Research Advisory Committee on Gulf War Veterans' Illnesses

Committee Meeting Minutes
June 25, 2016

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Department of Veterans Affairs
Washington, DC

Research Advisory Committee on Gulf War Veterans' Illnesses
Department of Neurology
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I hereby certify the following minutes as being an accurate record of what transpired at the June 25, 2016 meeting of Research Advisory Committee on Gulf War Veterans' Illnesses.

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Stephen L. Hauser, M.D.
Chairman
Research Advisory Committee on Gulf War Veterans' Illnesses

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Attendance Record

Members of the Committee:
Stephen Hauser, MD, Chairman
Kimberly Adams, JD
James Bunker
Fiona Crawford, PhD
Marylyn Harris, RN
Stephen Hunt, MD
Nancy Klimas, MD
Katherine McGlynn, PhD
Jeffrey Nast, JD
Stephen Ondra, MD
Frances Perez-Wilhite
Martin Philbert, PhD
Scott Rauch, MD
Mitchell Wallin, MD
Scott Young, MD

Committee Staff:
Jon VanLeeuwen, PhD, Managing Director

Designated Federal Officer:
Victor Kalasinsky, PhD

Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
June 25, 2016

Office of Research and Development, Department of Veterans Affairs,

THIS MEETING IS A TELECONFERENCE
(1-800-767-1750; access code 56978#)
(http://va-eerc-ees.adobeconnect.com/racgwvi/)

(ALL TIMES ARE EASTERN DAYLIGHT TIME)

Agenda
Saturday, June 25, 2016

3:00 – 3:05	**Welcome; Introductory Remarks**	**Dr. Stephen Hauser, Chairman Res Adv Cmte Gulf War Illnesses**
3:05 – 5:00	**Committee Discussion: IOM Report Gulf War &Health, Vol 10**	**Dr. Stephen Hauser, Chairman Res Adv Cmte Gulf War Illnesses**
5:00 – 5:30	**Public comment**	
5:30	**Adjourn**	

Minutes (June 25, 2016 Teleconference)

Welcome, Introductory Remarks

Dr. Stephen Hauser opened the meeting by welcoming participants and asking Committee members to introduce themselves. Dialing in to the call were Kimberly Adams, James Bunker, Fiona Crawford, Marylyn Harris, Steve Hunt, Nancy Klimas, Katherine McGlynn, Jeffrey Nast, Steve Ondra, Frances Perez-Wilhite, Martin Philbert, Scott Rauch, Mitch Wallin, and Scott Young. Caroline Tanner was the only member not present. Also on the call was Jon VanLeeuwen, Managing Director of the RAC.

Dr. Hauser stated that the Committee discussion would last from noon to 2pm Pacific Daylight Time, or from 3 to 5pm Eastern Daylight Time. This would be followed by a 30-minute Public Comment session.

Dr. Hauser asked Dr. Kalasinsky to mention some procedural issues. Dr. Kalasinsky indicated that the Committee is governed by the rules of the Federal Advisory Committee Act (FACA) and that the Committee is charged to give recommendations and advice to the Secretary of Veterans Affairs. Dr. Kalasinsky is the Designated Federal Officer and serves as a liaison between VA and the Committee. Dr. Kalasinsky also mentioned that there is a court reporter making an audiotape and ultimately a transcript of the meeting and that the meeting is being transmitted over the Internet using AdobeConnect. The AdobeConnect file will be archived, and links will be placed on the Committee webpage. Dr. Kalasinsky also reminded the members of the Committee to be cognizant of potential conflicts of interest as outlined in the ethics training from the meeting before.

Committee Discussion

Dr. Hauser also reminded everyone of the charge to the Committee to provide advice and recommendations to the Secretary of Veterans Affairs. The main topic of discussion during this teleconference will be the report of the Institute of Medicine (National Academy of Medicine, NAM) entitled Gulf War and Health, Volume 10. The RAC is interested in providing advice to the Secretary regarding the recommendations in the NAM report and in so doing indicate the RAC's ideas of how the VA should move forward in Gulf War research. The draft RAC letter recommends a few areas that are different from what the NAM has suggested.

The RAC's main concerns regarding the NAM report fall into three categories:

1. Exposures in animal studies,

2. Epidemiology studies, and
3. How to interpret recommendations related to brain-body interconnectedness.

Dr. Hauser indicated that it was essential for the Committee to provide objective, well-considered advice and making sure that that advice is consistent with other advisory bodies as much as possible, and even though individual members may disagree, the committee can still provide useful advice to the VA.

