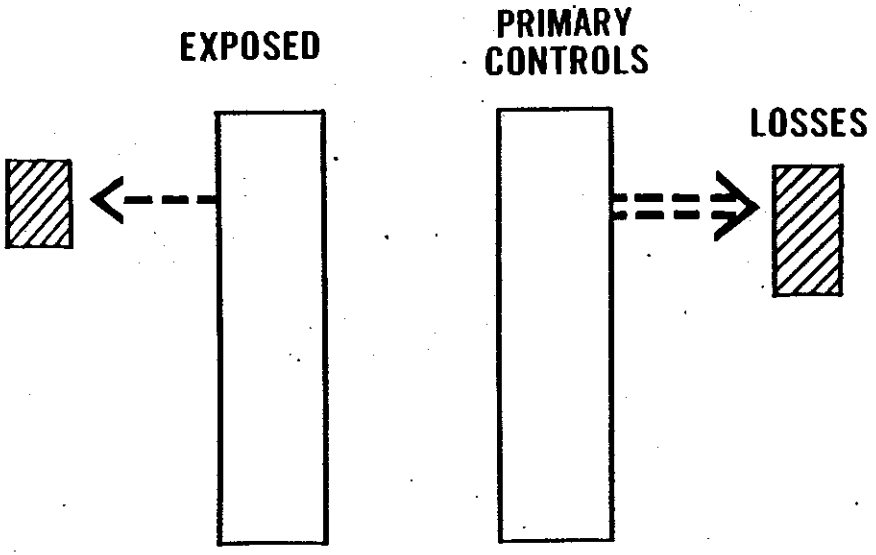
FIGURE 15

RATIONALE OF REPLACEMENT

DILUTIONAL BIAS



P(L/W) > P(L/I)

P(L/W) >>> P(L/I)

CONDITIONAL PROBABILITIES:

L = LOSS
W = WELL
I = ILL

his own state of health, the alteration of the control group distribution is offset; (i.e., an "ill" control is replaced with an "ill" individual, and a "well" control with another "well" individual.) This concept of replacement, coupled with the payment of stipends, and extensive efforts to encourage compliance will minimize losses to study and offset the adverse effects of those losses that do occur.

H. Statistical Power Limitations

(1) Problem

As discussed in Section VI, statistical power considerations are heavily dependent on loss to study rates. Since the design of the study is also limited by the size of the exposed population, statistical power for identifying the relative risk of an uncommon disease or symptom-complex (<1/100) is very low (<.50), (See Section VI. B.). This study will, to a greater extent, be able to detect increased risks in common diseases or symptom-complexes (>1/100).

(2) Discussion

The "herald sign" of TCDD exposure, chloracne, is expected to have the greatest likelihood of achieving adequate statistical power in this study. Recent findings from Seveso, Italy, support the importance of chloracne as the primary marker symptom. The incidence of chloracne has been reported by Reggiani (personal communication) and Homberger, et al., to be 14.9 cases per 1000 residents in the region of highest contamination of Seveso (Zone A) and 6 to 12 cases per 1000 in the Seveso community as a whole. These rates vary by age group, with children being at highest risk. Only 1 to 5 cases per 1000 were seen in other regions of Northern Italy (Milan, Como, and Lecco). The incidence of adolescent acne in all of these populations varies between 21% and 30%. These incidence rates probably place chloracne at the lower limit of adequate statistical power of this study. In the Nitro, West Virginia studies, residuals of chloracne, as well as exacerbations of previously active disease, continue to be seen 10 years after the most recent exposures, and 30 years after the industrial accident. Thus, it is likely that any chloracne in the exposed population may be detected, despite the intervening years since RANCH HAND exposures. In addition to chloracne, other recently reported human effects of TCDD exposure at Seveso, Italy, appear to fall within the capabilities of this study design (e.g., peripheral neuropathy, neuropsychiatric effects, and liver dysfunction). In general, with respect to statistical power, continuous data (clinical or laboratory measurements) even from relatively small samples fair much better than either categorical or dichotomous data (presence or absence of a given condition). Consequently, a concerted effort will be made to obtain physical examination data in a scored and/or continuous manner.

I. Variability of Procedures

(1) Problem

The variation of physical examination findings from differences in technique and the random errors inherent in laboratory testing are items of concern, particularly if attributable health effects are subtle or of low magnitude. Nonstandardized procedures and techniques are major contributors to this variance.

