

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
National Center for Toxicological Research**



**Ranch Hands Advisory Committee
September 7, 2006
Rockville, Maryland**

Record of the Final Proceedings

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ATTACHMENT 1

List of Participants

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Guest Presenters, Media and Members of the Public

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American Chemistry Council

Mr. Clark Brooks
Greenville News

Ms. Jeanne Brooks
Greenville News

Dr. Mark Brown
Department of Veterans Affairs

Dr. David Butler
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Dr. Frederick Erdtmann
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Ms. Darlene Superville
Associated Press

Mr. Rick Weidman
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**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH**

**FINAL MEETING OF THE RANCH HANDS ADVISORY COMMITTEE
September 7, 2006
Rockville, Maryland**

Minutes of the Final Meeting

The Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) National Center for Toxicological Research convened the final meeting of the Ranch Hands Advisory Committee (RHAC). The proceedings were held on September 7, 2006 at FDA's Washington Operations Office, 5630 Fishers Lane in Rockville, Maryland.

Opening Session

Dr. Michael Stoto, the RHAC Chair, called the meeting to order at 8:33 a.m. and welcomed the attendees to the proceedings. He opened the floor for introductions.

Dr. Leonard Schechtman, the RHAC Executive Secretary, read a statement into the record to confirm that no RHAC members had financial or other conflicts of interests with any of the topics listed on the September 7, 2006 meeting agenda.

Review of Previous Meeting Minutes. Dr. Stoto announced that the previous meeting minutes were distributed to RHAC for review and comment. The current draft reflected changes submitted by Dr. Stoto.

Dr. Stoto entertained a motion to approve the revised version of the minutes. A motion was properly placed on the floor and seconded by Drs. Trewyn and Hassoun, respectively. RHAC unanimously approved the revised version of the February 27, 2006 RHAC Meeting Minutes with no further changes or discussion.

Update on the Air Force Health Study (AFHS) Custodian

Dr. Stoto opened the floor for representatives of three different agencies to provide their perspectives on the AFHS custodian.

Medical Follow-up Agency (MFUA) Perspective. Dr. Frederick Erdtmann is the MFUA Director at the Institute of Medicine (IOM), National Academy of Sciences (NAS). He described MFUA's perspective on the AFHS custodian. Congress commissioned IOM to conduct a study with two major purposes: (1) determine the continued value of the AFHS data and materials and (2) identify an appropriate home if the research assets were found to have future benefit.

IOM formed the AFHS Disposition Committee (AFHSDC) with outside experts to assist in responding to its charge. AFHSDC determined that the AFHS database was unique and had enormous potential as a research asset in the future. AFHSDC proposed MFUA and seven other sources to house the AFHS data and materials, but did not recommend a "best" option. As a result, Congressional staff and members reviewed AFHSDC's report and implemented a decision-making process to identify the best option.

During a meeting with Congressional staff and members, Dr. Erdtmann expressed MFUA's strong interest and willingness in becoming a custodian of the AFHS materials. He also obtained formal approval from IOM's governance and leadership to undertake this responsibility. Following these discussions, the 2007 Defense Authorization Bill indicated that the Department of Defense (DOD) would transfer the AFHS assets to MFUA. However, MFUA's role as the AFHS custodian is not finalized at this time. The authorization bill has not been passed and signed into law. Funds have not been appropriated to transfer the AFHS assets to MFUA. Congress has not identified a funding source to support future research with the AFHS assets.

Dr. Erdtmann reminded RHAC that AFHSDC identified three elements of costs in using the AFHS research assets: (1) maintain, manage and secure data; (2) manage new research projects; and (3) and maintain biological specimens. AFHSDC also recommended the allocation of \$250,000 in seed funds for three consecutive years to market the AFHS assets and attract interest within the research community. These dollars could be used to support pilot projects that might eventually be expanded into large studies funded by federal agencies or private foundations.

Dr. Erdtmann made additional remarks about MFUA's perspective of the AFHS custodian in response to RHAC's questions and comments.