Dr. Hauser reminded Committee members that even though there were areas where the RAC disagreed with the NAM report, it is very important to recognize that there are many areas of agreement. He indicated that five of the eight NAM recommendations have broad support on the RAC. These include:

1. That VA partner with DOD to incorporate emerging diagnostic technologies to study Gulf War illness,
2. That there be follow-up assessments of Gulf War Veterans with neurodegenerative diseases,
3. That further assessments of cancer incidence and prevalence and mortality be conducted,
4. That gender-specific and race- or ethnicity-specific health conditions be studied, and
5. That the top priority should be on the development and identification of effective therapeutic interventions.

Dr. Hauser indicated that the letter to the Secretary needs only to be approved by a simple majority and that as Dr. Kalasinsky mentioned if there are conflicts of interest, some members may be required to recuse themselves from discussion and voting. Dr. Hauser suggested that the main focus would be on Recommendations #2, #3, and #5 in the RAC letter.

There was no disagreement about Recommendation #1, so Dr. Hauser moved immediately to Recommendation #2 which focused primarily on exposure and animal studies. The edits made to Recommendation #2 since the April meeting were very significant.

Dr. McGlynn suggested removing a phrase from Recommendation #2 which was confusing in its reference to the NAM report. Dr. VanLeeuwen began making edits in real time and planned to send the edited versions to Committee members by e-mail before any votes were taken. Dr. Rauch asked that the Chairman read the version that was being edited because individual Committee members might be looking at different versions of the updated letter. Dr. Hauser did so.

The gist of the recommendation is that the RAC believes that properly designed exposure studies and animal studies may be very valuable in understanding Gulf War related health outcomes, and this is in disagreement with the NAM report. Animal models of Gulf War exposures have been developed and have identified mechanisms through which such exposures might lead to Gulf War illness. Dr. Young agreed with the new text because the original version had the conclusions buried in the paragraph. He indicated that the new wording is unambiguous and that is very important. Kimberly Adams also agreed that the new edit makes it very clear that the RAC disagrees with the NAM, and it also explains why. Mr. Bunker agreed with Ms. Adams, and he continued to say that the Secretary should have the various webpages on the VA website made consistent in its use of terminology for Gulf War illness. Dr. Crawford and Dr. Rauch each indicated that they agreed with Dr. Young and Ms. Adams.

Dr. Hauser indicated that he still had a problem with the text because as an animal modeler of human disease he does not have an animal model which completely replicates human disease. Animal models are important in identifying specific aspects where the animal model can mimic certain features of human disease states, but he did not think that the models for Gulf War illness were mature enough yet. He favors the use of animal models, but is concerned that it is difficult to mimic Gulf War illness because of the complexity of the condition. Dr. Crawford agreed and indicated that it is unlikely that they will be able to develop a model that mimics every aspect of Gulf War illness but there are models of Gulf War exposures where certain symptom sets can be produced. Her concern was that the NAM suggested that the development of an animal model may not be possible, and this is the notion that RAC members disagree with. She suggested that the animal models for Gulf War illness are no worse than the animal models for other human diseases and emphasized that there may never be a single animal model for Gulf War illness. However, several animal models may be developed which would be useful for studying the condition.

Dr. Hauser indicated that there seems to be agreement in the basic premise of this RAC recommendation and that the wording is the part that needs to be refined. He continued that the RAC disagreed with the NAM that animal research is likely to be unproductive. He indicated that there are many ways in which animal models can help understand different aspects of Gulf War exposures and wondered if there was a way to word the recommendation to reflect this idea. He suggested simply saying that the RAC strongly endorses continued animal research relative to the Gulf War exposures and medical consequences or biological consequences.

Dr. Crawford felt strongly that the RAC needed to challenge the NAM report. She felt that the report was extraordinarily negative with regard to animal research and that the statement that the development of an animal model may not be possible makes it sound as if no relevant model can be developed. She emphasized that the RAC needs to state its disagreement with the NAM report very clearly.

Mr. Bunker agreed that more animal studies need to be conducted especially with regard to certain of the exposures in the Gulf region. He mentioned specifically the toxic nature of the crude oil in Kuwait. He continued that it would be unethical to expose humans to toxic materials in crude oil so animal studies are the only method of doing such studies.

