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
November 19, 2004

RECORD OF THE PROCEEDINGS

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
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RANCH HAND ADVISORY COMMITTEE MEETING
November 19, 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 convened a meeting of the Ranch Hand Advisory Committee (RHAC). The proceedings were held on November 19, 2004 at 5630 Fishers Lane, Rockville, MD.

Opening Session

Dr. Michael Stoto, the RHAC Chair, called the meeting to order at 8:08 a.m. and welcomed the participants to the meeting. Dr. Leonard Schechtman, the RHAC Executive Secretary, read a statement into the record to confirm that no RHAC members had any financial or other conflicts of interests with any of the topics listed on the November 19, 2004 meeting agenda. Dr. Stoto 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. Robert Sills
Dr. Ronald Trewyn

FDA/NCTR Representatives
Dr. Leonard Schechtman
RHAC Executive Secretary

Ms. Kimberly Campbell
Committee Management Specialist

U.S. Air Force Representatives
Dr. Joel Michalek
2nd Lt. Margaret Montgomery
Lt. Col. Julie Robinson

U.S. Air Force Contractors
Mr. Manuel Blancas
UD Tech

Dr. William Grubbs
Science Applications International Corporation
Dr. Judson Miner, Operational Technologies Corporation

Mr. Maurice Owens
Science Applications International Corporation

Ms. Meagan Yeager
Science Applications International Corporation

Guests
Dr. David Butler
National Academy of Sciences

Dr. Gary Kayajanian
Public

Ms. Jaclyn Petrello
Exponent

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. He submitted changes to the office of the RHAC Executive Secretary prior to the meeting and opened the floor for other members to propose revisions as well. He entertained a motion to approve the minutes as modified; a motion was properly made and seconded by Drs. Trewyn and Johnson, respectively. With no further discussion, the September 22, 2004 RHAC Meeting Minutes were unanimously approved as modified. Dr. Stoto requested that in the future, he receive changes to the minutes submitted by the U.S. Air Force (USAF) to ensure the comments are appropriate from a technical perspective.

Update on the Air Force Health Study (AFHS) Disposition Study

Dr. David Butler, of the National Academy of Sciences (NAS), explained that the Veterans Benefits Act of 2003 contained a Congressional mandate to conduct the AFHS disposition study. The law was signed in December 2003 and directed NAS to address several elements in conducting the study. First, the scientific merit of retaining and maintaining medical records, other data and laboratory specimens collected during the course of AFHS should be evaluated. Second, the existence of privacy concerns or other ethical and logistical obstacles to retaining and maintaining AFHS materials, data and laboratory specimens should be identified. Third, advice should be given on providing independent oversight of AFHS medical records, other materials and further study of the records, data and specimens. The mechanism for providing such oversight should also be outlined if further studies are conducted. Fourth, recommendations should be made on the potential value and cost of extending the AFHS and the most appropriate federal or non-federal entity to continue the AFHS. Fifth, guidance should be given on making laboratory specimens that have been collected during the course of

the AFHS available for independent research. This advice should include the value, relevance and potential cost of the research.

At this point, NAS has signed a contract with the Department of Veterans Affairs (DVA) and has received ~$850,000 to conduct the AFHS disposition study. NAS is now soliciting input from a variety of sources in three key areas. First, potential members to serve on a committee for the study are being identified. Government employees cannot be selected as committee members since the study is sponsored by a federal agency. Areas of expertise the committee should have are being assessed, such as environmental medicine; veteran's health or aging and military populations; longitudinal epidemiologic studies; analysis of biologic samples; long-term maintenance of records; sample size and other biostatistical issues; and informed consent and other bioethical issues.

Second, appropriate materials for the committee to consider are being evaluated since all NAS studies, recommendations and conclusions are science-based. Third, potential topics and speakers are being identified for a workshop NAS will convene in March or April 2005 in Washington, DC. The purpose of the meeting will be to gather additional information for the committee to consider. The workshop will be open to the public, posted on the NAS web site and also broadly announced to the public. NAS expects to produce a report on the AFHS disposition study by November 2005.

Dr. Butler encouraged RHAC members to e-mail him at afhs_study@nas.edu to provide input on potential committee members, areas of expertise and any other aspect of the AFHS disposition study or the 2005 workshop. He committed to providing Dr. Schechtman with more details about the workshop for distribution to RHAC.

