

DEPARTMENT OF HEALTH AND HUMAN SERVICES

and

**FOOD AND DRUG ADMINISTRATION
NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH**

convene the

RANCH HAND ADVISORY COMMITTEE MEETING

***Rockville, Maryland
September 22, 2004***

RECORD OF THE PROCEEDINGS

TABLE OF CONTENTS

	<u>Page</u>
Opening Session	1
Approval of Previous Meeting Minutes	2
Update by the AFHS Principal Investigator	2
Review of Chapter 19: Immunology	4
Review of Chapter 8: Covariates	5
Review of Chapter 12: Psychology	5
Review of Chapter 16: Hematology	6
Review of Chapter 15: Cardiovascular	6
Review of Chapter 7: Statistical Methods	7
Review of Chapter 5: Study Selection and Participation	8
RHAC Business	11
Public Comment Period.....	12
Closing Session.....	15

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**RANCH HAND ADVISORY COMMITTEE MEETING
September 22, 2004
*Rockville, Maryland***

Meeting Minutes

The Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) National Center for Toxicological Research (NCTR) convened a meeting of the Ranch Hand Advisory Committee (RHAC). The proceedings were held on September 22, 2004 at the Food and Drug Administration, 5630 Fishers Lane in Rockville, Maryland.

Opening Session

Dr. Michael Stoto, the RHAC Chair, called the meeting to order at 8:17 a.m. He welcomed the participants to the meeting and opened the floor for introductions. The following individuals were present for the deliberations.

RHAC Members

Dr. Michael Stoto, Chair
Dr. Paul Camacho
Dr. Ezdihar Hassoun
Dr. David Johnson
Dr. Sanford Leffingwell
Dr. Ronald Trewyn
Dr. Robert Sills

U.S. Air Force Representatives

Col. Karen Fox
Mr. William Keihl
Dr. Joel Michalek
Mr. William Murray
Mr. Richard Ogershok
Lt. Col. Julie Robinson
Mr. Larry Walden

FDA/NCTR Representatives

Dr. Leonard Schechtman
RHAC Executive Secretary

U.S. Air Force Contractors

Mr. Manuel Blancas
UDTech

Ms. Kimberly Campbell
Committee Management Specialist

Dr. William Grubbs
Science Applications International
Corporation

Dr. Diane Mundt
Environ

Dr. Judson Miner
Operational Technologies Corporation

Dr. Kenneth Mundt
Environ

Dr. Maurice Owens
Science Applications International
Corporation

Ms. Jaclyn Petrello
Exponent

Ms. Meagan Yeager
Science Applications International
Corporation

Mr. Fred Razzaghi
Consumer Healthcare Products
Association

Guests

Mr. George Hawley
Veterans of Foreign Wars

Mr. Rick Weidman
Vietnam Veterans of America

Approval of Previous Meeting Minutes. Dr. Stoto announced that the previous meeting minutes were distributed to RHAC for review and comment. The draft was modified to reflect Dr. Stoto's changes on the "Future Use of Biological Samples" presentation. Dr. Trewyn suggested that the third bullet on page 8 be revised as follows: "Provide a breakdown of in-country Vietnam versus other locations where the comparison group served."

Dr. Stoto entertained a motion to approve the previous meeting minutes as modified; a motion was properly made and seconded by Drs. Trewyn and Leffingwell, respectively. The April 30, 2004 RHAC Meeting Minutes were unanimously approved as modified with no further discussion. Dr. Stoto confirmed that in the future, draft meeting minutes will be immediately sent to Dr. Joel Michalek, the Air Force Health Study (AFHS) Principal Investigator for technical review and comment.

Update by the AFHS Principal Investigator

Dr. Michalek covered the following items in his status report. First, he gave a detailed briefing to the National Academy of Sciences (NAS) Institute of Medicine (IOM) panel. Second, he summarized his presentations at Dioxin 2004 and third, he summarized current AFHS research.

The purpose of the IOM presentation was to respond to a critique by the IOM panel of the AFHS cancer paper published in the *Journal of Occupational and Environmental Medicine* in February 2004. An earlier paper, published in the *American Journal of Epidemiology*, highlighted a main effects model in which Ranch Hands with high, low and background exposure levels were compared to comparisons. The analysis was published in 1998 and showed no exposure effect.