(2) Corrective Measures

Variability in examination procedures will be minimized by the use of standardized procedures, examination protocols, on-site monitors, and training. All laboratory procedures will be conducted at the examination center and quality control will be stressed at all times. (See Section IX)

J. Confounding Exposure Factors

(1) Problem

While virtually all of the media attention has been directed toward the 2,4,5-T-containing herbicide formulations, other herbicides were applied concurrently by the C-123 aircrews in Vietnam. Herbicide Blue (Cacodylic acid with 15.4% pentavalent arsenic) and Herbicide White (2,4-D and Picloram) were used throughout the 1962-1970 time period. Any long-term health effects from these additional compounds may confound the results of the study. Peripheral neuritis, tremors, skin and lung cancer, loss of hair and nails, skin rashes, and gastric symptoms have been alleged after exposure to arsenical pesticides. The organophosphate insecticide Malathion was also sprayed by some of these same aircrewmembers when RANCH HAND duties permitted their temporary assignment to mosquito/malaria control missions. Many of these individuals were involved in the aerial spray application of these and other pesticides both before, during, and after their Vietnam service. Long-term effects from these chemicals would confound the study results. The small size of the RANCH HAND population will allow very little opportunity for analytic stratification for these confounding variables. Differing patterns of exposure to aircraft fuels in the study populations have been suggested as confounding factors. The C-130 aircraft were powered by turbo-prop engines which used jet fuel (JP-4), while the C-123 and C-7 aircraft were powered by standard reciprocating engines which used leaded aviation fuel (AV-GAS). After June 1968, many C-123s were modified by the addition of auxilliary jet engine boosters for added power on takeoffs and in emergencies.

(2) Discussion and Corrective Measures

While the extent of confounding caused by exposure to these other pesticides is undetermined at this time, assessment of its magnitude must rely on responses of the subjects to that portion of the questionnaire dealing with other occupational exposures. For this reason, information

concerning exposures to other herbicides/insecticides used in Vietnam will be collected. Whenever possible, stratification techniques will be used to adjust for these confounding variables during data analysis. Variations in fuel between C-130 and C-123 aircraft would be significant factors if individuals in the study were heavily and repetitively exposed. However, the normal duties of the study participants did not involve aircraft refueling or other fuel handling activities. Thus, fuel exposures can be minimized as significant confounding factors.

IX. Quality Assurance and Management Considerations

A. Quality Control

(1) Overview

As in any major scientific effort the quality of the data and the comparability of the data over time are key factors in achieving valid results. Quality assurance in both scientific and management aspects of this study are planned, and will be fully integrated into each phase of the study.

(2) Scientific Aspects

(a) Protocol Development

The Air Force scientific protocol has been under development for more than one year. It has been subjected to an unprecedented five stage independent peer review process to insure the highest quality and validity of its science.

(b) Blind Assessment Protocols

The exposed or non-exposed status of each individual will not be revealed to any of the Health Examiners. Each aspect of the physical examination will be conducted by rigid adherence to the examination protocol. Past medical history and review of systems will be obtained by individuals not associated with the examining process.

(c) Population Ascertainment Quality Control

The study/control populations for this effort were ascertained through extensive computer, and hard copy record searches. The matching variables for each individual were entered and verified with a computer program to minimize transcription errors. Data collection for both exposed and control populations was conducted using identical techniques, thus avoiding systematic bias in population ascertainment.

(d) Precision Matching

Computer techniques will permit extremely close matching of the control participants to the RANCH HAND participants for three distinct variables. This will substantially enhance the analytic flexibility and validity of the study.

(e) Questionnaire Techniques

Detailed questionnaire methods are under development to provide comprehensive crosschecks between objective and subjective health information. Particular emphasis will be placed upon techniques to ascertain false positive information which might impact the validity of the study.

(f) Laboratory Quality Control

The contractor for acquisition of health data mandatorily must have a detailed in-house laboratory quality control program coupled with enrollment into the "CLIA" or "CAP" laboratory survey. In addition, randomly selected duplicate specimens will be sent to a central Air Force reference laboratory for verification.

(g) Single Physical Examination Site

All physical examinations conducted by the contractor will be performed at a single site by dedicated teams of health professionals to insure that data variability is at an absolute minimum. The contractor will be a fully accredited medical institution, and must provide organizational evidence of national/international preeminence.

(h) Personnel Qualifications

All examining physicians will be certified and accredited by a Medical Specialty Board. Paramedics, medical students and interns will not participate as examiners in this study.

(3) Management Aspects

(a) Informed Consent

All participants will be fully informed as to the nature and purpose of all medical diagnostic tests and examinations, and will certify their complete understanding by signing specially designed informed consent forms. Release of medical data will be in strict accordance with Privacy Act determinations, and Air Force policies. Total confidentiality will be granted to subjects who are not on active duty. Active duty subjects will be given limited confidentiality with release of medical information to the DOD only in instances in which there is a risk to public safety or national defense.

(b) Monitoring Group

A monitoring group of scientists and personnel outside the USAF will regularly review and assess the conduct of the RANCH HAND study. This group will interact closely with the Air Force principal investigators, and will provide written commentary and recommendations directly to the White House Office of Science and Technology Policy. Approximately equal representation will be maintained between government scientists, academic scientists, and scientific personnel nominated by veterans advocacy groups.

(c) Consultants

In addition to the structured Air Force management system, outside management and scientific consultants will be utilized to provide assistance to the principal investigators upon request.