Update by the AFHS Principal Investigator

Dr. Joel Michalek covered the following items in his status report. First, USAF will discontinue research on January 1, 2006 in accordance with its directive to terminate all AFHS activities on October 1, 2006. If NAS makes a recommendation in November 2005 to continue AFHS, proactive measures will need to be taken to revise USAF's time-line. However, the USAF shutdown plan is sufficiently flexible to address the NAS recommendations on disposition of AFHS.

Second, USAF has revised and resubmitted its paper on cancer in the control group to the *Journal of Occupational and Environmental Medicine*. The data show associations in the control group between cancer and dioxin as well as cancer and years in the Southeast Asia (SEA) region. The paper states that the reasons for these associations are unknown. USAF is also evaluating cancer in the Ranch Hand cohort due to the

findings in the control group and expects to complete this paper prior to the next RHAC meeting.

Third, USAF is summarizing its research that demonstrated participation in the AFHS did not statistically prolong the life or measurably improve the health of any subject. Fourth, USAF is conducting a case-by-case review of Ranch Hand enlisted ground crew who died of cardiovascular disease to better understand these patterns. Fifth, the Centers for Disease Control and Prevention (CDC) completed 500 randomly selected assays of the TEQ that provided measurements on 36 dioxin congeners, furans and PCBs for the first time. USAF and CDC are compiling these findings for a manuscript.

Review of Chapter 18: Endocrine

Dr. Leffingwell was charged with the review of Chapter 18. He was absent from the meeting, but submitted his comments in writing for RHAC to review and discuss. In general, both RHAC and USAF found Dr. Leffingwell's comments to be well written, thorough and helpful in strengthening the chapter. USAF confirmed that the majority of the comments could be addressed with minor editorial changes. In particular, USAF agreed to add language to respond to two specific points raised by Dr. Leffingwell.

First, text from USAF's published insulin paper will be included to clarify lines 163-165. A review of the paper pointed out that in the process of developing diabetes, an individual maintains glucose levels, but only through very high levels of insulin until the point is reached when insulin production fails and diabetes results. Second, language will be added to lines 311-314 to place the relative concentrations of dioxin levels in Ranch Hands in context with other cohorts. A member of the public suggested that USAF analyze the comparison group by assessing endocrine effects as a function of length of duty tour to determine whether a longer stay resulted in more harm. Dr. Leffingwell's comments are appended to the minutes as Attachment 1.

Review of Chapter 20: Pulmonary

Dr. Johnson was charged with the review of Chapter 20. In general, he found the chapter to be well written and agreed with the conclusions and summary. In particular, his comments and those of other RHAC members are outlined below.

- Revise line 166 to clarify whether the reduction in all examinations is "slight" or "significant."

- Place the paragraph on lines 171-177 on page 20-3 with other paragraphs on page 20-2 that discuss previous studies.
- Change "an herbicide" to "a herbicide" on lines 214 and 217.
- Specify "respiratory health" on lines 1089, 1142, 1302 and 1313 if AFHS found evidence of respiratory cancer.
- Determine whether the predicted values described on lines 1105-1108 are adjusted for race.
- Change lines 1141 and 1312 to "there is no consistent evidence."

Review of Chapter 11: Neurology

Dr. Sills was charged with the review of Chapter 11. In general, he found the chapter to be a comprehensive examination of cranial nerve function, peripheral nerve status and central nervous system coordination. He particularly commended USAF in several areas. The results and conclusions are supported by detailed statistical analyses of various neurological assessments. The summary contains a solid synthesis of both the group and initial dioxin analyses. The results section compiles the data in an easy to read, well-written and understandable format. The tables successfully capture statistically significant neurological endpoints and allow the reader to easily determine important p values. In particular, Dr. Sills' comments and those of other RHAC members are outlined below.

- Add "Achilles reflex," "coordination" and other clinically significant neurological endpoints to the "Conclusion" section on line 2628.
- Change line 2648 to, "In conclusion, based on these results, the evidence did not support."

Review of Chapter 13: Gastrointestinal

Dr. Hassoun was charged with the review of Chapter 13. In general, she found the chapter to be extremely well written and easy to understand. In particular, her comments and those of other RHAC members are outlined below.

- Explain the rationale for excluding USAF's peptic ulcer data from Chapter 13.
- Revise Table 13-1 on line 556 as follows. Divide the table into two parts in which the headers of "Variable," "Data Source," "Data Form" and "Cutpoints" are in Table 13-1 and the headers of "Covariates," "Exclusions" and "Statistical Analysis and Methods" are in a new Table 13-

2. Distinguish between "(a)" and "(b)" used for both "Covariates" and "Exclusions" by adding "*" or "**." Define "U," "A" and "D/C."