- No organization is serving as a “champion” or “watchdog” to ensure that the 2007 Defense Authorization Bill is appropriated. However, veteran’s service organizations would most likely make a strong public outcry if this action is not taken because a 25-year effort has been dedicated and an investment of \$174 million investment has been contributed to AFHS.
- RHAC might have a role in encouraging appropriation of the 2007 Defense Authorization Bill and ensuring that this effort remains on the critical path in the final decision-making process. For example, RHAC could write a letter to appropriate Congressional committees to (1) reiterate its position on the value of the AFHS assets; (2) reinforce the continued use of the AFHS assets in future research; and (3) list additional opportunities in this effort.
- The AFHS assets might have commercial value in which pharmaceutical companies and other industries in the private sector would pay for access to the data and materials for research purposes. However, research by private entities would be conducted under careful scrutiny to ensure that any studies would advance knowledge of health and health outcomes in both veteran and general populations. All future research efforts would be thoroughly reviewed by advisory boards to ensure that studies conducted with the AFHS assets were of high merit and value. The source of research funds would be fully acknowledged and carefully monitored to promote transparency to the public.
- If funds are appropriated to MFUA to serve as the AFHS custodian, efforts would be made to partner with a federal agency because NAS does not maintain serum or specimen repositories. MFUA would most likely approach DOD, the Centers for Disease Control and Prevention (CDC), or the National Institutes of Health (NIH) in this effort. MFUA would also approach private sector groups if a federal partner could not be secured.
- The cost to maintain the AFHS specimens was estimated to be \$250,000 per year, but MFUA would also need additional funds of ~\$1.2 million per year to support staff salaries to manage the AFHS database, specimens and pilot projects.
- Maintenance and use of the AFHS database would be limited to a five-year period. If the AFHS assets were not found to be self-sustaining or were not determined to have continuing utility after this period of time, MFUA would archive the database. MFUA would initiate a review and evaluation process to make this determination.
- MFUA was recently incorporated into the new IOM Board on Military and Veteran’s Health (BMVH). As the two IOM research oversight groups, BMVH and MFUA will broaden activities beyond epidemiologic studies to analyze all phases in the life cycle of military personnel from entry into the service to death. BMVH is also an outcome of DOD’s continuing efforts to

increase its knowledge and understanding of deployment health by tracking, documenting and maintaining records of deployment health effects.

Dr. Erdtmann concluded his remarks by reiterating MFUA's strong interest and willingness in serving as the AFHS custodian. If the 2007 Defense Authorization Bill is appropriated, he confirmed that MFUA would closely collaborate with the U.S. Air Force (USAF) in FY'07 to transfer the AFHS assets in a safe, seamless and swift manner. Dr. Erdtmann thanked the past and present RHAC members for contributing their time over the past 25 years to provide advice and guidance to USAF on the extremely important and valuable AFHS research assets.

Department of Veterans Affairs (VA) Perspective. Dr. Mark Brown is the Director of the Environmental Agents Service in the VA Office of Public Health and Environmental Hazards. He described VA's perspective on the AFHS custodian. Congress mandated VA to fund the AFHS disposition study, but the legislation did not require VA to reach conclusions or make recommendations on the outcomes of this research activity. However, VA closely followed the disposition study due to the role, influence and importance of AFHS in other research mandated by Congress on health outcomes from dioxin or herbicides in both veteran and general populations.

AFHSDC did not recommend the continuation of AFHS as an ongoing epidemiological study, but VA and seven other sources were proposed as potential custodians to maintain the data, biological samples and other health information for future studies. However, VA expressed the following concerns with AFHSDC's proposal for VA to serve as the AFHS custodian.

- The VA Office of Research and Development's research budget of ~\$400 million per year is small, strictly intramural, and specifically targeted to veteran's health issues. VA's intramural research program is based on proposals that are developed, originated and submitted by individual investigators.
- VA would need to obtain new informed consent forms from each AFHS participant or the families of deceased veterans.
- Interagency problems would arise if VA served as the AFHS custodian. The AFHS data set would be divided between DOD and VA, but these agencies have completely different missions.
- The AFHS data might not be applicable to other studies on veteran health issues because the Ranch Hand cohort is unique and is not representative of Vietnam veterans or the general veteran population.
- AFHS has a history of controversy due to misgivings among Vietnam veterans, their families and advocates about AFHS's approaches,

openness, transparency, credibility and independence. These groups have also expressed concerns about DOD's fairness in conducting the research. As the AFHS custodian, VA would inherit this public criticism and might also be expected to immediately reverse DOD's previous findings. For example, veterans might expect VA to identify a new association between health effects and exposure to Agent Orange.

- VA is extremely concerned about public perception of its role and involvement in AFHS, particularly with its current focus on other research priorities. For example, VA is now conducting studies on mental health issues among veterans returning from Afghanistan and Iraq. VA realizes that the public expects the agency to be fair and equitable across all veteran populations.
- AFHSDC indicated that the AFHS database would be self-supporting because researchers would pay to obtain access to these valuable biological samples and other data. VA did not necessarily agree with this conclusion.
- Existing statutory language requires DOD and VA to allocate funds of ~\$500,000 per year to MFUA to maintain other databases. VA is not entirely supportive of this legislation because its portion of these funds is taken from the medical care budget for the care of patients rather than the research budget. VA would be solely liable for the costs of serving as the AFHS custodian because its appropriators would not allocate additional funds for this effort.

Dr. Brown acknowledged that VA expressed numerous concerns in serving as the AFHS custodian, but he noted VA is also aware of four major benefits. First, AFHSDC concluded that the AFHS data and materials had value and should be maintained and used for other research purposes. AFHS's original intent and specific study design were to analyze health effects from herbicides in the Ranch Hand cohort. However, these data could be used for broader research purposes. For example, a cause-specific mortality study would be fairly easy and inexpensive to conduct. A longitudinal geriatric study could be performed on this segment of the U.S. population to identify health issues over time.