Based on RHAC's advice, USAF removed the main effects model from the analysis and applied new strategies. Most notably, the analysis of cancer incidence by dioxin category was readjusted to reflect years spent in Southeast Asia (SEA) and the potential for exposure to Agent Orange. The new analysis showed an effect when stratified and was driven by a significant interaction in which the relationship between cancer and dioxin category changed with years in SEA.

An AFHS paper on dioxin and peripheral neuropathy published in *Neurotoxicology* in 2002 was also discussed during the briefing. The data showed a significant increase in the risk of probable peripheral neuropathy with increased dioxin category, but the most recent NAS report found the analysis to be less than convincing. Moreover, NAS did not conclude that the data suggested an exposure effect. As a result, the IOM panel is currently re-analyzing the paper and has asked USAF to provide additional details on the data and study results.

Second, AFHS data were presented during the *Dioxin 2004* conference in Berlin in September 2004. The insulin sensitivity paper further explored the diabetes association seen in AFHS participants. The cancer paper displayed trends in comparisons only to better understand cancer in Ranch Hands. The mortality paper compared mortality between Ranch Hands and 19,000 comparisons. Advantages of the analysis include a large sample size and major covariates of date of birth, rank and military occupation. However, the study is limited because important covariates of smoking and family history of heart disease in the 19,000 comparisons are not available. Analyses of the mortality data showed a significant increase in the risk of cardiovascular death among Ranch Hand enlisted ground crew.

The metabolic syndrome paper showed an association between metabolic syndrome and subsequent cardiovascular death in controls, but not among Ranch Hands. USAF is thoroughly reviewing these data because several outcomes in the Ranch Hand group are not currently understood, such as a change in the expected pattern of metabolic syndrome in cardiovascular mortality; increased cardiovascular mortality in Ranch Hand enlisted ground crew; and lack of an exposure association among living persons who presented to Scripps Clinic. USAF is reexamining each death among Ranch Hand enlisted ground crew to determine whether competing risks were overlooked during the initial analysis.

Third, Dr. Michalek reported on several additional active research activities. Prostate cancer and dioxin papers are currently being developed with a larger database. The additional cases will provide more opportunities to analyze and display results. All cases of heart disease among Ranch Hand enlisted ground crew are being thoroughly examined. Responses are being prepared to address issues raised by the IOM panel on the AFHS peripheral neuropathy paper. A paper is currently being developed on cancer in the Ranch Hand group as a follow-up to the paper on cancer in the control group. Recent data are being incorporated into the new paper to build on trends seen in the control group.

The new paper on the Ranch Hand group will feature a larger sample size than the paper on the control group. The data set of controls contained 355 of 1,700 persons with at least one tumor, while the new data set of Ranch Hands contains 450 of 800 persons with verified malignancy. However, the Ranch Hands database is still being updated. The cancer paper will compare years spent in SEA and cancer risk among personnel who were and were not in Vietnam. Efforts are underway to also determine locations of these personnel in SEA, including Japan, Okinawa and Taiwan.

Dr. Stoto remarked that the ongoing activities illustrate the value of AFHS data and strong efforts USAF has made to expand the original study design beyond issues related to health effects from Agent Orange and other herbicides. The interesting outcomes USAF is now seeing in controls should be particularly emphasized while decisions are made about the disposition of AFHS. Dr. Robert Sills, of the National Institute of Environmental Health Sciences (NIEHS), was extremely pleased that USAF responded to RHAC's previous recommendation to publish AFHS data in peer reviewed publications. This strategy has increased the strength and credibility of the data. He commended USAF on its diligent efforts in compiling and analyzing the wealth of information that has been collected.

Chapter Reviews

RHAC members were assigned the different health study chapters to review prior to this September 22, 2004 meeting and submitted comments in advance of the meeting or provided written and/or oral comments at the time of the meeting.

Review of Chapter 19: Immunology

Dr. Leffingwell was charged with the review of Chapter 19 and Appendix F-11. His comments along with recommendations by other RHAC members are outlined below.

- Place abbreviations for Table 19-2 immediately after the section that is defined rather than at the end of the table.
- Explicitly state in Section 19.2.1 that the number excluded did not significantly differ between groups.
- Repeat the title of “Analysis of CD3+ Cells” in sub-tables (a)-(h) in Table 19-4.
- Change line 1628 to “which fights invading organisms such as ...”.
- Italicize “(Callithrix jacchus)” in the references.

