on the basis of presumption, if there is no evidence of the disability during service. 38 U.S.C. § 1117, implemented by 38 CFR 3.317, establishes presumptions of service connection for chronic undiagnosed illness or medically unexplained chronic multisymptom illness, such as chronic fatigue syndrome, fibromyalgia and irritable bowel syndrome, that first manifested during service or to a degree of 10 percent or more during an established period following service in the Southwest Asia Theater of Operations (SWA).

The Veteran need only establish, through competent medical or lay evidence, the presence of chronic disabling symptoms lasting 6 months or more, that exhibit objective indicators or signs, and that can not be attributed to any known clinical diagnosis (except for chronic fatigue syndrome, fibromyalgia and irritable bowel syndrome).

Regarding Gulf War Veterans' claims for chronic undiagnosed illness or medically unexplained chronic multi-symptom illness such as chronic fatigue syndrome, fibromyalgia and irritable bowel syndrome, VBA processed 38,359 claims as of September 30, 2009. Of these, 15,181 were granted service connection for at least one undiagnosed condition, and 23,178 were denied service connection for any undiagnosed condition.

Question 6: What is the percentage of denial of claims of Gulf War veterans as compared to the population at large that applies for benefits through the VA? Are Gulf War veterans denied at a greater rate than any other war?

Response: VA does not have the historical information necessary to respond to this question. We do have information for recent claims and for Veterans currently receiving VA compensation benefits. The data provided below was obtained from Compensation and Pension records that are currently active and does not include Veterans who received no grant of any service-connected disability or who have subsequently died. The data provided identifies the number of Veterans from each identified wartime period who have at least one service-connected disability or those who have no service-connected disability.

- For 300,000 Veterans of Operation Desert Shield/Storm with claims decisions, 85.7 percent were granted service connection for at least one condition, and 14.3 percent were not granted service connection for any condition.
- For over one million Veterans with in-country Vietnam service with claims decisions, 85.3 percent were granted service connection for at least one condition, and 14.7 percent were not granted service connection for any condition.
- For over 500,000 Global War on Terror (GWOT) Veterans with claims decisions, 83.5 percent have been granted service connection for at least one condition, and 16.5 percent were not granted service connection for any condition. The 500,000 GWOT claims came from Veterans with service after 9/11. The 300,000 claims noted above were from Veterans deployed to Desert Shield/Storm. These counts are for distinct periods of service, and Veterans who served in both may be included in both counts.

Question 7: After listening to the first panel explain the differences in their reports, could you please provide a step by step process by which the VA evaluates the reports once they are received from both the IOM and the RAC, and explain any differences in the mandate for each of these reports.

Response: The Agent Orange Act 1991, Pub. L. No. 102–4 (codified in part at 38 U.S.C. § 1116) and the Persian Gulf War Veterans Act of 1998, Pub. L. No. 105–277, title XVI (codified in part at 38 U.S.C. § 1118), direct the Secretary of Veterans Affairs to contract with the National Academy of Sciences (NAS) to evaluate the available evidence concerning the health effects of exposure to herbicides and exposure to certain hazards suspected to be associated with Gulf War service and to prepare biennial reports to the Secretary summarizing its findings based on such evidence. Pursuant to those statutes, NAS's Institute of Medicine (IOM) prepares such reports and provides them to the Secretary.

The process by which VA evaluates the IOM reports in order to assist the Secretary in making determinations is described below:

RECEIPTS OF REPORT AND IOM COMMITTEE BRIEFING

VA receives a draft copy of the IOM report about 1 week prior to the date of the report's public release. On the day of public release, a representative of the IOM Committee provides VA a briefing on the report. The briefing identifies any significant findings in the report, any changes in the IOM's categorization of specific diseases in comparison to prior reports, and any significant changes, and responds to any questions from VA participants. The briefing is attended by the Members of VA's Working Group (described below) and other interested VA personnel.

SUMMARY OF VA'S REVIEW PROCESS

VA has not adopted formal procedures governing its internal review of IOM reports under the two statutes discussed above. However, practice has been it involves a three-tiered review. In the first tier, a "Working Group" of VA employees from different operational elements of VA reviews the IOM report and any other relevant evidence and prepares a summary of its assessment and a statement of recommendations or options. This summary is intended for the benefit of a "Task Force" composed of high-level VA officials. In the second tier, the Task Force, based on the Working Group's input, provides recommendations to the Secretary, usually in the form of a separate written report. In the third tier, the Secretary determines, based on the Task Force's input, whether a presumption of service connection is warranted for any disease.