(d) Contract Performance

All data acquisition contracts will contain highly detailed schedule performance requirements. All statements of work will be coordinated with two procurement levels, appropriate Air Force program coordinators, and the outside monitoring group.

(e) On-Site Contract Monitor

An Air Force Medical Service officer will be assigned to the physical examination site to:

(1) provide visible Air Force representation to all participants,

(2) conduct detailed entry and exit briefings with all participants, particularly ensuring that the health assessment was conducted on a "blind basis",

(3) review all medical data for completeness and accuracy prior to computer entry, and

(4) examine all relevant features of the data acquisition process, and insure absolute compliance to the contract specifications.

(f) Data Security

All medical information obtained on each participant will be entered into a computer data respository. Access to these data will be limited to key scientific investigators by master code numbers.

B. Management Structure

(1) General Organization

Standard Air Force Systems Command research and development concepts and organization will be used to manage this study and assure effective control of all phases of the investigation. The organizational structure is outlined in Figure 16.

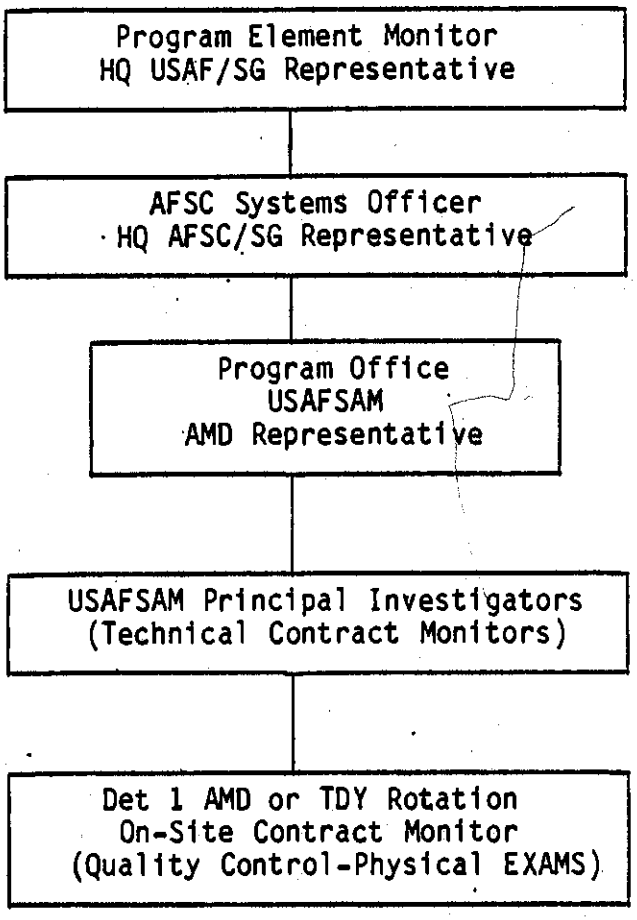
(2) Functions

(a) Program Element Monitor (PEM)

The tasks of the PEM will be preformed by a representative of the USAF Surgeon General's staff. The PEM will serve as the Air Staff Program Monitor, and as such, he will represent the needs and interests of the primary investigators to the Surgeon General and the Air Staff. He will support the needs of the study to the Deputy Chiefs of Staff, the Secretary of the Air Force, the Secretary of Defense, and Congress.

Figure 16

MANAGEMENT STRUCTURE



(b) Systems Officer (SYSTO)

The SYSTO will serve as the Program Manager at the Air Force Systems Command level. In this capacity, he will monitor program status, key issues, and problems. He will also serve as coordinator and expediter between the PEM and the primary investigators. Additionally, the SYSTO will prepare program documentation, coordinate all aspects of the program, monitor obligations and expenditures, and initiate reprogramming actions to support unfunded study requirements.

(c) Program Office

The Program Office will be staffed by a representative of the primary investigators and an Aerospace Medical Division (AMD) representative. This office is responsible for implementation of the complete program

management plan on a day-by-day basis. Routine periodic management assessments and program status information will be provided to the SYSTO. The office will assure that all professional and technical aspects meet the stringent quality requirements outlined in the study protocol. It is the responsibility of this office to insure that all schedules, milestones, and financial requirements are met. This office also interfaces with, and provides guidance and support to the onsite contract monitor(s).

(d) USAFSAM Principal Investigators/Scientists

This team is the leading technical resource for this program. Members of this team are responsible for the faithful execution of the protocol, and as such, approve/disapprove all protocol changes, working in concert with the outside monitoring group. The principal investigators are the tecnhical monitors on all contracts under the protocol. They are responsible for the security of all data, for all data analysis, and for all interpretation of analyses subject to review by the outside monitoring group. These investigators provide summary data to Air Force management personnel on request, to enable proper contract billing and program resource analysis. The primary flow of data, data analyses, and analysis interpretation from the principal investigators/scientist directly to the monitoring group is designed to obviate any appearance of Air Force management bias.