Second, the AFHS database has been well advertised at this point. Third, MFUA has a demonstrated track record in serving as the repository for databases DOD maintains on military populations. Fourth, investigators may develop innovative strategies in the future to use the AFHS assets. Dr. Brown did not have any new information on the pending legislation, but his understanding was that AFHS would be concluded on September 30, 2006 and MFUA would serve as the new custodian of the data and materials.

USAF Perspective. Col. Karen Fox is the AFHS Principal Investigator. She described USAF's perspective on the AFHS custodian.

- The 2007 Defense Authorization Bill indicated that USAF would need to leverage funds to support the transfer of the USAF data and materials. USAF is now attempting to identify monies for this effort.
- USAF plans to give its equipment to the new custodian in accordance with language in the 2007 Defense Authorization Bill.
- USAF will assign a small team to remain onsite to ensure that electricity for the freezers continues to operate after September 30, 2006.
- USAF initiated transition activities to address AFHSDC's recommendations. USAF's update on these activities is scheduled on the agenda.
- During informal conversations with USAF, some federal agencies expressed an interest in partnering with MFUA to maintain the AFHS serum and specimens.

Col. Fox concluded her remarks by emphasizing that USAF would be extremely pleased to obtain consent from the AFHS participants to transfer the data to a new custodian due to the richness of this asset.

Dr. David Butler, of IOM/NAS, provided additional details about AFHSDC's findings. The major recommendations were to (1) provide the custodian with seed funding for three years; (2) organize and format the data to facilitate future research; and (3) conduct an evaluation after five years to assess the continuing merit in providing access to the AFHS data for research.

AFHSDC concluded that five years would be a sufficient amount of time to implement the recommendations, determine if the research community had continued interest in using the AFHS data and specimens, and establish whether the AFHS resources had value and relevance as a resource. Additional provisions would need to be made if researchers expressed an interest in using the AFHS assets. Although AFHSDC did not specify an agency or organization to conduct the five-year evaluation, Dr. Butler reiterated that BMVH and MFUA represent two IOM research oversight groups with expertise in evaluating epidemiologic studies.

Dr. Stoto made several comments to guide RHAC's discussion on the AFHS custodian. Costs to maintain the AFHS assets and costs to conduct research with the AFHS data and materials are two separate issues. On the one hand, a government agency should allocate funds to the new custodian to maintain the AFHS assets. On the other hand, federal agencies or private foundations could allocate funds to investigators to conduct research with the AFHS assets. He asked RHAC to focus its discussion on

arrangements that should be made to ensure the AFHS data and materials were accessible to researchers in the future.

Dr. Stoto also requested RHAC's input on Dr. Erdtmann's suggestion for RHAC to play a role in the final decision-making process of the AFHS custodian. He raised the possibility of RHAC writing a letter to the VA authorization and appropriations committees to:

- endorse the findings of the AFHSDC report;
- reiterate RHAC's position about the value of the AFHS assets;
- emphasize the national interest in allocating funds to support the costs of maintaining and providing access to the AFHS assets for a limited period of time; and
- reinforce the importance of making arrangements to ensure that researchers continue to have access to the AFHS data and materials in the future.

Several RHAC members requested that the following suggestions be considered in the final decision-making process of the AFHS custodian.

- MFUA should consider VA as a federal partner to maintain the AFHS serum and specimens in addition to CDC, DOD and NIH.
- Evaluations should be conducted on an annual basis rather than at the end of five years. This ongoing process should be designed to answer the following questions: (1) Is the cost of maintaining the AFHS assets justified? (2) What are specific examples in which the AFHS assets were used? (3) What strategies could be applied to promote the use of the AFHS data and materials if these assets were not utilized?
- The AFHS assets should be marketed as having broad relevance to "humans" rather than advertised with a narrow focus on "military veterans" or "civilians."

Update on the AFHS Closeout Activities

USAF and its contractors provided updates on activities in several areas that have been completed or are underway to support the transition and closeout of AFHS.

Dioxin 2006 Conference. Col. Fox reported that USAF presented two posters and made two oral presentations during the Dioxin 2006 Conference in Oslo Norway. The two posters illustrated mortality in USAF veterans of Operation Ranch Hand and the viability of stored serum specimens. The two oral presentations focused on an overview

of AFHS and congeners in serum of 800 USAF veterans. USAF previously presented data from the posters and oral presentations to RHAC.

Col. Fox noted that the conference participants expressed concern about the closure of AFHS and asked USAF to provide information on efforts to maintain the data and collaborate with other entities. USAF informed the participants about its strong interest in another institution overseeing AFHS and ensuring that the data would be available for future research. Col. Fox pointed out that 800-1,200 persons typically attend the annual dioxin conferences.

Technical Reports and Manuscripts. Col. Fox reported that time constraints did not allow USAF to submit a number of studies to peer-reviewed journals for publication. As a result, the following four studies will be released as USAF technical reports to ensure that these data are available in the future: (1) the AFHS Compliance Report; (2) “Third Source Causation: An Alternative Explanation for the Check Mark Pattern;” (3) “A Matched Analysis of Diabetes Mellitus and Herbicide Exposure in Veterans of Operation Ranch Hand;” and (4) “Post-Service Mortality of Air Force Veterans Occupationally Exposed to Herbicides During the Vietnam War: Final Report.” USAF previously presented all four studies to RHAC.

