

RANCH HAND ADVISORY COMMITTEE MEETING MINUTES  
January 22-24, 2001

FDA Headquarters, Parklawn Building  
Rockville, Maryland

- The meeting of the Ranch Hand Advisory Committee (RHAC) was held from January 22 to 24, 2001. On each of those days, the sessions were convened and adjourned, respectively, as follows:
  - 1/22/01: convened at 1:20 PM; adjourned at 4:53 PM
  - 1/23/01: convened at 8:55 AM; adjourned at 4:01 PM
  - 1/24/01: convened at 8:53 AM; adjourned at 10:23 AM
  
- Attendees included:
  - RHAC members--
    - Robert W. Harrison, M.D. (Chair)
    - Michael A. Stoto, Ph.D.
    - Michael Gough, Ph.D.
    - Elissa Favata, M.D.
    - Paul R. Camacho, Ph.D.
  - Committee Staff:
    - Ronald F. Coene, P.E.
    - Leonard M. Schechtman, Ph.D.
    - Barbara J. Jewell
  - Other attendees and their affiliations--
    - LTC Karen A. Fox, Brooks Air Force Base
    - LTC Bruce Burnham, Brooks Air Force Base
    - Joel Michalek, Ph.D., Brooks Air Force Base
    - Judson Miner, Program Management Support, BAFB
    - Richard Ogershok, U.S. Air Force
    - Manuel A. Blancas, Program Management Support, BAFB
    - Meghan Yeager, SAIC
    - William Grubbs, SAIC
    - Maurice Owens, SAIC
    - Bill Chism, EPA
    - Rick Weidman, Vietnam Veterans of America
    - Gary Kayajanian, Ph.D.
    - Kim Pemland, FDA Week
    - Mary Lambert, Office of the Secretary, DHHS
    - Robert Newman, House Subcommittee on National Security and Veterans Affairs
    - Mary Ellen McCarthy, House Veterans' Affairs Committee

- Committee approval of previous (October 2000) meeting minutes was deferred for further revision. The draft minutes of the October 2000 meeting are to be sent to Dr. Michalek for technical editing and then to the Exec Sec and committee Chair, who will provide the final edited draft version.
- Reporting of future meeting minutes
  - The RHAC has requested that subsequent meeting minutes be in the form of a synopsis (executive summary) that highlights important issues, includes pertinent action items, and refers the reader to the meeting transcript for additional details as necessary.
  - Minutes are to be reviewed by RHAC members, with each committee member to be responsible for reviewing his/her section and for signing off on that section.
  - Technical editing is to be done by Dr. Michalek.
  - Final draft is to be generated by Exec Sec with input, as needed, from committee Chair.
- Review/discussion/editing of Statement of Work (SOW)
  - Search and replace will be done on the document to ensure consistency in terminology, e.g. change "offeror" to "contractor"
  - Committee conclusions regarding open issues (pg. ii): #1-5 no; #6 yes; #7 chemical exposure in the home (Dr. Favata)
  - Sec 3.2.2: Dr. Camacho will research the definition for hostility and communicate with Dr. Michalek
  - Sec 3.2.4.6.6: The committee discussed whether or not this section should be revised; it was decided that the Air Force (AF) will review all coefficients of variation
  - Sec 3.2.4.6.6: The meaning of "tri-level control" was questioned by Dr. Favata
  - Sec 3.3.2.3: Dr. Harrison suggested
    - deleting the variable "severity of diabetes"; the committee agreed that there's no great harm in retaining it.
  - Sec 3.5.2.2: Dr. Harrison stated that the jargon should be changed and replaced with proper language (e.g. Contractor shall clean the data ....)
  - Sec 3.5.3: The committee discussed the issue of "out of range", and use of a statistical method related to data clean up
  - Sec 3.6.1: The committee, led by Dr. Stoto, discussed statistical models in section 3.6.1.1 and 3.6.1.2
  - Sec 3.6.1.5: The committee proposed certain modifications to this section
    - Should always adjust for BMI
    - Occupational factors should be considered
    - The value of regional factors was discussed; the committee felt such data would not add value to the assessment of the 2002 data
  - Sec 3.6.2: No changes necessary
  - Sec 3.6.3: The use of SAS was discussed; also decided was that all data/information would not be stored solely on floppy disks
  - Sec 3.6.4.1: The definition of "hostility" is an issue that needs to be resolved by Dr. Camacho; also see page 13 and sec 3.6.4.1.1, pg. 27, line 4
  - Sec 3.6.4.1: Eliminate erythrocyte sedimentation rate (pg. 26 (d))
  - Table 3.6.4.3b: 8<sup>th</sup> cranial nerve is not addressed and should be
  - Table 3.6.4.3b: Remove item 19 and include eighth cranial/cochlear nerve evaluation