VA WORKING GROUP

The Working Group ordinarily consists of Members of the Office of Public Health and Environmental Hazards (OPHEH) of VHA, the Compensation and Pension Service (C&P Service) of the Veterans Benefits Administration (VBA), and representatives from the Office of the General Counsel (OGC). Additionally, the Working Group often includes other VHA personnel with specialized medical training or experience concerning a health issue implicated by a particular IOM report. Members are assigned to the Working Group by supervisory personnel within VHA, VBA, and OGC.

The Working Group convenes after receiving the briefing from the IOM committee. Prior to the meeting, VHA personnel seek to identify based on the IOM report and the Committee briefing, the diseases that may warrant special consideration because the IOM's findings with respect to those diseases appear to be potentially significant. At the initial Working Group meeting, VHA provides the Working Group Members with additional information concerning those diseases, including copies of any significant scientific studies identified in the IOM report and other information concerning matters such as the course of the disease, known causes or risk factors, related conditions or health effects, latency periods (if any), and any other known relevant information.

OGC representative briefs the Working Group on the legal standard governing the Secretary's decision. Members of the Working Group discuss whether any of the IOM's findings appear to be potentially significant, in that they might warrant a presumption of service connection for a particular disease or diseases, and will discuss the strength of the scientific evidence with respect to such diseases. The Working Group will attempt to reach consensus as to whether the scientific evidence appears to warrant a presumption of service connection for any diseases under the applicable legal standard. If the Working Group reaches agreement that a presumption is or is not warranted on the basis of the scientific evidence and the legal standard, it will agree to put forth a recommendation based on that conclusion. In arriving at such recommendations, the Working Group relies on scientific evidence and the legal standard, and does not consider matters of governmental policy or cost.

If the Working Group concludes that the scientific evidence and legal standard do not provide a clear basis for recommending for or against establishing a presumption, but permit a range of options, the Working Group agrees to set forth a range of options for decision by VA policymaking officials. In those circumstances, the Working Group will discuss the factors that preclude a clear recommendation, which may include ambiguity in the governing statutory standard as applied to certain IOM findings, the limited or conditional nature of the IOM's findings with respect to certain diseases, or other factors. The Working Group will discuss the decisional options available to the Secretary and may also discuss the factors that may be relevant to the Secretary's decision among those options. To this extent, the Working Group may discuss the policy considerations that would be relevant to the Secretary's choice among permissible courses of action.

Once the Working Group has reached agreement concerning its recommendations or presentation of options, a written report is completed. The Report will contain (1) a summary of the issues to be decided under applicable law and the IOM report, (2) a summary of the findings contained in the IOM report, (3) a summary of the legal standard governing VA's decision, (4) a summary of the Working Group's analysis of the medical evidence in relation to the legal standard, particularly with respect to any potentially significant findings in the IOM report, and (5) a statement of the Working Group's recommendations or of the options identified by the Working Group. The Working Group does not prepare or obtain a cost estimate for the options, although it may provide general information concerning, e.g., the prevalence rates of certain diseases under consideration. If the Working Group report lists a range of options available to the Secretary, it would identify the scientific and legal considerations relevant to the Secretary's choice among those options, and may also identify policy implications associated with various options.

VA TASK FORCE

The Task Force consists of the Under Secretary for Health, the Under Secretary for Benefits, the General Counsel, and the Assistant Secretary for Policy and Planning. There is no established procedure for the Task Force's deliberations. Task Force Members receive a copy of the Working Group report and, based on that report, provide advice to the Secretary concerning the Secretary's determination, which may include recommendations based upon the options, if any, outlined by the Working Group. The Task Force often, though not always, provides a separate report to the Secretary.

SECRETARY

Based on the Task Force's report, the Secretary determines whether or not to establish presumptions for any diseases discussed in the IOM report and directs appropriate action to implement the decision.

VA Charter: Research Advisory Committee:

At the direction of Congress, VA in 2002 chartered the VA Research Advisory Committee on Gulf War Veterans' Illnesses (RACGWVI) to advise the Secretary on the overall effectiveness of Federally funded research to answer central questions on the nature, causes, and treatments of Gulf War-associated illnesses. The RACGWVI's charter stipulates they are to provide information and recommendations to VA. Despite this limited charge, the RACGWVI published and released an independent report, including recommendations, in 2004 and again in 2008.