Dr. Klimas indicated that potential conflicts of interest may be a problem for her and Dr. Crawford because they are subject matter experts. She wondered if she would be allowed to speak on the subject. She indicated that in terms of wording the current version is a much stronger letter. And she would disagree with the NAM in that models are available now, particularly the O'Callaghan model developed with the pesticide and cortisol exposure. She was not sure how to change the wording because she liked it the way it was, but she could see why there was still disagreement.

Dr. Young indicated that he is not disagreeing; he was just concerned that it is not enough just to continue animal testing. The animal studies need to be combined with additional research.

Dr. Klimas reminded everyone that the NAM report included a section about systems biology. Dr. Young indicated that systems biology was exactly the kind of connection he meant. Dr. Hauser added that the next step is to link pathways identified in preclinical models with observations in humans.

Dr. Rauch suggested language to the effect that while the RAC would agree that there is no perfect or comprehensive animal model of Gulf War illness, animal models of Gulf War *exposure* have been developed. He said further that most Committee members might argue that there is no such thing as a perfect animal model. He also indicated that in connecting imaging studies it is common to identify an "intermediate phenotype" as the link between animals and humans.

Dr. VanLeeuwen asked for some specific language that he could insert into the recommendation. Dr. Hauser started with Dr. Rauch's suggestion "while we would agree that there is no perfect or comprehensive model for a comprehensive preclinical model of Gulf War illness, animal models of Gulf War exposures have been developed

and have identified mechanisms through which such exposures might contribute to GWI." This could be followed by "furthermore there may be new ways to approach exposure studies in animal modeling that incorporate cutting-edge research methods which could yield novel insights and that it helps accelerate progress towards effective therapies."

Dr. Crawford and Ms. Adams both agreed with the suggested wording. Ms. Adams also thought that listing specific examples was important. Dr. VanLeeuwen read back the edits that he made to the document and Dr. Wallin suggested one point of clarification. He thought it was important to be clear that the exposure mentioned in the recommendation was animal exposure. Dr. Rauch suggested that Dr. VanLeeuwen's edits be broken into two sentences for clarity. Dr. Hauser asked Dr. VanLeeuwen to send the edits to the committee so they could see the text in its entirety. Dr. Hauser indicated that the individual parts of the edits be considered separately so that members who needed to recuse themselves could do so. On the other hand, he preferred that there would be consensus without having a need for anyone to recuse himself or herself.

Dr. VanLeeuwen sent Version 5 to everyone and asked them to focus on page 3 and the track changes. Dr. VanLeeuwen read the edit "while we would agree there is no comprehensive preclinical model of GWI, animal models of Gulf War exposures have been developed and have identified mechanisms through which such exposures might contribute to GWI." Mr. Bunker, Dr. Crawford, Dr. Young, and others like the edits. Dr. VanLeeuwen was able to load a clean copy onto AdobeConnect so everyone could see it.

Dr. Hauser indicated that making two sentences could take the following form. After this phrase "accelerate progress towards effective therapies" the following should be added "For example, systems in computational biology provide exciting new direction for bringing together preclinical and human data. Application of approaches such as these to the Gulf War health outcomes research could significantly advance our understanding of how complex systems are perturbed." Mr. Nast, Dr. Crawford, and Dr. Klimas concurred with the edit. Dr. Hauser sent the modification that turns it into two sentences and asked Dr. VanLeeuwen to send it to group.

At this point Dr. Hauser suggested that the committee move on to Recommendation #3. It has to do with epidemiology studies of various conditions. There was a minor change in grammar that strengthens the recommendation. Dr. Rauch, Ms. Adams, Dr. Crawford, and others agreed with the change.

Dr. Hauser suggested the conversation move to Recommendation #5, an important recommendation which reaches out to the NAM. Dr. McGlynn agreed and felt the recommendation was well stated. Dr. Young wondered whether or not the recommendation should mention exclusively the National Academy of Medicine. Dr. Klimas agreed that perhaps it was unnecessary to specifically mention the NAM. She did agree, however, that NAM committees should be well balanced with content experts, as indicated in the recommendation. Dr. Rauch suggested that the wording say something like "such as the NAM." Dr. Young suggested "including but not limited to the NAM." Mr. Bunker suggested that the laws written by Congress specifically mentioned the IOM (NAM).

Dr. Hauser asked Dr. Kalasinsky for clarification, and Dr. Kalasinsky explained that the laws simplify the process of entering into a contract with NAM because the NAM was chartered by Congress to provide independent expert opinions to government agencies. Dr. Rauch suggested wording be changed to include "the RAC recommend VA continue to seek" something like "expert external independent input to review," "such as from the NAM" or "such as via the NAM to review," in the first part. And the second part suggests that the NAM committees should include Gulf War researchers.