- Table 3.6.4.3c: Items 24-27 needs an evaluation code
  - Sec 3.6.4.3.1: Modify paragraph (pg. 31)
  - Sec 3.6.4.3.1: The 2<sup>nd</sup> paragraph should include a graduated scale, i.e., 0 = absent, 1 = slight, 2 = normal, 3 & 4 = very active
  - Sec 3.6.4.3.4: The term “pesticide” should be used in place of “insecticide”
  - Sec 3.6.4.3.4: The term “degreasers” needs to be defined
  - Sec 3.6.4.4.3: Needs to be relocated and perhaps revised
  - Section 3.6.4.4: Is to be reviewed by Dr. Camacho; information from review forthcoming
  - Sec 3.6.4.4.4: Information was first provided in 1982; CDC recommendation is for re-use
  - Sec 3.6.4.4.4: Wechsler Memory Scale – is considered to be the best measure to use for short term memory
  - Sec 3.6.4.5: GI section – normals should serve as controls (Dr. Harrison)
  - Sec 3.6.4.5.3: AF to rewrite this section; Dr. Favata stated that this section should be revised with current thinking
  - Sec 3.6.4.6.1: Replace “all intersections” with “combinations”
  - Sec 3.6.4.6.1: Dr. Favata proposed that peri-emblical and scrotal should be added
  - Sec 3.6.4.6.5: This section should be deleted
  - Table 3.6.4.7: #6 Prothrombin time (seconds) should be moved under liver
  - Table 3.6.4.8: Add beta-2 macroglobulin
  - Table 3.6.4.8a: Add “family history” as a covariate
  - Table 3.6.4.8c: Addressed in comments by Dr. Osei
  - Sec 3.6.4.8.1: Decision to use the WHO/ADA cut point of 140
  - Sec 3.6.4.8.3: Add the term “bilateral” before “orchiectomies”
  - Sec 3.6.4.9.3: Eliminate “batch-to-group” adjustment
  - Sec 3.7.3: AF to rewrite this section
  - Section 3.7.3: – summary tables – Dr. Stoto suggested that the results should be presented in terms of clinically meaningful effects and p-values. Dr. Harrison proposed that this section needs to be rewritten and then resubmitted to the RHAC. Dr. Michalek is to provide the revision within two weeks.
  - Addendum A, page 62, #12: “...plus hip at its widest...” should be added
  - Addendum D, page 81: Details such as those regarding the modem should be added
- General Comments and Suggestions
    - All abbreviations will need to be defined
    - A glossary of terms (including abbreviations) should be prepared
    - Physician’s Handbook, item 11, should include abstinence from caffeine
    - AF is to send copies the IRB approvals to RHAC
    - AF is to compile a list of all contractors and consultants affiliated with the study
    - AF is to prepare a list of all hypotheses investigated and their outcomes/status
    - RHAC Chair is to write the Secretary of HHS, with copies to Secretaries of the DVA and AF, regarding the following:
      - Recommending implementation of PL 91-102-4 relative to the Sections 7 & 8
      - Pointing out the serious scientific and ethical considerations being faced by the study that need to be addressed in an expeditious manner, especially the issue of maintenance/disposition of specimens

- Requesting the Secretary to conduct meetings/discussions to resolve the issues
- RHAC needs guidance on ethical, legal, and scientific aspects of the study
  - Dr. Stoto has offered to help draft the letter
  - The draft will be provided to RHAC members for comment
  - The letter is to be copied to appropriate interested parties (VSO's)
- RHAC recommended that dioxin (TEQ) analyses be performed during this cycle
  - Prioritization will be as follows:
    - #1: everyone in the cohort
    - #2: all in the cohort who have only one result
    - #3: anyone with levels above 10 ppt
- Next meeting in April to review 4 research proposals only
  - RHAC is to identify expert reviewers for each of the 4 research proposals
  - All proposals are to be circulated to the RHAC members along with the justifications (provided by Dr. Michalek)
  - AF is to prepare a chart summarizing those findings determined in the first, second, and in all subsequent studies/exams (Dr. Gough)
  - A chart depicting timelines of status of the various hypotheses that were derived from the study was suggested (Dr. Harrison)
- IRB approval status
  - Committee views and discussion points from this RHAC meeting will serve as the basis for revisions/editing of the SOW
  - IRB is to review the study and consent forms
  - RHAC would like copies of:
    - List of contractors and sub-contractors
    - List of medical specialists who wrote the different chapters
    - All IRB approvals
- Discussion regarding Dr. Favata's replacement
  - Members of the RHAC present were of the opinion that the committee replacement for Dr. Favata should be another clinician.
  - Dr. Michael Weiss was mentioned; he is to be contacted to determine if he would be willing to be considered as a perspective nominee.
  - Dr. David Butler from the IOM was mentioned as another source for nominee candidates (Dr. Stoto to make contact).
  - Dr. Ron Trewyn may be asked if he would be interested in serving another four-year term.
  - The committee felt that consideration of this option would indicate a need to inform Dr. Caldwell and Mary Lambert as to this possibility and the other alternative of selecting another clinician.
- Additional study considerations
  - Dioxin measurements
    - Individuals who previously had only one dioxin measurement should be measured a second time