Question 8: Is the material provided to you by both the RAC and the IOM sufficient to meet the research needs of the Gulf War Veterans being treated at the VA? What has VA done beyond evaluating the RAC and the IOM reports to further research on Gulf War Veterans?

Response: Although the RAC and the IOM provide valuable advice in developing the VA research program, development and execution of meaningful research projects relies upon the skill and clinical experience of VA investigators who individually and collectively help develop specifics of the research agenda. Seventy percent of VA researchers are also clinicians who treat Veterans. This allows clinicians to develop research projects in response to the symptoms their patients exhibit including Gulf War Illnesses.

Additionally, in an effort to generate more Gulf War Illness-related research proposals, VA's Office of Research and Development (ORD) has issued the following Requests for Applications (RFA):

> **Oct 2002—Deployment Health Research RFA issued (ongoing for all Merit Review cycles)**
>
> . . . research focused on potential long-term health effects of exposures and risk factors among Veterans of hazardous deployments, such as the Gulf War, Project SHAD, Bosnia/Kosovo, or Afghanistan. . . . ORD recognizes five major research categories related to deployment health as priorities:
>
> - Long-term health impacts of hazardous deployments
> - Health impacts of specific military occupational and environmental exposures
> - Improvements in evaluation and diagnosis of deployment-related illnesses
> - Improvements in treatment of deployment-related illnesses

- Health risk communication for Veterans and health care providers.

Apr 2004—1st Gulf War Research RFA (14 of 54 proposals funded)

. . . for studies directly relevant to Veterans who were deployed during the 1990's to the Persian Gulf.—research studies that focus on potential long-term health effects of exposures and risk factors among Veterans of the Gulf War in several areas of interest. . . . We are particularly interested in studies in the following areas:

- Immunological changes (activation, suppression, interactions) that may be associated with the unexplained illnesses reported by Gulf War Veterans
- Autonomic system changes that may be associated with symptoms reported by Gulf War Veterans
- The prevalence of neurological disorders in Gulf War Veterans
- Proposals that address other important objectives regarding causes, mechanisms, and treatments for Gulf War Veterans' illnesses.

March 2005—2nd Gulf War Research RFA (12 of 44 proposals funded)

. . . ORD will fund relevant and scientifically meritorious . . . research studies that focus on potential long-term health effects of exposures and risk factors among Veterans of the Gulf War in several areas of interest. . . . proposals related exclusively to PTSD or stress-related conditions will not be funded under this program announcement. . . . Research priorities include:

- Long-term health effects of hazardous deployments
- Health effects of specific military occupational and environmental exposures
- Improvements in evaluation and diagnosis of Gulf War Veterans' illnesses
- Improvements in treatment of Gulf War Veterans' illnesses.

May 19, 2009—Gulf War Treatment RFA (5 proposals were reviewed in September 2009)

. . . solicits submissions of applications for studies that:

- Propose a controlled clinical trial or epidemiological investigation of the effectiveness of treatments for chronic multi-symptom illnesses in Veterans of the 1990–1991 Gulf War compared with subjects meeting case definition for fibromyalgia (FM) and/or chronic fatigue syndrome (CFS).
- Identify biomarkers (i.e., genetic, neuroendocrine, immunological, biochemical, physiological, etc.) that either predict or explain differences in response to new treatments. Biomarker studies proposed without an accompanying treatment trial will not be considered for funding.
- Trials to identify new symptom-specific treatments (i.e. memory, attention, sleep, pain, etc.) in ill Gulf War Veterans may be proposed.

Pharmacologic agents must have a plausible biological basis for anticipated efficacy. Treatments that have been tested in other chronic multi-symptom illnesses (i.e., FM or CFS) may be proposed, even if they have been shown to be moderately effective or ineffective in treating those conditions.
Applications not employing appropriate populations of Gulf War Veterans will not be considered for funding.

VA has a proactive history of initiatives to further research on Gulf War Veterans beginning with the 1994 launch of the first VA study on the Health of Gulf War Veterans. Since then, VA has continuously supported an extensive Gulf War research portfolio dedicated to understanding chronic multi-symptom illnesses, long-term health effects of potentially hazardous substances to which Gulf War Veterans may have been exposed during deployment, and conditions or symptoms that may be occurring with higher prevalence in Gulf War Veterans, such as Amyotrophic Lateral Sclerosis (ALS), multiple sclerosis, and brain cancer.