USAF also has two outstanding manuscripts under its contract with Science Applications International Corporation (SAIC) that were not previously presented to RHAC. “Serum Dioxin and Memory Among Veterans of Operation Ranch Hand” will be submitted to a peer-reviewed journal and the “Nerve Conduction Study Data Verification and Review Report” will be released as a USAF technical report. Col. Fox announced that all of USAF’s technical reports would be available on the DOD web site for public access.

Dr. Marian Pavuk, of SpecPro, Inc., provided an overview of USAF’s two manuscripts that were not previously presented to RHAC. In the “Serum Dioxin and Memory Among Veterans of Operation Ranch Hand” study, Ranch Hand veterans in the high category scored significantly higher than comparison veterans on the immediate and delayed recall trial of the Wechsler Memory Scale (WMS) logical memory sub-test during the 1982 examination. No substantial differences were reported for the immediate and delayed visual reproduction and associate learning sub-tests with WMS in 1982.

The 1982 memory data were re-analyzed in 2002 with the addition of 94 more veterans who had dioxin measurements in 2002 and participated in the 1982 memory assessment. Memory assessment data from the 2002 examination were also analyzed and the 1982 and 2002 results were compared as well. The re-analysis focused on logical memory delayed recall in 1982; immediate and delayed logical memory recall in

2002; and differences between the paired standardized scores for logical memory in 1982 and 2002.

Results of the re-analysis are as follows. Previous findings with the 1982 data that showed small memory deficits in immediate and delayed logical memory recall in the high exposed group of Ranch Hand veterans were confirmed. However, some of these results were no longer statistically significant because data from the 2002 examination did not show memory deficits observed with the 1982 data. The comparison of standardized memory scale scores between 1982 and 2002 showed no indication of memory function deterioration in Ranch Hand relative to comparison veterans.

Enlisted ground crew Ranch Hand veterans had the highest exposure to dioxin, but results in this group were consistent with those of other Ranch Hand veterans. The re-analysis indicated that Ranch Hand veterans who were exposed to Agent Orange functioned normally in the context of immediate and delayed memory function. The 1982 examination found small memory deficits in groups of veterans with the highest exposure, but the 2002 examination did not show significant memory deficits. The cause of memory deficits observed in veterans in 1982 is unknown and cannot be contributed at this time to confounding variables; structural, neurochemical or other neurological mechanisms; or other factors.

In the "Nerve Conduction Study Data Verification and Review Report," Dr. Pavuk reported that data collected in 1992 and 1997 indicated statistically significant increased odds of probable and diagnosed peripheral neuropathy among Ranch Hand veterans with higher dioxin levels. The goal of the data verification and review was to use nerve conduction study (NCS) results to validate clinical diagnoses of peripheral neuropathy among 60 selected AFHS participants. The subject matter expert who performed the review was not provided with data on diabetes and was blinded to the identity of Ranch Hand versus comparison veterans.

The review of the NCS data showed the following results: 56 veterans had peripheral neuropathy; 4 veterans had no evidence of generalized peripheral neuropathy; and 46 veterans showed signs of conduction slowing. Toxic neuropathies caused by toxicants typically do not result in the slowing of conduction velocity. In terms of diabetes, 34 of 56 veterans with peripheral neuropathy had diabetes; 18 of 28 Ranch Hand veterans had diabetes; and 16 of 28 comparison veterans had diabetes.

The review of the NCS results established a diagnosis of generalized peripheral neuropathy in 56 of the 60 selected AFHS participants based on conventional criteria. Of these 56 veterans, 82% had NCS evidence of generalized peripheral neuropathy characterized by conduction slowing. This finding supported the possibility that participants with diabetes mellitus or impaired glucose tolerance might causally

contribute to the pool of AFHS participants with clinically evident peripheral neuropathy. The presence of substantial conduction slowing was in contrast to findings associated with most forms of toxic or non-diabetic neuropathy.

The influence of aging on the neurologic examination and NCS results was found to be important. The mean age of the study population at the time of the NCS evaluation was 68.4 years with a range of 54-87.7 years. Although aging influenced results of the NCS and clinical neurological testing, the effects of normal aging on the peripheral nervous system are not well understood. Overall, the NCS confirmed the clinical cutoff of peripheral neuropathy and was found to be a superior method of diagnosing this condition.

External Collaborations. Col. Fox reported that USAF sent a letter to all principal investigators (PIs) involved with AFHS throughout its 25-year history. The purpose of the letter was to provide formal notification of the closure of AFHS and ask all PIs to destroy the AFHS data sets and biological specimens or return these materials to USAF. USAF took this action in response to recommendations in the AFHSDC report, but its legal advisors reviewed and approved the letter prior to dissemination.

USAF sent a total of 49 letters to 45 PIs with electronic data sets and 4 PIs with biological specimens. Certified follow-up letters were mailed to PIs who did not respond to the original letter. USAF's letter resulted in the following collaborative efforts.