(e) Onsite Contract Monitor (Physical Examination Contractor)

The onsite monitor will act as the Air Force representative at the examination site. He will monitor and assess the quality and timeliness of the contractor's performance, and will advise the Program Office of any performance decrements, as well as other problems encountered at the examination site. He will be responsible for the quality control of all aspects of the examination process (physical examination, laboratory procedures, and psychological and physiological testing). He will also welcome each study subject, review the results of the complete evaluation, and debrief each subject at the conclusion of the examination process.

X. Reporting Procedures

Interim synoptic progress reports will be provided to the Surgeon General through Quarterly Management Reviews conducted each January, April, July and October. Key data analyses will be displayed, but inferences and conclusions will await full data analysis at the conclusion of each phase. A formal report for each of the three phases will be completed with forecasted submission dates of: Mortality Study, June 1982; Morbidity Study, June 1983; and Follow-up Study, June 1985, 1987, 1992, 1997, 2002. Findings and conclusions of each phase will be published in a journal of stature. Total study design, findings, and conclusions will be published in the USAFSAM Aeromedical Reviews or Technical Reports.

XI. QUESTIONNAIRE

The release of the actual questions within the questionnaire could possibly result in irreparable damage to the study from an avoidable source of responder bias. Consequently, this section provides a summary of the general subjects to be covered on the questionnaire and a brief discussion of those specific areas that will receive particular emphasis.

The questionnaire will, of necessity, be lengthy, but it will be administered at a time convenient to the subject. Subjects who refuse to participate in a face-to-face interview will be encouraged to cooperate with modified questionnaires given by telephone. The questionnaire will verify personal identification data such as name, SSAN/AFSN, date of birth, address, telephone numbers, race, military status, effective date of status, location of military medical records, and marital history information. RVN tour information will be rechecked and expanded to include specific data such as date of tour, tour end date, AFSC, organization of assignment, PCS and TDY status, combat missions, and whether or not the tour was a RANCH HAND affiliated tour.

Pre- and Post-RVN exposure information, both occupational and avocational, to asbestos, radiation, herbicides, pesticides, and carcinogens will be elicited. Data concerning the frequency and duration of these exposures are very important. RVN exposure to these chemical and physical agents will also be collected.

Medical information obtained during this interview will include a statement of general health, smoking history, alcohol consumption history and long-term medication/drug use. In addition, questions dealing with infertility, birth defects of offspring, as well as the wife's obstetrical history (i.e., total conceptions, live births, miscarriages, stillbirths and premature pregnancies) will be obtained. A family history emphasizing cancer, heart disease, liver disease and inherited disorders in both the subject's and spouse's families will be collected.

A comprehensive medical inventory will be included emphasizing the neurologic, dermatologic, reproductive, and hepatic systems.

At the time of the physical examinations, each subject will be given a comprehensive face-to-face medical history which will expand and verify the health information that was obtained in the initial questionnaire and records review. An extensive review of systems will be covered at that time, including an extensive occupational and avocational exposure history.

Just prior to the time of follow-up adaptive physical examinations, a preliminary telephone contact will establish the subject's current health status and his willingness to continue participation in the study. Appointments for the follow-up examinations will also be arranged. Adaptive questionnaires will be given emphasizing those symptoms and systems that were found to be significantly associated with the exposed population on analysis of earlier study results. If the subject expresses a desire to cease participation at

this time, he will be encouraged to reconsider his decision, and the reasons for dropping out of the study will be sought. At the time of subsequent followup evaluations, subjects who have left the study will be given the opportunity to rejoin the study.

XII. Physical Examination Design

A. General Instructions

This phase of Project RANCH HAND II is a cross sectional study of the subject's health at the time of examination. The physical examination and all required laboratory procedures will be performed by physicians and technicians at a major civilian medical center under contract to the Air Force. It is important that examiners remain unaware of the subject's status as a RANCH HAND participant or as a control subject. The physician examiner is tasked to examine and objectively record his findings. The examining physician is not, and cannot be expected to arrive at any definitive diagnosis, as the full history and laboratory results will not be available to him. Medical history, laboratory results, and physical examination findings will be evaluated by an independent diagnostician employed by the contractor. This diagnostician will formulate diagnoses and differential diagnoses, if appropriate. In addition, he will present a detailed analysis and debriefing to the study subject, and provide a copy of the analysis to the subject's personal physician, if so requested.

If, during the examination, the physician discovers evidence of serious illness requiring immediate treatment, the normal emergency or urgent care procedures of the medical facility would apply. Such care will be arranged by the diagnostician and will be supplied by the contractor at Air Force expense. If during the examination, evidence of illness requiring non-emergency medical attention is found, the diagnostician should inform the subject and offer to have forwarded pertinent information to the subject's physician. A clear record of any such advice and treatment should be recorded. The ultimate value of the RANCH HAND II Study will lie in the collection of complete, accurate and, whenever possible, quantitiative data permitting the most stringent and powerful statistical analysis. For that reason, the physical examination protocol requires exact measurements in many instances, and the use of defined meanings of semiquantitative indicators in other places.