VA is committed to funding new clinical trials to identify new therapies for ill Gulf War Veterans as well as using emerging technologies to move in new directions. VA recently announced funding available for VA researchers interested in conducting clinical trials to test treatments used for other chronic multi-symptom illnesses such as chronic fatigue syndrome and fibromyalgia. The five applications were received and reviewed in September 2009. The results of these and other clinical investigations, together with new discoveries using the newest and most ad-

vanced technology, are expected to lead to improved treatments and a better quality of life for Gulf War Veterans.

VA has provided funding to UTSW Medical Center, through a contract from the Dallas VA Medical Center, for research that focuses on a new national survey of Gulf War Veterans; a proposed genome-wide association study of participants in the national survey to identify genetic markers of illness and potential susceptibility to illness; and identification of alterations in brain imaging that correspond to specific neuropsychological measurements (i.e. memory, attention, executive function, etc.). Due to unsatisfactory contract performance, the option to extend the contract 1 year was not exercised. The funding will be redirected to other VA-funded Gulf War research projects, moving in similar directions, and utilizing research capacities in place. Specifically, VA will undertake the following efforts:

- Genome Wide Association Study (GWAS) of GWVI, Chronic Fatigue and Fibromyalgia;
- Request For Applications (RFA) for new treatments for ill Gulf War Veterans;
- RFA for Gulf War Research including, but not limited to:
    - Diagnostic Tests to identify ill Gulf War Veterans
    - Diagnostic tests to identify subpopulations of ill Gulf War Veterans
        - Neuroimaging paired with neurocognitive/neuropsychological testing
        - Structural and/or functional neuroimaging
        - Proteomics
        - Gene expression/polymorphisms
    - Genetic susceptibility
        - Gene expression and/or polymorphisms
    - Other illnesses potentially affecting Gulf War Veterans (studied in a Gulf War Veteran population)
        - ALS
        - Multiple Sclerosis
    - Animal Studies
        - New treatment targets
        - Pathophysiological mechanisms
        - Mechanisms that underlie persistence of symptoms

These studies should lead to improved understanding of these diseases and development of new treatments by identifying disease susceptibilities, underlying damage pathways, and potential treatment targets.

VA research program for Gulf War illnesses is robust and we are confident that through this and other Federal research initiatives, such as the Congressionally Directed Medical Research Program (CDMRP) for Gulf War research, we will discover ways to provide enhanced health care for these ill Veterans.

Question 9: What areas of Gulf War Illnesses is VA funding research? When do you expect to see the results of these studies?

Response: Attached is a Gulf War research project list for FY07, FY08 and FY09. Data analysis, for any research project, usually takes at least 12 and often 15—18 months before any results—peer-reviewed scientific literature—are published.

The average length of a research study is 4 years. It typically takes several years after funds have been provided before sufficient data can be accumulated, analyzed, and written as a manuscript. Once a manuscript has been submitted, it usually takes a minimum of 6–12 months for the manuscript to be peer reviewed and published by a scientific journal. Results are not considered final until results are peer reviewed and published. Clinical trials can even take longer before the results appear in a publication because results come only after the trial has been completed. This can take many years from beginning to the end. Additional results/publications may occur after a project is presented to scientific groups, professional associations, etc. or from further data analysis.

Public Law 102–585, as amended by Public Law 105–368, requires the VA to submit an annual Report on the status of Federally sponsored research on Gulf War Veterans' illnesses. Known as "The Annual Report to Congress on Federally Sponsored Research on Gulf War Veterans' Illnesses"—this report provides Congress with an overview of Federal research activities for a given calendar year and highlights important research findings and milestones. Their have been 15 reports submitted to Congress.

The reports can be found at the following Web link: http://www.research.va.gov/resources/pubs/pubs—individual.cfm?Category=Gulf%20War%20Reports

The annual report covers the research activities of the Departments of Veterans Affairs, Defense (DoD), and Health and Human Services (HHS). Although each annual report contains the same sections as previous reports, key differences exist in the information reported. These reports discuss the results of Gulf War research that were published in a calendar year. Published research results and Federally funded programs are categorized into 5 primary Focus Areas: Brain and Nervous System Function; Environmental Toxicology; Immune Function; Reproductive Health; and Symptoms and General Health. In addition, the appendices are revised each year to reflect changes in funding amounts, new research findings, the addition of new programs, and the completion of previously funded studies.