- Add language to clarify the current and lifetime cigarette smoking history sections on lines 696-708. For example, current cigarette smoking is a covariate for all liver enzymes in all current laboratory measurements, while lifetime cigarette smoking is only assessed for historical medical records variables, such as hepatitis and cirrhosis. Lifetime cigarette smoking is not a covariate for all 60 endpoints.
- Add the following definitions to Appendix F: the maximum and minimum coefficients for Pearson's chi square and "$p \leq 0.05$."

Review of Chapter 14: Dermatology

Dr. Johnson was charged with the review of Chapter 14. In general, he found the chapter to be well written and science-based. He commended USAF on its diligent efforts overall, and specifically, the inclusion of solid data and results to support the conclusions. In particular, his comments and those of other RHAC members are outlined below.

- Duplicate text from USAF's published paper to describe the rationale for focusing on acne. Repeat the explanation in the "Introduction" on line 94, "Discussion" on line 1356 and "Conclusion" on line 1571. For example, historical reported information was used for AFHS because individuals would be unable to distinguish between and accurately report acne or chloracne. USAF used self-reports of the anatomical location of "acne" on the body to determine the presence or absence of chloracne.
- Revise the "Background" on line 95 to clarify "acne" and "chloracne" up front. For example, state that the association between chloracne and dioxin is scientifically well established by prior occupational studies, but not with acne.
- Change lines 194-195 to "Also, in an AFHS 1998 publication."
- Distinguish between "acne" and "chloracne" on lines 214-216 and other places where appropriate throughout the chapter.
- Modify line 246 to "the occurrence of reported acne" and make this change in other places throughout the chapter where acne was based on self-reports.
- Revise line 461 to "Younger participants reported lifetime acne."
- Change line 466 to "Non-Black participants reported a longer mean."
- Outline "the reasons for the higher occurrence of acne in Ranch Hand enlisted ground crew" since dioxin is associated with chloracne rather than acne.

- Change line 1587 to "revealed no pattern suggesting chloracne."

Review of Chapter 10: Neoplasia

Dr. Trewyn was charged with the review of Chapter 10. In general, he found the chapter to be well written, but noted that several areas lacked important content. In particular, his comments and those of other RHAC members are outlined below.

- Include USAF's published and unpublished data, internal research, completed models and new observations in their entirety that demonstrate significant cancer results. Incorporate relevant cancer research on Vietnam veterans completed by the Institute of Medicine (IOM) as well. For example, reference 179 on line 3771, "Cancer in U.S. Air Force Veterans of the Vietnam War, was considerably shortened and the abbreviated version does not adequately reflect the importance of the publication. Moreover, USAF's newer data more accurately capture the fact that certain individuals suffered adverse health effects based on service in Vietnam or SEA.
- Add a substantial amount of text to the "Epidemiology" section on line 188 to show that controls served in Vietnam. Explain that a series of studies have been conducted to analyze these data differently. Point out that the studies and abstracts have been published, presented at meetings, or will be published in peer-reviewed journals or USAF technical reports. Summarize relevant findings of the cancer research and incorporate references for the reader to locate published results.
- Appropriately revise and interpret the "Introduction" on line 130, "Summary" on line 3102 and "Conclusion" on line 3254 after USAF's internal research and other publications are summarized in the "Epidemiology" section.
- Ensure that the text of the chapter reflects references 171-177 on lines 3752-3764.
- Reference toxicological and epidemiological studies in the published literature that cite cacodylic acid and other toxic components of herbicides used in Viet Nam.

Review of Chapter 21: Conclusions

All RHAC members were charged with the review of Chapter 21; their comments are outlined below.