- Dr. Amit Gupta, of the University of Texas Southwestern Medical Center, submitted "Anthropometric and Metabolic Factors and Risk of Benign Prostatic Hyperplasia: A Prospective Cohort Study of Air Force Veterans" to *Urology* for publication.
- Dr. Steven Boyle, of Duke University Medical Center, submitted the following two papers to the *International Journal of Behavioral Medicine* and *Brain, Behavior and Immunity*, respectively, for publication: (1) "The Relation of Hostility, Anger and Depression to Five-Year Increases in Lipids and Lipoproteins" and (2) "Hostility, Anger and Depression Predict Increases in C3 Over a Ten-Year Period."
- Dr. Laurie Haws, of ChemRisk, and Dr. Michael Gough, of the George C. Marshall Institute, presented the following abstract at the Dioxin 2006 Conference and submitted the following paper to *Environmental Health Perspectives*, respectively, for publication: (1) "Are Dioxin Body Burdens Surrogates for Other Risk Factors in Association Between Dioxin and Diabetes?" and (2) "Evaluation of the Association Between Serum Dioxin Levels and Type 2 Diabetes in Air Force Veterans Occupationally Exposed to Herbicides in Vietnam."

- Dr. Lynn Frame, of Texas Tech University Health Sciences Center, produced a paper on the association between sleep disorders and dioxin that was accepted for publication by the *Journal of Epidemiology*. USAF reviewed and cleared Dr. Frame's other two papers for publication on "sleep disorder and dioxin levels as a metabolic syndrome," but has been unable to obtain the final status of these studies. Dr. Frame has been unavailable due to her long-term illness.

Col. Fox provided additional details about USAF's external collaborations in response to specific concerns raised by several RHAC members. Dr. Joel Michalek is the former AFHS PI and author of the cancer study. In addition to sending the formal PI letter, USAF also had numerous telephone conversations and e-mail communications with Dr. Michalek to establish an agreement to finalize and publish the study.

USAF confirmed Dr. Michalek's receipt of these communications and his knowledge of the clearance requirements, appropriate channels and process to collaborate with USAF. Although he did not pursue an external collaboration with USAF, Dr. Michalek is free to establish a relationship with the new AFHS custodian and obtain permission to finalize and publish the cancer study.

Col. Fox added that to USAF's knowledge, typical research contract restrictions between federal agencies and employees of academic institutions did not play a role in Dr. Michalek's failure to enter into an agreement with USAF as an external collaborator. As with another PI, USAF intended to use its existing contract with SAIC to allocate funds to Dr. Michalek to finalize and publish the cancer study. These efforts were planned because USAF's scientific group reviewed the cancer study and recognized the benefits in completing this research.

Although USAF made strong efforts to engage Dr. Michalek as an external collaborator, Col. Fox expressed concerns about the analysis. The cancer study and its findings of diabetes were based on different years and various days of spraying in Southeast Asia. Significant outcomes were reported, but the study design did not indicate that a hypothesis was developed before the data were analyzed. Due to these concerns, Col. Fox emphasized the critical need for the cancer study to be peer reviewed.

Col. Fox clarified that Dr. Michalek and all other PIs would only be required to destroy or return AFHS data sets or biological specimens specified in the letter. The PIs have given USAF the original data and are allowed to retain the raw data. USAF intends to provide the new custodian with data, but submission of this information would depend on new consent forms submitted by AFHS participants. Col. Fox emphasized that USAF took every possible action to facilitate the publication of the cancer study in the scientific literature for future access.

RHAC was divided in providing advice and recommendations on publishing Dr. Michalek's cancer study in the peer-reviewed literature or releasing the paper as a USAF technical report. On the one hand, some members took the following position.

- USAF should make every effort to ensure that all AFHS studies and analyses conducted by credible scientists are published in the scientific literature for future access and availability to the research community.
- AFHS studies are a matter of public record because the data were previously presented to IOM, RHAC and other groups.
- The cancer study produced several significant outcomes. Due to these findings, a number of RHAC members previously advised USAF to re-analyze the data on cancer and other health effects.
- The omission of the cancer study in the peer-reviewed literature or as a USAF technical report might decrease the credibility of AFHS or contribute to public perceptions that AFHS was "suppressed" because this research showed significant findings.

On the other hand, other members took the following position.

- Dr. Michalek and all other PIs received appropriate notice about the closure of AFHS and were given numerous opportunities to enter into agreements with USAF as external collaborators.
- The termination of AFHS in less than 23 days required USAF to take actions to closeout this activity.
- Dr. Michalek informed individual RHAC members of his interest in finalizing and publishing the cancer study, but he did not state these intentions privately to USAF or publicly to RHAC.

Dr. Stoto acknowledged that RHAC and USAF would be unable to resolve the dilemma on publication of the cancer study during the meeting. As a result, he closed the discussion by expressing his personal opinion on this issue. AFHS analyses that were conducted beyond the five cycle reports and previously presented to RHAC should be available to the research community in the future for further review and evaluation.