Review of Chapter 8: Covariates

Dr. Sills was charged with the review of Chapter 8. His comments along with recommendations by other RHAC members are outlined below.

- Add asterisks to the tables to more easily identify significant associations, such as “*p<0.05” or “**p<0.001.”
- Delete “The purpose of the chapter” on lines 571 and 629 and begin the sentences with “It was determined whether the covariates used throughout this report ...”.
- Delete “in this report” on line 631.
- Add a references section of statistical methods to the chapter to better inform readers who may be unfamiliar with covariate associations with estimates of dioxin exposure.

Review of Chapter 12: Psychology

Dr. Hassoun was charged with the review of Chapter 12 and Appendix F-4. Her comments along with recommendations by other RHAC members are outlined below.

- Add asterisks to the tables to clearly define significance levels, such as “*p ≤0.05.”
- Add a reference to clarify that the “Verbal Paired Associates test” described on line 427 is an algorithm cited from the literature or provided by the Centers for Disease Control and Prevention on scoring psychological tests.
- Explain that the “alcohol use” covariate in Section 12.1.3.2 is used as both a covariate and dependent variable.

- Describe the “Unadjusted and adjusted analyses for Models 2 and 3” on line 496.
- Add the maximum possible values for the Wechsler Memory Scale-Revised in Table 12-1. Change the heading of the fourth column in the table to “Cutpoints/Maximum Scores.”
- Include text in Appendix F-4 to define significance levels.
- Clarify in Appendix F-4 that the maximum correlation for Pearson’s correlation coefficient is 1.0 and the minimum correlation is -1.0.

Review of Chapter 16: Hematology

Dr. Trewyn was charged with the review of Chapter 16 and Appendix F-8. His comments along with recommendations by other RHAC members are outlined below.

- Broaden the introduction to highlight research on non-dioxin herbicides, related chemicals and other types of species, such as toxicological studies on 2-4-D and cacodylic acid. Add a paragraph to describe the evolution of the study. For example, the AFHS progressed beyond research on Ranch Hand occupational exposures to a more comprehensive focus on dioxin due to increased capacity over time to measure serum dioxin.
- Emphasize that new analyses are showing hematological effects when adjusted for years spent in SEA, but this covariate is not reflected in the report. Include language to inform readers that these data are forthcoming.
- Clarify that line 126 refers to the “animal species” of dioxin.

Review of Chapter 15: Cardiovascular

Dr. Leffingwell was charged with the review of Chapter 15 and Appendix F-7. His comments along with recommendations by other RHAC members are outlined below.

- Insert text on lines 398-401 to explain that ECG variables can be mutually exclusive categories.
- Change “strongest” to “stronger” on line 441 since only two Doppler signals exist.
- Place abbreviations for Table 15-1 immediately after the section that is defined rather than at the end of the table.
- Incorporate language to explain that significant differences were seen between the number excluded in Ranch Hands and comparisons for both the “Resting Pressure Index” and “Family History of Heart Disease Before

- Age 45" variables in Table 15-2. Clarify that the differences were seen in both the "Group" and "Categorized Dioxin" categories.
- Repeat the title of "Analysis of Essential Hypertension" in sub-tables (a)-(h) in Table 15-3.
 - Change the titles as follows: "Analysis of Abnormal Tibial Pulses" for Table 15-26; "Analysis of Abnormal Leg Pulses" for Table 15-27; and "Analysis of Abnormal Peripheral Pulses" for Table 15-28. Repeat the titles in sub-tables (a)-(h) for the respective tables.
 - Italicize "(*Callithrix jacchus*)" on line 2784 and "(*Orizias latipes*)" on line 2816.
 - Revise line 2819 to read "cytochrome P5401A."
 - Widen the space between columns in Table F-7, particularly since the "w" in the "Enlisted Groundcrew" column is on a line by itself.
 - Change the title of Section 15.1.12 from "Mode of Action" because the text actually refers to toxicological effects in animals.
 - Modify the "Discussion" section on page 15-112 to immediately present the study findings rather than discuss cardiovascular disorders. Move the first three paragraphs of the "Discussion" section to the "Background" section on page 15-1.

Review of Chapter 7: Statistical Methods

Dr. Stoto was charged with the review of Chapter 7 and Appendix E. His comments along with recommendations by other RHAC members are outlined below.