Question 10: How much weight does VA place on IOM and RAC reports when determining presumptions for service-connected disabilities for the purposes of benefits and health care? Does VA ever make determinations of service-connection for disabilities without the use of IOM and RAC reports? Please explain.

Response: Under the provisions of Public Law 105–277, The Persian Gulf War Veterans Act and Public Law 105–368, the Veterans Programs Enhancement Act, VA entered into a contract with the National Academy of Sciences (NAS) to review and evaluate the scientific and medical literature regarding associations between illnesses and environmental exposures associated with Gulf War service. VA considers reports from the NAS in determining whether any medical condition warrants a presumption of service connection based on Gulf War service. Recently, VA announced it was establishing presumptions of service connection for certain conditions based on the most recent IOM Study.

The Research Advisory Committee on Gulf War Veterans' Illness, (RAC–GWVI) was established by the Secretary of Veterans Affairs in March 2002 to provide advice and make recommendations to the Secretary of Veterans Affairs on proposed research plans and strategies related to understanding and treating the health consequences of military service in the Southwest Asia theater of operations during the 1990–1991 Gulf War (Operations Desert Shield and Desert Storm).

The Secretary considers all advice and recommendations of both the NAS and the RAC–GWVI when determining whether a presumption of service connection should be established for a particular condition. As described above, VA has an informal process of tiered review and recommendations with respect to IOM reports, to enable the Secretary to meet the statutory requirements applicable to such reports.

The Secretary of Veterans Affairs has statutory authority to make determinations of presumptive service connection for disabilities without relying on IOM and RAC reports.

Question 11: How recently was the Veterans Health Initiative (VHI) Independent Study Guide for treating 1991 Gulf War Veterans updated? Do you have a copy of that study guide which you can provide to the Committee?

Response: VHA has just started a major revision of this document. The last update was completed in 2002. A copy of that VHI is attached. Our new initiative is to make the information in this program more relevant to busy providers and to modularize the content so that it is more accessible. The Office of Public Health and Environmental Hazards and the Employee Education System are working together on this project. We have an American Association for the Advancement of Science (AAAS) fellow with advanced degrees in postsecondary education and computer technology to spearhead this initiative.

Attachment 1: FY 2007 ORD Support for Ongoing War Research Projects

End Date		FY 07			
10/15/08	VA–138	$ 235,241	$ 209,289		
12/31/09	VA–137	$ 224,294	$ 199,550		
12/31/08	VA–108	$ 224,917	$ 200,104		VA–108
09/30/07	VA–142	$ 991,510	$ 882,126		
09/30/07	VA–119	$ 168,600	$ 150,000		VA–119

Attachment 1: FY 2007 ORD Support for Ongoing War Research Projects—Continued

End Date		FY 07			
09/30/07	VA–133	$ 112,400	$ 100,000		
06/30/09	VA–101	$ 112,010	$ 31,250	$ 68,403	68403
12/31/09	VA–132	$ 112,400	$ 100,000		
09/30/07	VA–131	$ 163,579	$ 145,533		
03/31/09	VA–107	$ 210,638	$ 187,400		VA–107
12/31/07	VA–096	$ 135,127	$ 120,220		VA–096
12/31/09	VA–125	$ 743,779	$ 661,725		VA–125
09/30/07	VA–126	$ 165,565	$ 147,300		VA–126
09/30/07	VA–129	$ 168,600	$ 150,000		VA–129
09/30/08	VA–113	$ 110,152	$ 98,000		
12/31/08	VA–134	$ 77,640	$ 69,075		
12/31/08	VA–135	$ 79,242	$ 70,500		
03/31/08	VA–130	$ 217,056	$ 62,600	$ 130,510	
03/31/09	VA–109	$ 317,503	$ 149,900	$ 132,576	VA–109
03/31/07	VA–097	$ 134,628	$ 119,776		VA–097
06/30/08	VA–117	$ 115,772	$ 103,000		VA–117
06/30/07	VA–118	$ 119,453	$ 106,275		VA–118
06/30/07	VA–148	$ 71,009	$ 63,175		
				$ 6,727,775	
03/31/10	VA–149	$ 129,861	$ 115,535		$115,535
09/30/07	VA–143	$ 112,400	$ 100,000		
09/30/07	VA–144	$ 112,400	$ 100,000		
03/31/09	VA–145	$ 224,800	$ 200,000		
12/31/09	VA–146	$ 256,160	$ 227,900		
09/30/07	VA–123	$ 178,447	$ 158,761		VA–123
03/31/08	VA–090	$ 449,990	$ 250,000	$ 150,347	VA–090
09/30/07	VA–080	$ 252,602	$ 106,000	$ 118,735	VA–080