Dr. Stoto agreed that Dr. Michalek should not maintain personal data on individual AFHS participants due to privacy and confidentiality issues. However, he raised the possibility of USAF giving Dr. Michalek permission to publish the statistical summaries, tables, regression analyses and other data from the cancer study that were previously presented to RHAC. Dr. Stoto's position was that USAF should make every possible effort to facilitate the publication of the cancer study in the scientific literature.

Program Management Activities. Dr. Judson Miner is the Research Director of Operational Technologies Corporation (OTC) and a former AFHS PI. He provided an update on activities Program Management has completed or is currently conducting for the closeout of AFHS. All permanent civilian and technical contractor slots will be removed from the technical team as of September 30, 2006.

Lt. Col. Julie Robinson, another former AFHS PI, will remain onsite as a term civil service employee. She will oversee a transition administrative team of 6.5 full-time equivalents (FTEs). The transition team will complete tasks as recommended by AFHSDC, such as transferring the AFHS assets to the new custodian; providing technical assistance for the data sets and records; shipping materials; and obtaining permission and consent from the AFHS participants. Program Management will also have a transition team of 1.5 FTEs

In terms of contracting efforts, Program Management has asked SAIC to ensure that AFHS data in the Relational Informational Warehouse (RIW) are more usable to the new custodian. Program Management will attempt to extend this activity to FY'07 to provide even more assistance to the new custodian. SAIC has also been asked to complete a report on the AFHS and Project Ranch Hand II Program History. The report would summarize AFHS activities that were conducted and Program Management's best practices and lessons learned. In addition to SAIC, contracts would also be established with SpecPro, Core6 and OTC for transition and Program Management activities related to contracting efforts.

With respect to funding, Congressional language in the pending FY'07 Defense Authorization Bill is identical in both the House and Senate. Program Management would carry over contingency funds from its FY'06 budget in the event that Congress does not pass the federal budget by October 1, 2006 and federal agencies would be required to operate under a continuing resolution. The contingency funds would ensure that electricity to the freezers would remain operational after September 30, 2006. However, these dollars would only provide support for ~3 months.

Program Management informed the USAF Headquarters Program Element Monitor about the funding disconnect until Congress passes the federal budget. In 2001, Program Management also informed the House and Senate VA committees about the closure of AFHS on September 30, 2006 and the need to allocate funds to transfer the data and materials. The pending FY'07 Defense Authorization Bill would require USAF to use its individual funds to maintain the data and specimens for one year after the closeout of AFHS.

Dr. Miner concluded his remarks with some personal observations about AFHS from Program Management's perspective. AFHS has been a political and controversial issue

for a variety of sources, including RHAC, veteran's groups and the media. Program Management monitored and managed a \$139.6 million budget for more than 26 years; 50 separate contracts over the course of conducting AFHS; and logistics for ~12,000 person-trips to physical examinations. Program Management's integrated product team systems approach was highly successful in completing the AFHS protocol as directed by the White House. Dr. Miner thanked RHAC for providing valuable support to Program Management over the past 25 years.

Transition Activities. Col. Fox reported that USAF has completed or is currently conducting transition activities in response to AFHSDC's recommendations. More than 2,000 boxes with hard copies of the AFHS medical records and other pertinent materials are ready to be shipped to St. Louis, Missouri for storage for 30 years. After this period of time, the hard copies would be sent to the National Archives for permanent archiving. All of the hard copies of the AFHS medical records and other materials have been digitized for electronic storage. More than 80,000 biological specimens were reorganized.

Efforts are underway to construct electronic files of the AFHS data to provide the new custodian with a data dictionary and ensure the new custodian understands the values of the database. USAF expects its remaining personnel to complete this activity. Efforts are also underway to load all AFHS data into the RIW to provide the new custodian with a single and searchable program. The RIW will be populated with specific AFHS databases.

USAF's legal advisors reviewed and approved a letter and transfer consent form that will be mailed to all AFHS participants. The purpose of these documents would be to formally notify the participants about the closure of AFHS, provide information on the new custodian, and request permission to transfer personal data to the new custodian. USAF is now attempting to locate participants who cannot be found with addresses in the existing database.

For deceased participants, USAF would automatically transfer their data to the new custodian. For participants who do not give USAF permission to transfer their data, these materials would be maintained for one year and then destroyed if the participants still do not grant permission after this time. However, hard copies of the medical records and other data that will be sent to and stored in St. Louis are a part of AFHS and would be retained. Col. Fox thanked RHAC for providing solid support to USAF over the past 25 years.

Public Comment Period

Mr. Rick Weidman is the Director of Government Relations for Vietnam Veterans of America (VVA). He made the following remarks in response to the presentations and RHAC's discussions.