- Cost estimates to perform measurements range from \$500 to \$1000 per person (average \$750/person); 1500 people would incur a cost of approximately \$1,125,000
- It is preferred that the measurements be performed on both Ranch Handers and controls, which would total approximately 2200 - 2300 people
- AF representatives suggested that it is possible that the CDC would perform the measurements on both populations at a cost estimated to be \$1,840,000 (i.e. 2300 people x \$800 per person = \$1,840,000)
- If this is not feasible, then at a minimum, the measurements should be performed on those persons with high dioxin levels (>10 ppt), estimated to be approximately 500 people
- AF requested that, if possible, funds for this purpose be made available directly to CDC
- Disposition of study specimens
  - Approximately 51,000 biological specimens are currently stored at -70° C at BAFB, all collected under informed consent.
  - A letter was sent from Donna Shalala, previous Secretary of HHS, to Dr. Ken Olden, NIEHS, pointing out the need to utilize the specimens for their intended purpose at this time (before the study ends), and citing the importance of obtaining the financial support necessary for maintenance of the biological samples. (If these efforts are delayed, it may be too late to help the Vietnam Veterans [see Dr. Michalek's slides: "Issues"]).
  - Dr. Olden, although acknowledging receipt of the letter, indicated that no funding was available.
  - Decisions need to be made before 2006 (completion date of the study).
- RHAC recommendations
  - The RHAC recommended administering the spousal questionnaire this cycle
  - Recommendation for a toll free 1-800 telephone number that should be available to Ranch Handers 24 hours/day (Dr. Harrison)
  - Dioxin measurement prioritizations:
    - Priority 1: Two points on every subject (~1500)
    - Priority 2: Do a dioxin measurement of all subjects (~2300)
    - Priority 3: Measure those with values above 10 (~600)
  - Personality testing to be conducted by Dr. Harrison
  - Prepare a chart of all parameters flagged and follow these each cycle (pg. 8)
  - SOW will include a dioxin draw and storage
  - It remains to be decided whether the SOW will include an analysis of the samples and what kind of analysis
- Next RHAC meeting (April, 2001)
  - Tentative travel on 4/8/01; meeting all day 4/9/01
  - Mary Lambert (Tel. # 202-205-1848) to be notified; she will need to inform VSO's regarding meeting date and time
  - Agenda items proposed
    - Response to Dr. Gough's request, letter of 12/5/00
    - Science presentations

- Proposal reviews (4)
- Proposal review process
  - Reviews are to be done according to the NIH-style review
  - Two experts drawn from the RHAC or outside reviewers will assess each proposal
- Action Items
  - Mechanism to improve documentation of meeting minutes (see page 1, above, “Reporting of future meeting minutes”)
  - Meeting (2 days) to be scheduled for September 2001; calendar to be circulated via email for scheduling (week of 9/10 Dr. Michalek not available)
    - AF science presentation to address publications and research projects
    - VA presentation to provide update on the Chemical Corps study (tentative); Han Kang to be contacted
  - Create a public WebPage for RHAC and link to VA organizations and appropriate search engines.
  - Question individuals regarding exposure to chemicals in the home (Dr. Favata)
  - RFP is currently scheduled to be announced March 2, 2001; therefore need quick turn-around of SOW, highlighting changes noted at this RHAC meeting (Dr. Michalek)
  - Need for guidance regarding ethical issues:
    - Request appearance of expert (e.g. legal counsel) to discuss the ethics issues.
    - Can we ethically use the samples?
    - Can we find resources to support proper use of the samples?
- Proposals:
  - RHAC to contact the VA through Secretary HHS
  - Discuss with National Academy of Sciences (NAS) the practical and ethical issues.
- Public comment session
  - Mr. Gary Kayajianian of Arlington, VA, shared data comparisons between Ranch Handers and controls. (A full reporting of his information is available in the verbatim transcript).
  - Mr. Rick Weidman, representing Vietnam Veterans of America, offered comments. He indicated that he was meeting with Tommy Thompson, Secretary of HHS, this week and would be recommending that (a) the RHAC effort receive better overall and financial support, or (b) the stewardship of the RHAC project be dissociated from FDA and redirected to another more appropriate organization. He pointed out that HHS and FDA have failed to support the RHAC efforts, as exemplified by the poor handling of meetings and the failure to conduct meetings under the Sunshine Law (open to public). He suggested that this suggests a lack of organizational commitment to the RH project. He recommended (a) press releases/notifications regarding availability of data, (b) web site postings of committee meetings well in advance of the meeting dates, (c) notices sent to VSO's, (d) spot-lighting of committee activities in order to call attention to it, and (e) conducting meetings at an alternative (Washington, DC proper) location.
- Future meeting: Spring 2002 meeting at Scripts in CA.