Dr. VanLeeuwen said that the verbiage he had written says "the RAC recommends VA continue to seek expert external independent input, such as from the NAM, to review, evaluate, and summarize scientific literature and health issues relevant to Gulf War Veterans," and the rest was unchanged. Many members concurred with that statement.

Dr. Hauser asked Dr. Kalasinsky how NAM committee members are selected for Gulf War and Health reports. Dr. Kalasinsky indicated that neither the Office of Research and Development nor the Office of Public health (now Post-Deployment Health Services) have been involved with selecting or nominating individuals for NAM committees for the express purpose of allowing the NAM to maintain its independence.

Dr. Hauser asked Dr. VanLeeuwen to send the latest version of the letter (v 5.2) to the Committee members. Then Dr. Hauser suggested that the committee consider an earlier part of the letter which had cautions and recommendations, specifically those related to the brain-body interconnectedness.

Dr. McGlynn asked for clarification on Caution #1 before moving to Caution #3. Caution #1 deals with the ICD-9 code. Dr. Klimas commented that there is no ICD-9 code that captures Gulf War illness. This is a problem for determining how many patients in the VA are affected, and it is virtually impossible to know how many patients who use private healthcare are affected. Ms. Adams agreed.

Dr. McGlynn suggested that it was still not clear what is being recommended regarding ICD-9 codes. Mr. Bunker said that with the move from ICD-9 to ICD-10 some of the codes that were used for Gulf War Veterans are no longer in the coding system. Dr. VanLeeuwen reminded the committee that the conversation in April included concerns that ICD-9 codes are not always reported accurately; therefore, one has to be careful in using ICD-9 codes to categorize Veterans. Dr. VanLeeuwen suggested that there are actually two issues being considered - first, that there is no reliable way of using ICD-9 codes to identify patients with Gulf War illness, and second, that there are illnesses other than GWI which are also affecting Gulf War Veterans that need to be coded properly. Mr. Bunker suggested separating the two factors into different bullet points. Troops who were in the non-deployed group during 1990- 1991 might have been deployed in later conflicts and, thus, should not be considered "non-deployed" for research purposes. The other point is that there is no ICD-9 code for GWI and the existing ICD-9 codes are not reported reliably for Gulf War Veterans. Mr. Bunker and Ms. Adams reminded the group that it is also possible that ICD-9 codes that were used in the past may not exist in the ICD-10 system. Dr. Klimas indicated that there is no ICD-10 code for chronic fatigue syndrome. Dr. Klimas further indicated that with the case definition there could be an ICD-10 code for Gulf War illness because it is a diagnostic entity. She also explained that in ICD-9, chronic fatigue syndrome was categorized under neurological inflammatory disorders. In ICD-10, chronic fatigue became a *symptom* of fatigue which is not a disease code but rather a symptom code. Dr. McGlynn wondered if this issue is appropriate for a response to the NAM report.

Dr. VanLeeuwen modified the text to say that "there is reason to believe that non-deployed Veterans may have deployed to later conflicts. Secondarily there is no ICD-9/10 code for GWI. Conditions for which there are codes may not be reliably reported." Dr. Hauser suggested that the second part should contain the following: "as examples, there are no ICD-9 or 10 codes for GWI, and chronic fatigue syndrome is a condition in ICD-9 but not 10." Dr. Hauser agreed with Dr. McGlynn that this is not a major point of difference between the NAM and the RAC.

Dr. Hauser suggested that the Committee move to the brain-body interconnectedness issue and review the edits that had been made. Dr. Klimas and Dr. Rauch agreed that the current version is much better than the original. There was a brief discussion of the relevance of brain cancer to the brain-body interconnectedness, but it was determined that that discussion should be deferred to a later time.

Dr. Hauser asked Dr. VanLeeuwen to send current version of the letter to all the members. Dr. VanLeeuwen indicated that the earlier section now said "there is reason to believe that non-deployed Veterans may have deployed to later conflicts. Secondarily

ICD-9/10 codes may not be reliably reported. For example, GWI has no ICD-9/10 code, and CFS has been coded in ICD-9 but not ICD-10." Dr. Rauch suggested changing the wording about the ICD system to suggest that there were limitations with regard to GWI. He suggested "moreover, there are fundamental limitations in the ICD system with regard to characterizing GWI - both that GWI doesn't have a code and the codes that are being used for the component systems are limited and lack continuity across the subsequent versions." This was modified to read "... are limited and lack continuity from one version to the next, such as CFS which is charted differently in ICD-9 and ICD-10." The last part was further edited to read "…one version to the next (e.g., CFS has a code in ICD-9 but not ICD-10)."