These examinations will define the health status of the subjects at a point in time, and will establish the presence or absence of abnormal physical findings. After statistical review of the study groups, these findings may permit definition of a chronic effect due to exposure. An inaccurate examination may lead to falacious study results in two ways: a presumed syndrome may be defined which does not in fact exist, or a syndrome which in fact exists may not be defined with enough validity to warrant further actions.

B. Conduct of the Examination

SECTION	PHYSICAL EXAMINATION	SUBJECT NUMBER

1. GENERAL APPEARANCE

a. ___ Appearance/Stated Age ☐ Younger Than ☐ Older Than ☐ Same As

b. ☐ Well-nourished ☐ Obese

☐ Under-nourished ☐ Older Than

c. Appearance of illness or distress ☐ Yes ☐ No

d. Hair Distribution ☐ Normal ☐ Abnormal

SPECIFY:

2. HEIGHT cm | **WEIGHT** *(Undressed)* kg | **SITTING BLOOD PRESSURE RIGHT ARM AT HEART LEVEL** SYSTOLIC_____ DIASTOLIC_____

3. PULSE RATE_____ **REGULAR:** ☐ YES ☐ NO Describe any irregularities.

a. Irregular ☐

b. Irregularly irregular ☐

c. VPBs per minute _____

4. EYE GROUNDS ☐ NORMAL ☐ ABNORMAL Describe any vascular lesions, hemorrhages, exudates, papilledema.

☐ A-V nicking ☐ Hemorrhages ☐ Papilledema

☐ ↑ light reflex ☐ Exudates ☐ ↑ Cupping

☐ Arteriolar spasm ☐ Disk Pallor

5. ARCUS SENILIS ☐ PRESENT ☐ ABSENT 5a. Abnormal Ocular Pigmentation ☐ Yes ☐ No

6. ENT ☐ NORMAL ☐ ABNORMAL Describe any abnormality.

Tympanic membranes intact ☐ Yes ☐ No R ☐ L ☐

Nasal ulcerations ☐ No ☐ Yes

7. NECK *(Especially thyroid gland)* ☐ NORMAL ☐ ABNORMAL Describe any abnormality.

Thyroid gland palpable ☐ ☐ Parotid gland enlargement

Enlarged ☐ ☐ R ☐ L

Nodules ☐

Tenderness ☐

8. THORAX AND LUNGS ☐ NORMAL ☐ ABNORMAL Describe any abnormality, especially basilar rales.

☐ Asymmetrical expansion ☐ Wheezes Circumference at nipple level

☐ Hyperresonance ☐ Rales Expiration _____cm

☐ Dullness Inspiration _____cm

9. HEART ☐ NORMAL ☐ ABNORMAL Describe any enlargement, irregularity of rate, murmurs, or thrills.

Displacement of apical impulse ☐ No ☐ Yes Precordial thrust ☐ No ☐ Yes

Heart sounds normal ☐ Yes ☐ No ☐ S_1 ☐ S_2 ☐ S_3 ☐ S_4

(Continued in Item 18 on Reverse)

10. ABDOMEN ☐ NORMAL ☐ ABNORMAL Describe any abnormality with special attention to the spleen and liver. Record waist measurement on attached form.

☐ Heptomegaly ☐ Other mass - Specify:

_____cm Liver Span

☐ Splenomegaly ☐ Tenderness

☐ Liver ☐ Spleen ☐ Other, specify:

11. EXTREMITIES ☐ NORMAL ☐ ABNORMAL Describe any edema or signs of vascular insufficiency.

☐ Absence, specify:

☐ Edema ☐ Clubbing of nails

☐ Pitting ☐ Non-pitting ☐ Varicosities

☐ Loss of hair on toes

☐ R ☐ L

SECTION PHYSICAL EXAMINATION (Continued)

12. PERIPHERAL PULSES	NORMAL	DIMIN.	ABSENT	COMMENTS
RADIAL				
FEMORAL				
POPLITEAL				
DORSALIS PEDIS				
POSTERIOR TIBIAL				

13. SKIN ☐ NORMAL ☐ ABNORMAL Indicate type and location of lesions on the attached anatomical figure

☐ Dermatographia
☐ Comedones
☐ Acneiform lesions
☐ Acneiform scars
☐ Depigmentation
☐ Inclusion cysts
☐ Cutis Rhomboidalis
☐ Hyperpigmentation
☐ Jaundice
☐ Spider angiomata
☐ Palmar erythema
Full-Face and Bilateral profile photos taken ☐ Yes ☐ No
☐ Palmar Keratosis
☐ Petechiae
☐ Ecchymoses
☐ Soles of feet
☐ Nails
Biopsy Taken Yes No