- VA did not request additional research and development dollars from the Office of Management and Budget to fund MFUA's ongoing databases, studies and other veteran-related activities. VA only received increased funding for these efforts in response to strong advocacy by military and veteran service organizations.
- The pending legislation in both the House and Senate proposes the allocation of \$850,000 to USAF to continue to catalogue the AFHS data and materials, transfer freezers and provide other equipment to the new custodian. The pending legislation also proposes the allocation of up to \$200,000 to the new custodian to prepare for receipt of the AFHS biological specimens and other data from USAF.
- VVA provided public testimony to strongly support the recommendation for MFUA to serve as the custodian of the AFHS data and biological specimens. MFUA's unimpeachable integrity for over 70 years would most likely ensure that all of the AFHS assets would be publicly available to the scientific community for future research. VVA's position is that no governmental entity could serve as a "neutral" custodian based on AFHS's 25-year history.
- VVA is in favor of a valid and reputable academic institution in the metropolitan Washington, DC area maintaining the AFHS biological specimens, such as The Johns Hopkins University, Georgetown University, George Washington University, the University of Maryland, James Madison University, George Mason University, or Howard University. NAS should use its facilities at the Keck Building in Washington, DC to house the other AFHS data due to existing security controls at this location.
- VVA strongly supports valid, legitimate and reputable scientists and institutions submitting requests for applications rather than requests for proposals to conduct research with the AFHS assets. This approach would require applicants to develop solid hypotheses prior to applying for research dollars. This strategy would also ensure that earmarked funds are set aside for scientists.
- VVA intends to closely collaborate with Congressional staff and provide additional public testimony to ensure that the following actions are taken.
(1) Funding should be allocated to support AFHS for five years after the September 30, 2006 closeout date.

(2) Seed monies should be provided to the new AFHS custodian, but this amount should far exceed \$250,000 per year for three years as recommended by AFHSDC.

(3) NIH should allocate a portion of its tremendous research budget to veteran-specific studies. NIH has a history of funding epidemiological studies of cohorts in foreign countries rather than U.S. citizens who pledged their lives to protect the United States against all foreign and domestic enemies.

(4) VA should be required to comply with its federal mandate to conduct the National Vietnam Veterans Longitudinal Study with cohorts of veterans who served in Vietnam, veterans who served in the military outside of Southeast Asia, and non-veterans. Vietnam veterans typically die 20 years earlier than the general U.S. population and this research could potentially fill data gaps about the morbidity and early mortality rates among Vietnam veterans. However, studies conducted or funded by the NIH National Cancer Institute generally do not test against the null hypothesis by asking participants questions about their military experience in Korea or Vietnam.

In addition to his public comments, Mr. Weidman also asked RHAC to consider taking the following actions. One, RHAC should write letters to appropriate Congressional committees to formally endorse the findings of the IOM AFHS disposition study. Two, RHAC should write letters to NIH and the Labor HHS Committee and Appropriations Subcommittee in the House and Senate to emphasize the need to target funding to veteran-specific research.

Three, RHAC should write letters to the DOD, HHS and VA Secretaries to reinforce the need to allocate funds to MFUA to serve as the AFHS custodian. data. The letter should also note that these dollars must be made available for legitimate scientists and research institutions to have access to the AFHS analyses, tables and other data paid for by American taxpayers. RHAC's letters and solid reputation might have an influence on VA conducting studies in the future on veteran health effects from ionizing radiation and Agent Orange.

Mr. Weidman concluded his remarks by thanking the RHAC members for their vigorous and long-standing efforts in advocating for the health of Vietnam veterans and the entire nation. He also thanked USAF and its contractors for their outstanding efforts in conducting AFHS.

RHAC Business

Dr. Stoto made several remarks to guide RHAC's discussion on unresolved or additional issues. He asked the members to consider Mr. Weidman's three recommendations to RHAC. One, RHAC should formally endorse the IOM AFHS disposition study and support the recommendation for MFUA to serve as the custodian of the AFHS assets. Two, RHAC should formally support the allocation of NIH funding to veteran studies. Three, RHAC should urge DOD and VA to support future research with the AFHS data and materials and should also write letters to appropriate Congressional committees in this effort.

Dr. Stoto provided his perspectives about Mr. Weidman's three recommendations. For recommendation 1, RHAC should formally endorse the findings of the IOM AFHS disposition study in general terms, but should not advocate for MFUA or any other specific group to serve as the new AFHS custodian. For recommendation 2, formal support of NIH funding to veteran studies is beyond RHAC's purview. RHAC is not chartered to provide advice and guidance to NIH. For recommendation 3, each RHAC member is a special government employee and is prohibited from writing letters to Congress in this capacity. However, the members would be free to write letters to Congress as private citizens after their terms on RHAC ended.

Dr. Stoto also asked the members to consider whether the following three guiding principles should be reflected in the meeting minutes as RHAC's final consensus opinion about AFHS. First, RHAC commends USAF for its diligent efforts in conducting outstanding activities related to AFHS, producing solid data, and generating high-quality and excellent science over the past 25 years. USAF's efforts have been tremendously valuable to IOM, VA, veterans and the entire nation. AFHS was an extremely complex endeavor, but USAF produced a national treasure. RHAC also acknowledges USAF's complete professionalism during contentious discussions with RHAC and in controversial settings with other groups.