- Ensure that "Conclusion" sections in each chapter are consistent with the "Conclusions" Chapter.
- Include references to "(see Chapter X)" or "(see Appendix X)" where appropriate throughout the chapter.
- Change line 40 to "Throughout this report, serum dioxin levels."
- Modify line 53 to "The use of serum dioxin as a surrogate measure."
- Revise and substantially expand the "Introduction" on line 55 in five key areas. First, describe the purpose of AFHS. Ensure that the explanation is consistent with the "Executive Summary." For example, the AFHS was launched in the 1970s due to concerns about health effects among persons in the Ranch Hand Unit from high exposure to herbicides, particularly Agent Orange. The purpose of the epidemiologic investigation was to determine whether long-term health effects exist and can be attributed to occupational exposure to Herbicide Orange. Second, clarify that the serum dioxin measurement technique was invented after the AFHS was initiated and allowed for consistency between certain analyses and the AFHS protocol. Third, describe the historical context of the AFHS. For example, discuss the Agent Orange Workgroup with CDC, the National Institutes of Health and other federal agencies; Congressional hearings, testimonies and other political actions; USAF's possession of the herbicides tapes; the Vietnam Veterans Comprehensive Readjustment Act of 1979; Vietnam Veteran's Week and other activities by the Vietnam Veterans in Congress Caucus; and the USAF program objective memorandum to include the AFHS as a line item in the Department of Defense budget. Fourth, note that the current AFHS report only reflects the 2002 follow-up examination. Fifth, explain that epidemiology is an imperfect science and the AFHS may have missed some adjustments or confounders, such as "More Comparisons than Ranch Hands had high scores on the SCL-90-R" on line 193. Point out that the AFHS was adjusted for relevant variables, but some components are unknown. However, add a sentence to point out that more exploratory analyses may uncover new findings.
- Define "passive refusals" and "hostile refusals" on line 65.
- Modify the "Statistical Models" section on line 77 to clarify that the AFHS statistical methods were used for longitudinal purposes, but other models have been applied in different settings and are cited in the published literature.

- Edit the "Neoplasia Assessment" on line 117 to reflect USAF's published and unpublished results and internal research that will be added to Chapter 10.
- Make the same changes to the "Dermatology Assessment" on line 224 and the "Pulmonary Assessment" on line 352 as the revisions RHAC proposed for Chapters 14 and 20, respectively.
- Clarify lines 268-269 because the text can be inaccurately interpreted as "dioxin plays a role in decreasing high blood pressure." Point out that many AFHS participants were taking anti-hypertensive medications.
- Move the "Strengths and Limitations of the Report" section on line 362 after the "Statistical Models" section on line 77.
- Remove the language on RHAC's contributions to the AFHS from the "Strengths and Limitations of the Report" section on line 362 and place the text in a new "Acknowledgments" section.
- Expand the "Summary" section on line 375 to explain that the AFHS analyzed a variety of health outcomes, but found diabetes to be the most important dioxin-related health problem from a clinical perspective. Clarify that the remainder of the findings were chemistries, isolated laboratory results and physical examinations, but diabetes was the only disease seen.
- Describe AFHS publications, recent analyses and other new efforts that may influence prior findings of health outcomes. For example, a USAF paper was published in *Neurotoxicology* in 2002 and showed an increased risk of peripheral neuropathy. The IOM is currently conducting a critical review of the USAF paper that may impact the interpretation of the neurology results. USAF will soon publish a paper that shows a significant increase in the risk of cardiovascular death among enlisted ground crew. USAF is currently developing a paper that demonstrates a correlation between dioxin and number of days spent on the Ranch Hand Unit, specific dates in Vietnam and operational activities.
- Cite confounders, statistical models and studies that have been published for any clinical outcomes. Modify the respective chapters to be consistent with changes in the "Conclusions" chapter.
- Add a reference of "(see Table X)" after a result is described in each section and list the appropriate model in each table.
- Replace the tables in Appendix G with summary tables from each chapter. For example, only include Tables 18-47 and 20-19 in Appendix G to show significant results in Chapters 18 and 20, respectively. Modify the "Introduction" to be consistent with the revised Appendix G.

Review of the Executive Summary (ES)

All RHAC members were charged with the review of the ES; their comments are outlined below.