Attachment 2: FY 2008 ORD Support for Ongoing War Research Projects

Full Name	VAMC	Title	Focus	Total FY 2008*	Start Date	End Date		FY 08			
Clinical Trials				**$ 487,937**							
Amin, Mohammad M	Northport, NY	Inspiratory flow dynamics during sleep in GWS & the effect of CPAP	Prevelance and treatment of sleep disturbances in GW veterans	$ 258,136	10/16/05	10/15/08	VA–138	$ 258,136	$ 20,369	$ 189,289	$20,000
Downing, Mia M. (Ph.D.)	East Orange, NJ	Telemedicine Treatment for Veterans with Gulf War Illness	Feasibility of performing Cognitive Behavioral Therapy (CBT) via telephone with Gulf War veterans	$ 12,476	01/02/05	12/31/07	VA–108	$ 12,476	$ 11,100		
Tuteja, Ashok K. (M.D., M.P.H.)	Salt Lake City, UT	Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans	Treatment of GW veterans with gastrointestinal symptoms	$ 217,325	01/01/06	12/31/09	VA–137	$ 217,325	$ 193,350		
Biomarkers				**$ 4,652,315**							
Fink, John K. (M.D.)	Ann Arbor, MI	Novel Cause of Motor Neuron Disease	Gene mutations in veterans with ALS (includes 40 GW veterans from registry)	$ 110,152	10/01/04	09/30/08	VA–113	$ 110,152	$ 98,000		110152
Fiore, Louis D. (MD)	Boston, MA	VA Gulf War Biorepository Trust	Gulf War Brain and DNA Bank	$ 1,091,547	08/01/02	09/30/08	VA–142	$ 1,091,547	$ 971,127		
Klimas, Nancy G. (M.D.)	Miami, FL	Immunologic Mechanisms and Biomarkers in Gulf War Illness	Immune dysfunction as a mediator of persistent illness in both CFS and ill GW veterans	$ 112,400	01/01/06	12/31/09	VA–132	$ 112,400	$ 100,000		
Molina-Vicenty, Hector D. (M.D.) Blanchard, Melvin (M.D.) Reda, Domenic J. (Ph.D.)	St. Louis, MO	Evaluation of Stress Response Systems in Gulf War Veterans with CMI	Autonomic system and neurohumoral dysregulation in Gulf War veterans	$ 173,321	10/01/04	03/31/09	VA–107	$ 173,321	$ 154,200		VA–107

Attachment 2: FY 2008 ORD Support for Ongoing War Research Projects—Continued

Oddone, Eugene Z. (M.D.)	Durham, NC	Genetic Epidemiology of ALS Veterans	Identify genes that may confer susceptibility to the development of ALS and examine the interplay between environmental exposures and genetic susceptibility to ALS	$ 2,116,602	07/01/08	09/30/12	VA–151	$ 2,116,602	$ 1,883,098		
Pasinetti, Giulio M. (M.D., Ph.D.)	Bronx, NY	Biomarkers Discovery in ALS	Identification of biomarkers for ALS in CSF and serum from Gulf War veterans	$ 299,165	07/01/07	06/30/09	VA–101	$ 299,165	$ 125,000	$ 141,161	
Cook, Dane B. (Ph.D.)	East Orange, NJ	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain	Functional imaging of Gulf War veterans with unexplained musculoskeletal pain	$ 95,382	04/01/06	12/31/07	VA–096	$ 95,382	$ 72,359	$ 12,500	VA–096
Weiner, Michael W. (M.D.)	San Francisco, CA	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla	Magnetic Resonance Imaging (MRI) and Spectroscopy (MRS) of Gulf War veterans	$ 653,747	01/01/05	12/31/09	VA–125	$ 653,747	$ 581,625		VA–125
Gulf War Veterans Illnesses				**$ 758,497**							
Li, Mian (M.D., Ph.D.)	Washington, DC	Autonomic Functions of Gulf War Veterans with Unexplained Illnesses	Autonomic dysfunction as an underlying cause of unexplained symptoms in GW veterans	delayed	09/30/06	06/30/11	VA–134	$—			
Li, Mian (M.D., Ph.D.)	Washington, DC	Motor Neuron Function of Gulf War Veterans with Excessive Fatigue	Loss or damage of motor nerve cells in GW veterans with muscle and joint pain, muscle spasm, or fatigue	delayed	09/30/06	12/31/10	VA–135	$—			