Second, RHAC agrees with and formally endorses the overarching findings of the IOM AFHS disposition study. Most notably, AFHS data and materials that have been gathered beyond the published reports are extremely valuable. The availability of these assets to other researchers in the future is in the national interest. The findings of the IOM AFHS disposition study are consistent with RHAC's previous recommendations to USAF.

Third, USAF should make every effort to ensure all AFHS analyses that were conducted and presented to RHAC are available to the research community in the scientific literature. Overall, USAF has already ensured that cycle reports and other studies or papers have been or will be published in peer-reviewed journals or released to the

public as technical reports. However, the inability of the public to access the cancer study might diminish AFHS's credibility, particularly since this research showed different findings than other papers. USAF should make every possible effort to provide public access to results of the cancer study analyses that were conducted during the course of AFHS.

Several RHAC members made comments in response to the three guiding principles that Dr. Stoto described.

- USAF should develop a follow-up method to address AFHS manuscripts that were "submitted" to peer-reviewed journals. For example, submission of these papers to journals would not necessarily guarantee acceptance and publication. USAF should have strategies available to rapidly release "submitted" AFHS manuscripts as USAF technical reports in the event these papers are not actually "accepted" by peer-reviewed journals. This approach would ensure that all AFHS data are available to and accessible by the research community in some form.
- USAF made every effort to enter into an agreement with the author of the cancer study. The burden is now on the author rather than USAF to solicit an external collaboration and complete and publish the study.

RHAC **generally agreed** that the three guiding principles proposed by Dr. Stoto should serve as RHAC's final consensus opinion about AFHS.

Recognition and Appreciation

Col. Fox and Lt. Col. Robinson presented certificates of appreciation from USAF to three persons in recognition of their diligent efforts: (1) Dr. Leonard Schechtman, the RHAC Executive Secretary; (2) Ms. Kimberly Campbell, the RHAC Management Specialist; and (3) Ms. Nadine Rivera, the writer/editor of the RHAC meeting minutes. The participants applauded the valuable contributions of these persons.

Dr. Schechtman expressed HHS's and FDA's sincere gratitude and appreciation for the time and dedication that each RHAC member contributed to providing valuable advice and direction in the conduct and evaluation of AFHS. His formal recognition of the current RHAC membership is outlined below.

- Dr. Michael Stoto is a Professor of Health Services Administration and Population Health at the Georgetown University School of Nursing and Health Studies. He served as both an RHAC member and the chair from February 1999-2003 and 2003-September 2006.

- Dr. Paul Camacho is the Director of Special Projects at the William Joyner Center, University of Massachusetts-Boston. He served as an RHAC member from October 2000-January 2004 and from February 2004-September 2006.
- Dr. Ezdihar Hassoun is the Vice Chair of the Department of Pharmacology at the University of Toledo College of Pharmacy. She served as an RHAC member from February 2004-September 2006.
- Dr. David Johnson is the Executive Medical Director of the Division of Environmental Health at the Florida Department of Health. He served as an RHAC member from February 2004-September 2006.
- Dr. Sanford Leffingwell is an Occupational and Environmental Medicine Consultant with HLM Consultants. He served as an RHAC member from July 2003-September 2006.
- Dr. Kwame Osei is the Director of the Division of Endocrinology, Diabetes and Metabolism at the Ohio State University College of Medicine. He served as an RHAC member from August 2000-January 2004 and from February 2004-September 2006.
- Dr. Robert Sills is the head of the Molecular Pathology Laboratory of Experimental Pathology at the NIH National Institute of Environmental Health Sciences. He served as an RHAC member from August 2000-January 2004 and from February 2004-September 2006.
- Dr. Ronald Trewyn is the Vice Provost for Research and Dean of the Graduate School of Kansas State University. He served as an RHAC member from July 1995-January 1999 and from November 2001-September 2006.

Dr. Schechtman confirmed that certificates of appreciation and letters of recognition signed by the HHS Secretary would be sent to the RHAC members. He also acknowledged the valuable contributions of five other persons: (1) Drs. Michael Gough and Robert Harrison, former RHAC Chairs; (2) Mr. Ronald Cooney, the former RHAC Executive Secretary; (3) Ms. Barbara Jewell, the former RHAC Management Specialist; and (4) Ms. Kimberly Campbell, the current RHAC Management Specialist, for overseeing the logistics of RHAC meetings.

Dr. Schechtman clarified that his formal acknowledgment of the current RHAC membership in no way diminished the importance of the participation and service of former members. He emphasized that FDA also expresses deep gratitude to these persons.

Closing Session

Dr. Stoto closed the final meeting by thanking each RHAC member, USAF and FDA staff for their outstanding efforts and tremendous contributions to AFHS over the past 25 years.

With no further discussion or business brought before RHAC, Dr. Stoto adjourned the meeting at 1:14 p.m.

I hereby certify that to the best of my knowledge, the foregoing Minutes of the proceedings are accurate and complete.



12/1/2006
Date

Michael A. Stoto, Ph.D.
Chair,
Ranch Hands Advisory Committee

12/1/2006
Date



Leonard M. Schechtman, Ph.D.
Executive Secretary,
Ranch Hands Advisory Committee