- Explain that the statistical models were used in previous reports and remain the same for the sake of continuity. However, emphasize at the beginning of the chapter that different models are used in AFHS studies published in the scientific literature.
- Outline the rationale for not adding summary tables to the statistical methods chapter.
- Change the title of Section 7.2.2.1 to "Prior Knowledge Regarding Dioxin Elimination" and reorganize the text for clarity. Add language to discuss the adequacy of serum dioxin measures taken in 1987 and thereafter as proxies of doses received in Vietnam in the 1960s.
- Incorporate lines 176-183 into Section 7.2.2.1 since this text also refers to serum dioxin measures.
- Clarify the assumption in Section 7.2.2.1 that <10 ppt lipid-adjusted dioxin levels are equivalent to background levels.

- Revise Model 1 to clarify the underlying assumption that herbicide and dioxin exposures are proportional, and the latter is not measured or assessed.
- Include an additional advantage and disadvantage in Model 1: it follows the original AFHS design. The disadvantage is that Model 1 does not incorporate new data on the degree of exposure and may result in an inaccurate classification.
- Include an additional disadvantage in Model 2 to discuss the limitations of using body mass index (BMI) as a covariate to assess health. BMI is not sufficient to fully control for the complex relationship between dioxin and obesity.
- Revise “does not account for dioxin exposure after SEA” in Model 2 to clarify that dioxin was actually measured in 1987 or thereafter. Add text to explain that the estimate in Model 2 is in response to the interest of AFHS participants in using their initial doses only.
- Clarify the assumption in Model 3 that “dioxin body burden has been eliminated with time.” The model actually assumes a first-order elimination rate. Also, note that the model assumes that adding BMI as a covariate may not fully adjust for any relationship between obesity and the dioxin elimination rate.
- Clarify the statement in Model 3 that the data are “less dependent on the accuracy of the estimation algorithm for initial dioxin than Model 2.” Explain that power is actually lost by treating continuous variables as categorical.
- Revise the statement that Model 3 “makes no use of prior belief that some Ranch Hands received unusually large doses in Vietnam”. It is well documented that some enlisted ground crew actually were exposed to large doses.
- Add text in Model 3 to clarify that some comparisons were employed by U.S. industries, received substantial dioxin doses, possibly through occupational exposures, and are experiencing approximate first-order elimination, and have dioxin pharmacokinetics and associations between health and dioxin.
- Modify Model 4 to illustrate that “ppt” was measured if the result was present in 1992 and extrapolated to 1987 if the lipid-adjusted dioxin level was >10.
- Delete the advantage in Model 4 of “using 1987 dioxin has less inherent variation than initial dioxin” because the two models are statistically equivalent.
- In Section 7.5.5, another approach is to think of a statistically significant but clinically not meaningful difference as evidence that a fraction of those exposed might have clinically meaningful differences.

- Replace “ppq” in the formula on line 139 with a “w” to illustrate wet weight measured in femtograms.
- Add text or a footnote to Model 1 to explain that a significant number of comparisons were stationed in Vietnam.

Review of Chapter 5: Study Selection and Participation

Dr. Camacho was charged with the review of Chapter 5 and Appendix C. His comments along with recommendations by other RHAC members are outlined below.

- Distinguish between the “hostile” and “final refusal” classifications on line 64.
- Include additional information to more clearly delineate the “Replacement Protocol” on page 5-2, such as the number of replacements over the course of AFHS; outcomes with persons who replaced original comparisons; length of time individuals remained in AFHS; and number of original participants who remained in AFHS throughout its duration. Describe specific components of the algorithm used in the replacement protocol. For example, original comparisons were replaced, but not replacements. The original comparison and replacement could participate in AFHS at the same time because invitations to reenter AFHS were extended to all original participants. Replacements were not assigned to original comparisons who were deceased, could not be located or refused participation in AFHS.
- Acknowledge on line 129 that refusals who were asked to provide “their self-perception of health” may create a bias in AFHS. However, explicitly state the benefits and potential problems of this strategy. Replicate the flow chart in the statement of work as an appendix to the chapter to further illustrate known or suspected factors that would influence participation in AFHS.
- Add language to line 205 to clarify that “no replacement was made if formerly invited comparisons in a matched set were deceased.” Explain that the Ranch Hand case remained in AFHS in this instance. Repeat this text in the “Statistical Methods” chapter.
- Modify Table 5-3 to illustrate that “Reasons for Refusal by Group” are for 2002 only.
- Explicitly state on line 320 whether the reasons for refusal based on age, military rank and race are statistically significant or practically important.