Attachment 2: FY 2008 ORD Support for Ongoing War Research Projects

Bach, Ronald R. (Ph.D.)	Minneapolis, MN	Tissue Factor and Gulf War-Associated Chronic Coagulopathies **Gulf War-Associated Chronic Coagulopathies: Tissue Factor, Coagulation, and Immune System Activation**.	Impaired blood flow and circulation as a cause of cognitive difficulties, somatic pain, fatigue	$ 248,741	04/01/06	**9/30/209**	VA–130	$ 248,741	$ 221,300		
Diamond, David M. (Ph.D.)	Tampa, FL	Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics	Neurobiological basis of memory and development of new therapies for memory storage and retrieval dysfunction	$ 321,148	04/01/05	03/31/09	VA–109	$ 321,148	$ 149,900	$ 135,819	VA–109
Kang, Han K. (Dr.P.H.)	Washington, DC	Estimates of Cancer Prevalence in Gulf Veterans Using State Registries	Prevalence of cancer (including brain cancers) in Gulf War veterans	$ 66,597	07/01/05	06/30/08	VA–117	$ 66,597	$ 59,250		VA–117
Mitchell T. Wallin (M.D., M.P.H.)	**Washington, DC**	**Multiple Sclerosis in Gulf War Veterans**	**Evaluation of the risk of developing MS in GW veterans**	**$ 122,010**	**10/01/07**	**09/30/10**	**VA–152**	$ 122,010	$ 108,550		
Animal Models of GW Exposures				**$ 738,996**						**$ 6,637,745**	
Shetty, Ashok (Ph.D.)	Durham, NC	Behavior of Neural Stem Cells in a Rat Model of GWS	Effects of pyridostigmine bromide, DEET, and permethrin	$ 268,901	04/01/07	03/31/10	VA–149	$ 268,901	$ 239,236		
Mullan, Michael (M.D., Ph.D.)	Tampa, FL	Proteomic Analysis of Cellular Response to Biological Warfare Agents	Effects of pyridostigmine bromide, DEET, and permethrin	$ 224,800	04/01/06	03/31/09	VA–145	$ 224,800	$ 200,000		
Panter, Scott (Ph.D.)	San Francisco, CA	Direct Delivery of Neurotoxins to the Brain by an Intranasal Route	Effects of pyridostigmine bromide, DEET, and permethrin	$ 245,295	01/01/06	12/31/09	VA–146	$ 245,295	$ 208,234	$ 10,000	
Research Advisory Committee on Gulf War Veterans' Illnesses	Topeka, KS	Annual Operating Budget		**$ 400,000**			not a project				

Attachment 2: FY 2008 ORD Support for Ongoing War Research Projects

				$ 7,037,745							
				Total FY 2008							
		UTSW IDIQ Contract		$ 15,000,000							
				$ 22,037,745							

* Includes 12.4% administrative overhead *

Attachment #3: Projected FY 2009 ORD Support for Ongoing Gulf War Research Projects

Full Name	VAMC	Title	Focus	Total FY 2009*	Start Date	End Date
Clinical Trials				$ 18,196		
Amin, Mohammad M	Northport, NY	Inspiratory flow dynamics during sleep in GWS & the effect of CPAP	Prevelance and treatment of sleep disturbances in GW veterans	$ 9,819	10/16/05	10/15/08
Tuteja, Ashok K. (M.D., M.P.H.)	Salt Lake City, UT	Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans	Treatment of GW veterans with gastrointestinal symptoms		01/01/06	12/31/09
Lin, Henry C. (M.D.)	Albuquerque, NM	Bacterial Overgrowth Associated with Chronic Mult-Symptom Illness Complex	Treatment of GW veterans with gastrointestinal symptoms	$ 8,377	10/01/08	09/30/11
Biomarkers				**$ 7,327,628**		
Fiore, Louis D. (MD)	Boston, MA	VA Gulf War Biorepository Trust	Gulf War Brain and DNA Bank	$ 5,664,976	08/01/02	09/30/08
Klimas, Nancy G. (M.D.)	Miami, FL	Immunologic Mechanisms and Biomarkers in Gulf War Illness	Immune dysfunction as a mediator of persistent illness in both CFS and ill GW veterans	$ 56,200	01/01/06	12/31/09
Molina-Vicenty, Hector D. (M.D.) Blanchard, Melvin (M.D.) Reda, Domenic J. (Ph.D.)	St. Louis, MO	Evaluation of Stress Response Systems in Gulf War Veterans with CMI	Autonomic system and neurohumoral dysregulation in Gulf War veterans	$ 93,226	10/01/04	03/31/09
Oddone, Eugene Z. (M.D.)	Durham, NC	Genetic Epidemiology of ALS Veterans	Identify genes that may confer susceptibility to the development of ALS and examine the interplay between environmental exposures and genetic susceptibility to ALS	$ 377,557	07/01/08	09/30/12