- Reformat the ES and "Conclusions" to distinguish between the two chapters and make them applicable to different audiences. For example, maintain the "Conclusions" chapter as the scientific or technical summary and revise the ES as a summary for the lay public.
- Modify the ES with the following outline. In Paragraph 1, explain AFHS's purpose and historical context. Clearly point out that the current report only reflects the 2002 follow-up examination. In Paragraph 2, describe AFHS's study design and execution by discussing the Ranch Hands and comparisons; historical records and medical examinations of the subjects; and the overall number of participants. Add language to note that all studies may miss covariates. In Paragraph 3, outline statistical analyses used in the AFHS, describe the rationale for applying these models in the AFHS, and mention that different models were used in other publications. In Paragraph 4, list the strengths and limitations of the AFHS. In Paragraph 5, specify the different parameters studied in the AFHS across all health outcomes and highlight the statistically significant variables. In Paragraph 6, include evidence to demonstrate that diabetes was found to be the most clinically significant health outcome. Mention that other disease conditions were analyzed in the AFHS which may not play a role in risk following dioxin exposure. Note that the AFHS found no relationship between dioxin and diseases other than diabetes, but an association may still exist.
- Ensure that the format of the 2002 ES is consistent with those generated in 1992, 1995 and 1997 if another AFHS report will be developed in the future.
- Cite the AFHS protocol on line 2 to clarify that "The purpose of the epidemiologic investigation was to determine whether long-term health effects exist and can be attributed to occupational exposure to Herbicide Orange." [Make this change only if necessary in the revised paragraph 1].
- Delete "randomly selected" on line 12. [Make this change only if necessary in the revised paragraph 2].
- Modify line 16 to clarify that each living Ranch Hand gave informed consent and did not merely sign a consent form. [Make this change only if necessary in the revised paragraph 2].
- Correct lines 41-42 to reflect that Model 4 assumed all AFHS participants had the same serum dioxin elimination. [Make this change only if the paragraph is maintained in the new ES structure].

- Expand line 280 to explain in more detail that Vietnam veterans developed health effects from agents other than dioxin. Repeat this text in chapters that describe the AFHS study design and dioxin levels of AFHS participants. For example, USAF's 1989 published data demonstrate that Agent Purple and Pink phenoxyherbicides used in the earlier years of the Vietnam War contained dioxin at far greater concentrations than Agent Orange. The findings show that service personnel stationed in Vietnam from 1961-1965 have higher dioxin levels than those stationed in Vietnam from 1967-1968.

Over the course of the chapter reviews, RHAC also suggested universal changes that should be considered across the entire report. These comments are outlined below.

- Add a reference or footnote to "(see Chapter 7-Statistical Methods)" when Pearson's chi-square, the proportional hazards model or other statistical methods are described in individual chapters.
- Formulate text in laymen's terms for Vietnam veterans and the general public in the "Conclusion" section of each chapter. For example, clearly and succinctly state that "dioxin exposures did or did not cause a health effect."
- Structure the report in the same succinct format and order as General Accounting Office documents in which the executive summary is first; a bullet list of major findings is second; the methodology is third; and conclusions are fourth.
- Format the press release of the AFHS report to be easily understood by and accessible to the lay public.

Public Comment Period

Dr. Gary Kayajanian is an individual scientist who evaluates human cancer data. He raised two points about data Dr. Michalek presented during the *Dioxin 2004* conference in Berlin in September 2004. For the first issue, an increase in all cancers was not seen when cancer incidence was assessed in the comparison group based on length of duty tour. Dr. Kayajanian considered this finding to be in error because a significant decrease would have been seen based on length of duty tour if basil and squamous cell cancers were analyzed. The analysis was designed to include or exclude cancers.

For example, a cancer had to have occurred 15 years after the duty tour ended to be included in the analysis. A significant peak was seen 16-20 years after the duty tour began that was clearly not associated with dioxin, but 40% of skin cancers were excluded from Dr. Michalek's analysis. These results, according to Dr. Kayajanian,

were skewed due to the exclusion of service personnel with >3.6 years of service and cancers occurring 18.6 years after the duty tour began. If the analysis is redesigned to include all cancers and count cancers from the beginning rather than the end of the duty tour, a similar curve for basil and squamous cell cancers will most likely be seen, Dr. Kayajanian opined.

The second issue Dr. Kayajanian raised related to veterans with metabolic syndrome. Dr. Michalek's data showed a multi-variate relative risk of 2.1 with a 95% confidence interval from 0.7-6.7 in the comparison group. The Ranch Hand group had a multi-variate relative risk of 0.5 with a 95% confidence interval from 0.1-1.8. The difference between the multi-variate relative risks in the two groups is significant, but was not demonstrated in Dr. Michalek's data, according to Dr. Kayajanian.

Dr. Kayajanian suggested that the comparison and Ranch Hand groups be divided into seven exposure categories to determine whether a sharp decline in incidence is seen in the comparison group when the analysis moves from non-detect to 8-10 ppt. He saw a similar pattern of an extremely sharp drop in incidence for prostate cancers in Black males by moving the analysis from the lowest to highest exposure groups. The significant difference between the two groups he observed for chronic heart disease also applied to cardiovascular disease.