General Comments on Health Study Chapters

Several overarching comments were made about the seven chapters reviewed during the meeting. In general, RHAC noted that USAF responded effectively to its previous recommendation to add summary sections and tables to the chapters. This text was found to be extremely helpful. RHAC also pointed out that the chapters were clear, well written and easy to understand.

In particular, Dr. Sills found the tables and text in the covariates chapter to be consistent and in the appropriate order. The chapter accomplished its goal of determining whether covariates used throughout the report were associated with estimates of herbicide or dioxin exposures. The data supported the fact that dioxin was significantly associated with military occupation in which officers, enlisted flyers and enlisted ground crew had the lowest to highest exposure levels, respectively. The covariates chapter also contained a clear explanation of the data to assist readers, particularly significant associations between dioxin and health measurements on page 8-42.

Dr. Sills commended USAF for citing research on cardiovascular morbidity and mortality in the cardiovascular chapter, including study results by the Dow Chemical Company, International Agency for Research on Cancer, and National Institute for Occupational Safety and Health. Overall, he was pleased about the tremendous progress USAF has made in reporting critical AFHS data. These efforts clearly represent a model for future studies on potential exposures to hazardous substances and agents. Dr. Sills recognized USAF's diligent efforts in compiling a vast amount of information that has been collected over the years for AFHS. He was confident that these activities would result in an outstanding product.

Dr. Stoto was aware that USAF encountered several difficulties in writing the statistical methods chapter. For example, the chapter contains highly technical information, but some readers may have no training or knowledge in the field. USAF made outstanding efforts in explaining these complex data to a non-technical audience. Moreover, models used in the original AFHS design would not currently be implemented due to more recent data collected and new statistical capacity developed over time. USAF adequately describes and justifies its rationale for applying these outdated models.

RHAC suggested that the following global changes be considered across all chapters of the report. First, table titles should be repeated in each instance where a table has corresponding sub-tables. Second, "Discussion" sections should be modified to immediately discuss the findings of the particular chapter. For example, the first few paragraphs of "Discussion" sections should be moved to "Background" sections. Relevant text in "Discussion" sections should be repeated in the "Executive Summary."

Third, USAF should note that Ranch Hands and controls were told their respective dioxin categories because this knowledge may impact the overall assessment of well-being.

USAF thanked RHAC for its thorough reviews of the chapters. In accordance with general practice, USAF and its contract authors will review, evaluate, and respond to all RHAC comments that were raised during the meeting and other editorial changes submitted in writing. USAF will distribute a matrix to illustrate RHAC's recommendations and USAF's resolution of each comment. Dr. Stoto asked USAF to report on its resolution of RHAC's recommendation to revise "Discussion" sections during the next meeting.

RHAC Business

Dr. Stoto provided an update on an action item that was raised at the previous meeting. RHAC agreed that Dr. Stoto would write a letter to HHS Secretary Tommy Thompson with a copy to Congressional staffers and Mr. Anthony Principi, the Department of Veterans Affairs (VA) Secretary. The letter would outline the following points. Congress mandated a study to determine the disposition of AFHS data. The 2003 Benefits Act directed the VA Secretary to enter into a contract for the study 60 days after the legislation was signed on December 16, 2003, but the VA has yet to sign the contract or provide funds. RHAC is on record with its concern that the VA has not fulfilled its responsibility according to the legislation.

Dr. Stoto invited the VA Secretary or his representative to attend the September 2004 RHAC meeting to discuss this issue. To date, neither HHS nor the VA has responded to RHAC's letter, nor did the VA send a representative to the meeting. Dr. Stoto will extend another invitation for the VA to attend the next RHAC meeting. He acknowledged RHAC's awkward position in this matter because the disposition of AFHS data falls under the purview of Congress, USAF and the VA, but RHAC's charter is limited to advising the HHS Secretary.

Dr. Camacho expressed an interest in raising more awareness about the disposition of AFHS data and the VA's failure to fund the study. He planned to discuss this issue in a letter to major veterans' organizations, such as the American Legion, American Veterans, Disabled American Veterans, Veterans of Foreign Wars, and Vietnam Veterans of America. Each organization could then broadly disseminate the letter to its respective constituency. Dr. Stoto noted that Dr. Camacho would take this action as an individual citizen rather than as an RHAC member.