Pasinetti, Giulio M. (M.D., Ph.D.)	Bronx, NY	Biomarkers Discovery in ALS	Identification of biomarkers for ALS in CSF and serum from Gulf War veterans	$ 274,432	07/01/07	06/30/09
Cook, Dane B. (Ph.D.)	East Orange, NJ	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain	Functional imaging of Gulf War veterans with unexplained musculoskeletal pain	$ 300,782	10/01/08	09/30/12
Weiner, Michael W. (M.D.)	San Francisco, CA	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla	Magnetic Resonance Imaging (MRI) and Spectroscopy (MRS) of Gulf War veterans	$ 560,455	01/01/05	12/31/09
Gulf War Veterans Illnesses				**$ 758,294**		
Li, Mian (M.D., Ph.D.)	Washington, DC	Autonomic Functions of Gulf War Veterans with Unexplained Illnesses	Autonomic dysfunction as an underlying cause of unexplained symptoms in GW veterans	$ 25,880	09/30/06	12/31/08
Li, Mian (M.D., Ph.D.)	Washington, DC	Motor Neuron Function of Gulf War Veterans with Excessive Fatigue	Loss or damage of motor nerve cells in GW veterans with muscle and joint pain, muscle spasm, or fatigue	$ 79,242	09/30/06	12/31/08
Bach, Ronald R. (Ph.D.)	Minneapolis, MN	Tissue Factor and GulfWar-Associated Chronic CoagulopathiesGulf War-Associated ChronicCoagulopathies: Tissue *COM001*Factor,Coagulation, and Immune System Activation	Impaired blood flow and circulation as a cause of cognitive difficulties, somatic pain, fatigue	$ 273,861	04/01/06	9/30/209
Diamond, David M. (Ph.D.)	Tampa, FL	Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics	Neurobiological basis of memory and development of new therapies for memory storage and retrieval dysfunction	$ 241,520	04/01/05	03/31/09
Mitchell T. Wallin (M.D., M.P.H.)	Washington, DC	Multiple Sclerosis in Gulf War Veterans	Evaluation of the risk of developing MS in GW veterans	$ 137,791	10/01/07	09/30/10
Animal Models of GW Exposures				**$ 581,415**		
Shetty, Ashok (Ph.D.)	Durham, NC	Behavior of Neural Stem Cells in a Rat Model of GWS	Effects of pyridostigmine bromide, DEET, and permethrin	$ 273,801	04/01/07	03/31/10
Mullan, Michael (M.D., Ph.D.)	Tampa, FL	Proteomic Analysis of Cellular Response to Biological Warfare Agents	Effects of pyridostigmine bromide, DEET, and permethrin	$ 112,400	04/01/06	03/31/09
Panter, Scott (Ph.D.)	San Francisco, CA	Direct Delivery of Neurotoxins to the Brain by an Intranasal Route	Effects of pyridostigmine bromide, DEET, and permethrin	$ 195,214	01/01/06	12/31/09

Attachment #3: Projected FY 2009 ORD Support for Ongoing Gulf War Research Projects—Continued

Full Name	VAMC	Title	Focus	Total FY 2009*	Start Date	End Date
				$ 8,685,533		
				Total Distributed by ORD in FY 2009		
UTSW Medical center	Dallas, TX	Gulf War Veterans Illnesses' Research IDIQ Contract		$ 6,862,503		
				$ 15,548,036		
				Total Distributed (ORD) and Obligated (Contract) in FY 2009		

Includes 12.4% administrative overhead (all projects except IDIQ Cotnract)*

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