14. MUSCULOSKELETAL ☐ NORMAL ☐ ABNORMAL

☐ Muscle - Specify:
☐ Weakness
☐ Tenderness
☐ Abnormal Consistency
☐ Atrophy
☐ Spine
☐ Scoliosis
☐ Kyphosis
☐ Tenderness, Level ____
☐ Decreased range of motion
☐ Pelvic tilt
☐ Straight Leg Raising: Right/Left

15. GENITOURINARY - RECTAL - HERNIA ☐ NORMAL ☐ ABNORMAL

☐ Inguinal hernia ☐ R ☐ L
☐ Testes

	Absent	Enlarged	Atrophic
☐ R	☐	☐	☐
☐ L	☐	☐	☐

☐ Varicocele
☐ Epididymis
☐ Scrotal Mass ____ cm dia
☐ Hemorrhoids
☐ Prostatic Enlargement
☐ Rectal mass

16. LYMPH NODES - CHECK ALL AREAS. ☐ NORMAL ☐ ABNORMAL - SPECIFY CERVICAL, OCCIPITAL, SUPRACLAVICULAR, AXILLARY, EPITRACHLEAR, INGUINAL, FEMORAL
☐ Enlarged ___ ☐ Tender ___ ☐ Hard ___ ☐ Fixed ___ ☐ Confluent

17. NERVOUS SYSTEM - SEE ATTACHED FORMS

18. HEART AND OTHER OBSERVATIONS
(Continued from Item 9)

Murmur ☐ No ☐ Yes Area ☐ Ao ☐ Pu ☐ Apex
Sys ☐ ☐ ☐ ☐
Dia ☐ ☐ ☐ ☐

DATE OF EXAMINATION MONTH DAY YEAR

TYPED OR PRINTED NAME OF EXAMINING PHYSICIAN

EXAMINING FACILITY

SIGNATURE

CLINICAL RECORD NEUROLOGICAL EXAMINATION

HEAD AND NECK - Normal to Palpations/Inspection ☐Y ☐N Specify Scar ☐
Asymmetry ☐ Depression ☐
Carotid Bruit ☐No ☐R ☐L
Neck Range of Motion ☐ Normal or Decreased to ☐ Left ☐ Right
☐ Forward ☐ Backward

TRUNK

MOTOR SYSTEM - Handedness Right ☐ Left ☐

Gait ☐ Normal or ☐ Broad Based ☐ Ataxic ☐Small Stepped ☐Other-Specify

Associated Movements ☐Arm Swing ☐Normal or Abnormal ☐R ☐L

Muscle Status (strength, tone, volume, tenderness, fibrillations)
Bulk ☐ Normal ☐Abnormal

Tone Upper Extremities ☐Normal or ☐Increased ☐Decreased
☐Right ☐Left

Lower Extremities ☐Normal or ☐Increased ☐Decreased
☐Right ☐Left

Strength - Distal wrist extensors ☐Normal ☐Decreased
Ankle/Toe Dors/Flexors ☐Normal ☐Decreased ☐R ☐L

Proximal Deltoids ☐Normal ☐Decreased ☐R ☐L
Hip Flexors ☐Normal ☐Decreased ☐R ☐L

Abnormal Movements (tremors, tics, choreas, etc.) Fasiculations ☐No ☐Yes (1-4+)
Tenderness ☐No ☐Yes (1-4+)

Tremor ☐No ☐Yes - Specify

Upper Extremity ☐R ☐L ☐Resting ☐Essential ☐Intention

Lower Extremity ☐R ☐L ☐Other

Coordination (a) Equilibratory - Eyes Open
Eyes Closed - Romberg ☐Positive (Abnormal) ☐Negative (Normal)

Right Foot Left Foot

(b) Nonequilibratory (F to N; F to F; H to K) Finger-to-nose-to-finger
☐Normal ☐Abnormal ☐Right ☐Left ☐Both
Heel-Knee-Shin ☐Normal ☐Abnormal ☐Right ☐Left ☐Both

(c) Succession Movements (including check, rebound, posture-holding)
If indicated, check ☐Normal ☐Abnormal ☐R ☐R

Rapidly alternative movements ☐Normal ☐Abnormal ☐R ☐L ☐Both

Skilled Acts

( ) Handwriting. If indicated, ☐Normal ☐Abnormal

( ) Speech (articulation, aphasia, agnosia) Grossly ☐Normal
☐Abnormal - Specify Dysarthria ☐
Aphasia ☐

Reflexes (0-absent; 1-sluggish; 2-active; 3-very active; 4-transient clonus; 5-sustained clonus)

Deep	R	L	Deep	R	L	Other	R	L	Abnormal	R	L
									Babinski		
Biceps			Patellar								
Triceps											
			Achilles								
Remarks											

MENINGEAL IRRITATION

Straight Leg Raising ☐Normal ☐Abnormal ☐R ☐L ☐Both

NERVE STATUS (tenderness, tumors, etc.)