Dr. Leonard Schechtman, the RHAC Executive Secretary, proposed potential dates for the 2005 meetings: the week of February 14 or 21, 2005 for the first meeting; the week

of May 1 or 23, 2005 for the second meeting; the week of September 11 or 18, 2005 for the third meeting; and the week of November 1, 2005 for the fourth meeting. Days that meetings cannot be convened include May 26 and 27, 2005 for the second meeting and November 1 and 4, 2005 for the fourth meeting. FDA will poll RHAC by e-mail with as much advance notice as possible to confirm dates. USAF pointed out that two of the 2005 meetings will be needed to present the final report and provide an update on closure activities, ongoing research and additional findings. As a result, USAF estimates that only two RHAC meetings may need to be convened in 2005. USAF will determine in the near future whether additional meetings will be needed.

Dr. Schechtman thanked the RHAC members for completing and submitting their conflict of interest (COI) forms in a timely manner. The COI form that needs to be completed for 2005 will be e-mailed to each RHAC member in July 2005. The deadline for completing and submitting the document to FDA will be two weeks following the mailing. FDA will provide members with a copy of their respective COI forms for 2004.

Dr. Schechtman noted that HHS requires *Federal Register* notices for upcoming meetings to be published well in advance of the meeting date. As a result, FDA and RHAC will need to draft agendas no later than 60 days in advance of the upcoming meeting. Changes to agendas that will be published in the *Federal Register* can be submitted up to 45 days in advance of the meeting. However, only critical modifications that can be justified will be approved.

Dr. Stoto listed assignments for the third cycle of reviews that will be conducted during the next meeting. Dr. Trewyn will review Chapter 10-Neoplasia; Dr. Sills will review Chapter 11-Neurology; Dr. Hassoun will review Chapter 13-Hepatic; Dr. Johnson will review Chapter 14-Dermatology and Chapter 20-Pulmonary; Dr. Leffingwell will review Chapter 18-Endocrine; and all RHAC members will review Chapter 21-Conclusions and Executive Summary, but Dr. Camacho will serve as the lead reviewer.

Dr. Kwame Osei will be assigned Chapter 14 if he is able to attend the next meeting. FDA will provide each RHAC member with the assignment list and all chapters for the next review cycle. Dr. Sills commended Ms. Kimberly Campbell, the Committee Management Specialist, for her outstanding efforts in distributing materials and making logistical arrangements for the meetings.

Public Comment Period

Mr. Rick Weidman, Director of Government Relations for Vietnam Veterans of America (VVA), outlined the organization's perspective of AFHS. Although AFHS has been an ongoing activity for more than 25 years, the original study questions have still not been

answered. AFHS samples and other data gathered to date will be extremely useful in addressing these issues. For example, Ranch Hands were selected as the study population because the Department of Defense and VA claimed no evidence had been produced to validate that individuals were exposed to herbicides. Data collected since that time show that military personnel, particularly enlisted ground crew, were indeed exposed.

Despite the collection of these valuable data, VVA has noted several major flaws and is now questioning whether AFHS should continue in its current form. First, AFHS was initiated as a study on herbicides, but the original design will not be useful to Vietnam veterans and their families. AFHS should be expanded beyond its focus on dioxin to include other chemicals, participants and confounders that may be relevant to the overall validity of the findings, such as veterans who were hostile to or non-compliant with AFHS and replacements of original comparisons. These confounders should then be compared to a null hypothesis. The IOM previously considered VVA's recommendation and reviewed studies on health effects from PCBs.

Second, no scientific evidence has been produced to validate that levels <10 ppt are not harmful. Third, AFHS was not designed with a non-veteran cohort. Time in SEA has been measured, but no comparative research has been conducted to identify differences in overall health effects between USAF personnel who served in Vietnam and non-veterans. AFHS needs four separate cohorts to clearly make this determination: Ranch Hands, non-veterans, USAF personnel with no service in SEA, and USAF personnel with service in SEA. Congress authorized and appropriated funds for AFHS to provide Vietnam veterans and their families, the veterans community and the American public with confidence that the findings will make a tremendous contribution in addressing whether Vietnam veterans were significantly harmed by exposure to herbicides in SEA while serving their country.