Dr. Michalek responded to the public comments as follows. For the first issue, the data Dr. Kayajanian cited are from an older version of USAF's paper in which a 15-year lag was used to assess cancer. Since this methodology is no longer applied, the exclusions are not seen now in USAF's most recent version of the paper. Moreover, an increase in basal and squamous cell incidence was seen based on years in SEA. The latest version of USAF's paper does not count cancers from the duty tour; instead, cancers are counted from the beginning of medical follow-up that occurred at baseline in 1982.

For the second issue, Dr. Michalek responded that the relative risk relates to the development of metabolic syndrome to cardiovascular death among comparisons and separately among Ranch Hands. The data show that comparison groups that are developing metabolic syndrome are at a much higher risk of cardiovascular death than those that are not, but this finding was not seen in the Ranch Hand group. USAF has not yet analyzed the association between the three-factor interaction and dioxin.

Mr. Rick Weidman, Director of Government Relations for Vietnam Veterans of America, stated that the final AFHS report will be judged on its scientific validity. However, the document will also be widely reviewed by the non-scientific community, including the lay public, policymakers, veterans and the Vietnamese government. As a result, the report should broadly include more confounders and epidemiological data beyond Agent

Orange. Although the current report only reflects the 2002 follow-up examination, the political and veteran communities will judge the document based on the entire AFHS process.

Drs. Michalek and Miner responded to the public comments as follows. The cardiovascular, cancer and diabetes data are historical and reflect clinically verified outcomes from 30 years of medical follow-up. The analyses include all findings collected since Vietnam and serve as a longitudinal study over the entire health history of the AFHS participants. However, the remainder of the data only reflects the Scripps Clinic examinations in 2002-2003.

A longitudinal overview will be conducted to incorporate all findings from all physical examinations and published papers. USAF and Science Applications International Corporation (SAIC) are currently negotiating this activity and expect to complete the report at the same time the AFHS concludes on September 30, 2006. Dr. Stoto expressed RHAC's strong interest in participating in a review of USAF's upcoming longitudinal overview.

RHAC Business

Dr. Schechtman announced that FDA initially planned to convene up to four RHAC meetings in 2005, but USAF has indicated the need for only two technical meetings. FDA will schedule a third meeting in 2005 for RHAC to conclude its business, discuss next steps if necessary, and review the NAS report on the AFHS disposition study. FDA is now proposing the following schedule for the 2005 RHAC meetings. No meeting will be held in February 2005; instead, a conference call will be convened during that time if necessary for RHAC to review and discuss the revised "Conclusions" chapter and "Executive Summary." The three face-to-face meetings will be convened one day during May 2-6, 2005 or May 24-27, 2005; one day during September 12-16, 2005 or September 19-23, 2005; and one day during the months of November 2005-March 2006.

FDA will be in a better position to schedule the third meeting after the NAS report on the AFHS disposition study is released and the availability of RHAC members and USAF staff is confirmed. Dr. Schechtman reminded the members that FDA is required to submit RHAC agendas and other meeting information to the *Federal Register* at least 60 days in advance of a meeting. FDA must also provide strong justification to change a meeting announcement after submission to the *Federal Register*. This requirement will be particularly important since the third meeting will be convened based on availability of the NAS report on the AFHS disposition study.

Mr. Grubbs and Lt. Col. Robinson provided additional time-lines for RHAC to consider for its upcoming meeting schedule. SAIC will revise the "Conclusions" chapter and "Executive Summary" based on RHAC's comments and submit the new drafts to USAF by January 9, 2005. SAIC will complete another revision of the two chapters based on USAF's comments by the first week in February 2005. The new iterations of the "Conclusions" chapter and "Executive Summary" will be distributed to RHAC in January 2005. SAIC will also revise the "Neoplasia" chapter based on RHAC's comments and submit the new draft to USAF for distribution to RHAC.

USAF is scheduled to review Chapters 1-8 of the draft final report by December 9, 2004; the next eight chapters in January 2005; and the remaining chapters in February 2005. SAIC expects to make all changes and complete the final report the first week in March 2005. In terms of meetings, USAF would like to hold technical meetings with RHAC in 2006 to discuss USAF's longitudinal study, historical study of AFHS, internal research, and articles to be published in peer-reviewed journals and USAF technical reports.

Closing Session

Dr. Stoto thanked the members for thoroughly reviewing their respective chapters; USAF and its contractors for their diligent efforts in compiling data for the AFHS report; FDA staff for making logistical arrangements for the meeting; and members of the public for their valuable input.

With no further discussion or business brought before RHAC, Dr. Stoto adjourned the meeting at 12:36 p.m.

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

June 23, 2005
Date

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

July 1, 2005
Date

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