SENSORY SYSTEM (tactile, pain, vibration, position. If positive sensory signs are present, summarize below and indicate details on Anatomical Figure, Std. Form 531)

Light Touch ☐Normal ☐Abnormal

Pin Prick ☐Normal ☐Abnormal (Map on Anatomical Figure)

Vibration (at ankle, 128 hz tuning fork): ☐Normal ☐Abnormal ☐R ☐L ☐Both

Position (Great toe): ☐Normal ☐Abnormal ☐R ☐L ☐Both

CRANIAL NERVES

I R Smell ☐Present ☐Absent

L Smell ☐Present ☐Absent

II Fundus R Normal ☐ Abnormal ☐ Disk Pallor/atrophy
☐Exudate ☐Papilledema ☐Hemorrhage

Fundus L Normal ☐ Abnormal ☐ Disk pallor/atrophy
☐Exudate ☐ Papilledema ☐Hemorrhage

Fields (to confrontation)
Right ☐Normal ☐Abnormal Left ☐Normal ☐Abnormal

III Normal ☐ ☐Abnormal - Specify
IV
VI Pupils-Size (mm) Equal ☐ Unequal ☐ Difference mm____
Shape, position Round ☐ Other ☐ ☐R ☐L
Light, Reaction Normal ☐ Abnormal ☐ ☐R ☐L
Position of Eyeballs

Movements R L

Nystagmus Rotary ☐ Horizontal ☐ Vertical ☐
(Draw position)

XI

Ptosis R☐ L☐

V Motor R Clench Jaw - Symmetric ☐ Deviated ☐ R☐ L☐
L

Sensory R Normal ☐ Abnormal ☐ V_1☐ V_2☐ V_3☐
L Normal ☐ Abnormal ☐ V_1☐ V_2☐ V_3☐

Corneal Reflex R L

VII Motor R Normal smile ☐Yes ☐No Palpebral Fissure ☐Yes ☐No
L Normal smile ☐Yes ☐No Palpebral Fissure ☐Yes ☐No

IX Palate and Uvula
X Movement Normal ☐ Deviation to ☐R ☐L

Palatal Reflex R ☐Normal ☐Abnormal
L ☐Normal ☐Abnormal

XII Tongue-Protruded-Central ☐ R☐ L☐
Atrophy ☐No ☐Yes

MENTAL STATUS (alert, clear, cooperative, etc.) Gross abnormalities: ☐No
☐Yes - Specify

DIAGNOSTIC SUMMARY

SYNOPSIS OF POSITIVE FINDINGS

Medical History:

Physical Examination:

General

Dermatologic

Neurological

Psychological

Laboratory Results:

Diagnosis:

Differential Diagnosis, if applicable:

Date

Signature
of Diagnostician

C. Special Procedures

(1) Nerve Conduction Velocities (NCV)

These studies have been determined to be an important parameter in long-term follow-up studies of persons thought to have been exposed to Herbicide Orange components. The Nerve Conduction Velocities should be performed by a physician or by a specialty qualified technician under the supervision of a physician trained in neurophysiological methods.

(a) Specific NCVs

(1) Ulnar Nerve (one side only)

(a) motor (above elbow, below elbow)

(b) values recorded

(i) distal latency

(ii) NCV

(2) Peroneal Nerve (one side only)

(a) motor

(b) values recorded

(i) distal latency

(ii) NCV

(3) Sural Nerve (one side only)

(a) sensory: orthodromic

(b) values recorded: NCV

(b) Methods

Standardized, published methods will be used (e.g., Smorto, Marcio P., and John V. Besmajian; Electrodiagnosis; Harper and Row; NY, 1977).

(2) Psychological Test Battery

(a) General

This battery yields objective numerical data, and is well-standardized and clinically validated. The individual tests were chosen to insure an adequate analysis of one of the major alleged manifestations of

Herbicide Orange toxicity. Each test either validates the other tests or is considered to be a "definitive" test for analysis of a suspected psycho-neuropathic effect under study. Compared to the general civilian population, characteristic response tendencies are observed on the MMPI and Cornell Index among active duty aircrewmen being evaluated in an aeromedical setting. It is also important to consider the effect that pending retirement has exerted on the reporting of medical history and symptomatology. This may also alter responses to psychological testing.

(b) Specific Tests

(1) Wechsler Adult Intelligence Scale (WAIS)

Individually-administered collection of verbal and nonverbal intellectual measures; also useful for clinical inferences when combined with the neuropsychological battery below.

(2) Reading subtest of the Wide Range Achievement Test (WAIT)

Individually-administered measure of word recognition ability. Important to rule-out reading inefficiency should the response to the personality instruments below be of questionable validity (e.g., high F scale on MMPI).