VVA is extremely pleased that Dr. Stoto wrote a letter on behalf of the RHAC to the HHS Secretary about the disposition of AFHS data and the VA's failure to fund the NAS study in this effort. VVA agrees with RHAC that AFHS samples and other data should be transferred to the custody of NIEHS and made available to reputable researchers and legitimate research institutions. VVA plans to file a lawsuit, submit a Freedom of Information Act request, or take other political or legal actions that may be necessary if the AFHS data are not made available for further scientific study. AFHS belongs to the American public because the research was funded with taxpayer dollars to determine whether deleterious health effects of Vietnam veterans were related to their service in Vietnam. Additional research with AFHS data should be privately conducted and publicly funded through both requests for proposals and notices of funding availability to ensure future studies are appropriately designed and tested.

VVA also holds the VA accountable for not providing funds to support the National Vietnam Veterans longitudinal study in accordance with Public Law 108-183. Although NAS is expected to submit a report to Congress on the study in 2005, the VA has yet to enter into a contract. Despite its concerns, however, VVA acknowledges the contributions of all current and former RHAC members as well as the dedication and diligent efforts of USAF and its contractors in collecting and compiling a wealth of information for AFHS. VVA maintains its confidence in the VA Secretary, but recognizes that he is being poorly advised by certain sectors within the VA.

Mr. Weidman also made comments in response to RHAC's discussion of its business. The HHS and VA Secretaries should be asked to consider holding the next RHAC meeting at VA Headquarters, 810 Vermont Avenue in Washington, DC. This location could increase attendance by the public and participation by high-ranking VA officials.

Several remarks were made in response to Mr. Weidman's comments. Dr. Stoto clarified that providing guidance to extend AFHS and utilize the data in future studies are beyond RHAC's charter. RHAC is only charged with advising the HHS Secretary on the technical and scientific merits of AFHS in its current form. However, RHAC certainly agrees that AFHS samples and other data collected to date are extremely valuable and should be made available to legitimate researchers in the future. Dr. Stoto was pleased VVA agreed with RHAC's position that the VA has not fulfilled its Congressional mandate to fund the AFHS disposition study. As a federal advisory committee, RHAC is prohibited from taking certain actions, but VVA and other private organizations are free to make external efforts. Dr. Stoto confirmed that Mr. Weidman's suggestion to hold the next RHAC meeting at VA Headquarters will be considered.

Dr. Leffingwell agreed that establishing a referent cohort of the general population rather than USAF personnel would be a valuable, but daunting effort. Consideration should be given to creating a repository to apply AFHS data to studies in the civilian population. However, AFHS represents an outstanding body of research and the ability to maintain the same high level of quality in future studies is questionable. Dr. Leffingwell also appreciated external actions VVA will take in ensuring AFHS data are maintained.

Dr. Trewyn agreed that the AFHS design is flawed in some areas and RHAC's ability to make modifications is limited due to its role as a federal advisory committee. However, he was pleased to note that USAF acted on its interest and willingness to expand AFHS and publish data in peer reviewed publications. For example, USAF is now finding significant differences in the general cancer prevalence between the civilian population and Vietnam veterans in several ongoing research projects. Dr. Trewyn hoped USAF's additional efforts with the cancer data would provide opportunities for future research on cardiovascular and other health effects among Vietnam veterans.

Dr. Michalek explained that USAF and its peer review panel thoroughly discussed the concept of multiple control groups when AFHS was conceived in the mid-1970s. Due to budget limitations, AFHS could only be designed with one control group. USAF ultimately selected the control group of personnel stationed in SEA due to the realization that exposures may exist in SEA alone regardless of Agent Orange. Dr. Johnson underscored the critical need to obtain appropriate consent from AFHS participants if the data are used in the future for other research. He also emphasized that AFHS samples and other data should not be used for any purposes beyond the original intent.

Closing Session

The next RHAC meeting will be held on November 19, 2004. Dr. Stoto thanked the members for reviewing their respective chapters; USAF and its contractors for their diligent efforts in compiling the data; FDA staff for making logistical arrangements for the meeting; and members of the public for their attendance.

Dr. Stoto adjourned the meeting at 11:16 a.m. with no further discussion or business brought before RHAC.

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

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

Date

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

Date