Mr. Bunker also suggested that the recommendation include language to remind VA to use the term Gulf War illness and not the various terms that are currently in use on the VA website.

Dr. Houser asked if there was a motion to approve the edited version of the letter. Mr. Bunker so moved, and Dr. Crawford seconded. Individual members were asked for a "yes" or "no" vote, and the vote was unanimous to accept the letter as edited.

Public Comment

The Public Comment session began at two minutes past the hour. The first speaker was Brian Sell; he had submitted a letter to Dr. Kalasinsky prior to the meeting.

Mr. Sell is a Gulf War Veteran and a Veteran of Panama. His main concern with the Volume 10 NAM report is that it appears to suggest no further research on the causes of Gulf War illness and would focus only on research linked to health care. Mr. Sell has sarcoidosis, fibromyalgia, chronic fatigue syndrome, and PTSD, and he indicated that he receives excellent care at the Miami VA Medical Center. His problem with VA and the NAM is that he did not believe they did a thorough enough investigation of health issues affecting Gulf War Veterans. His submitted letter deals specifically with sarcoidosis and wonders why NAM has not considered that condition.

Denise Nichols called in to compliment the committee on their excellent review of the NAM recommendations. She wanted to stress, however, that research studies need to include the units that people were assigned to, the unit locations, and the age at which various conditions were diagnosed in patients. She also wanted to emphasize that cardiovascular problems are not receiving enough attention. She is also concerned about PTSD, mortality issues, strokes, pulmonary emboli, and rashes. There is also

concern among family members about birth defects and other problems that appear to be transmitted to offspring.

Ronald Brown mentioned two very rare endocrine cancers that he has discussed with Drs. Hunt, Klimas, and Drew Helmer. Mr. Brown is concerned about cancers developing now that it has been 25 years since the Gulf War. He also wanted to thank the Committee for the outstanding job they did with their recommendations.

Steve Hohman wanted to follow-up with Ms. Nichols' comments and indicated that he is currently being treated for tachycardia. He is also concerned that diabetes may start showing up Gulf War Veterans as it has Vietnam Veterans. He indicated that some of the members of his unit thought they were on the registry list but found that they are not because they enrolled prior to 1995. He also wanted to indicate his appreciation to the Committee for all their efforts and, in particular, the letter that they were discussing during the first part of the call.

Tracie Johnston's husband visited the WRIISC in March and received a diagnosis of Gulf War illness. When he returned to his local VA last week, he was told that since there was no code for Gulf War illness he could not be treated for Gulf War illness. He is being treated for fibromyalgia, chronic fatigue, asthma, sleep apnea, and Mrs. Johnston was glad that the RAC discussed the codes for GWI.

Gina Smith served nine months in the Gulf. Prior to that time, she was very healthy but has had health problems since then - a splenectomy, major surgery, and a recent hysterectomy. Every time she goes to the doctor it seems like they find something new that they cannot explain. She goes to VA and recently was diagnosed with Gulf War illness at the WRIISC. She filed for benefits almost 10 years ago and has been denied at every appeal. She thanked Mr. Brown and Mr. Bunker for their advocacy for Gulf War Veterans.

Wayne Leifried also wanted to thank Mr. Brown and Mr. Bunker, but he had a comment about the VA as a whole. He is receiving better care of the VA then he received from civilian doctors for so many years.

Denise Nichols asked if she can make two more comments. She is concerned about hypercoagulation and the research conducted by Dr. Ron Bach which supports the original studies that she conducted with Dr. Brewer in 1999. Dr. Bach is running a treatment trial using prednisone, but in the meantime she is trying to get the VA to test Veterans clinically for hypercoagulation. She is also concerned about a viral connection because Veterans are testing positive for parvovirus HHV-6. Ms. Nichols had one

additional comment that was prompted by an earlier reference to Vietnam Veterans. She would like to see a comparison of the presumptive conditions available to atomic Veterans, Vietnam Veterans, and Gulf War Veterans because their problems are linked to exposures. She also thanked the Committee again for their work.

In closing, Dr. Hauser asked Dr. VanLeeuwen about the next RAC meeting. It will be on August 8 and 9 at the San Francisco VA Medical Center. The details will be posted on the RAC webpage.

The teleconference was adjourned at 5:30pm (EDT).