(3) Halstead-Reitan Neuropsychological Test Battery

Individually-administered collection of brain behavior relationship measures for establishing the functional integrity of the cerebral hemispheres. The battery must include the following subtests: Category, Tactual performance, Speech-Sounds, Seashore Rhythm, Finger Tapping, Trail Making, and Grip Strengths. The Aphasia Screening and Sensory-Perceptual Exams are considered optional in view of their redundancy with the clinical neurologic exam included in this project. Individualized test debriefing is conducted to clarify test performances in the WAIS and Neuropsychological Battery.

(4) Three subtests of the Wechsler Memory Scale I (WMS I)

Individually-administered measures of immediate and delayed recall of verbal and visual materials. The Logical Memory, Associate Learning and Visual Reproduction subtests are to be administered in the standard, immediate-recall fashion initially. After 30 minutes has elapsed, the examinee is asked, without prior alerting, to recall as much as he can about the Logical Memory and Visual Reproduction subtest stimuli. Standard scoring is used for both test-retest administrations.

(5) Cornell Index (CI)

Self-administered and standardized neuropsychiatric symptom and complaint inventory, including items involving asthenia, depression, anxiety, fatigue, and GI symptoms in lay language. Endorsement of items are to be explored and clarified in test-debriefing.

(6) Minnesota Multiphasic Personality Inventory (MMPI)

60 to 90 minute self administered clinical psychiatric screening instrument; also capable of estimating response biases (e.g., "fake good," or "fake bad"). The shortened version of Form R (i.e., items 1 to 399) may be substituted for the 566-item Long Form. Standard scoring and Minnesota norms are to be used, with the possible exception of active duty examinees where USAFSAM aircrew norms may be applied. Clarification of profiles showing response biases, questionable validity, and/or unusual item endorsements will be conducted in individual test debriefing.

(3) 12-Lead Electrocardiogram

(a) Procedures

A standard 12-lead scalar electrogram is required. If an arrhythmia is observed, a one minute rhythm strip will be obtained. The electrogram will be done following a minimum fast of four hours.

(b) Interpretation

The electrocardiograms will be interpreted by cardiologists at the examining center, and then forwarded to Brooks AFB where physicians in the USAF Central ECG Library will compare the tracing to previous individual ECG records in the case of rated (pilot or navigator) subjects.

(c) Disposition (USAF Central ECG Library)

(1) Pilots and Navigators

The original tracings will be microfisched and permanent record established for each individual.

(2) Enlisted Subjects

The original tracings will be microfisched and a permanent record established for each individual.

(4) Radiographic Examination

A standard 14x17 in., standing, roentgenogram in the PA position using small nipple markers will be accomplished.

(5) Pulmonary Function Studies

Standard evaluation of vital capacity and forced expiratory volume at 1 second will be performed.

(6) Laboratory Procedures

(a) Specific Tests to be Performed on all Participants

(1) Hematocrit

(2) Hemoglobin

(3) RBC Indices

(4) While Blood Cell Count and Differential

(5) Platelet Count

(6) Erythrocyte Sedimentation Rate

(7) Urinalysis

(8) Semen Analysis (Number, % Abnormal, Volume)

(9) Blood Urea Nitrogen

(10) Fasting Plasma Glucose

(11) Creatinine

(12) 2-hour Post Prandial Plasma Glucose

(13) Differential Cortisol (0730 and 0930 hours)

(14) Cholesterol & HDL

(15) Triglycerides

(16) SGOT

(17) SGPT

(18) GGTP

(19) Bilirubin, Total and Direct

(20) Alkaline Phosphatase

(21) LDH

(22) Serum Protein Electrophoresis

(23) CPK

(24) VDRL

(25) LH

(26) FSH

(27) Testosterone

(28) Thyroid Profile (RIA) (T_3, T_4, TSH,FTI)

(29) Delta-aminolevulinic Acid

(30) Urine Porphyrins

(31) Hepatitis B antigen/antibodies

(32) Prothrombin time

(33) Blood Alcohol

(b) To be performed on selected subjects

(1) Anti-nuclear Antibody on subjects with indications of autoimmune disorders

(2) Hepatitis A Antigens/antibodies for those with current or past history of liver disease

(3) Karyotyping for those fathering children with birth defects

(4) Skin photography and skin biopsy on subjects with suspected chloracne

(5) To be performed if medical history indicates a subject has an increase in infectious diseases:

(a) Immunoelectrophoresis

(b) Quantitative Immunoglobulin Determinations

(6) To be performed on a randomly selected group of subjects

(a) Enumeration of B and T cells

(b) Enumeration of Monocytes

(c) B and T cell function tests

(7) Rationale for laboratory procedures

(a) Studies on the toxicity of TCDD in animals have shown that the following organ systems are damaged:

(1) Liver: Hepatic necrosis, liver enzyme changes, hypoproteinemia, hypercholesterolemia, hypertriglyceridemia.

(2) Reticuloendothelial System: Thymic atrophy, altered cellular immunity, decreased lymphocyte counts.

(3) Hemopoietic System: Anemia, thrombocytopenia, leukopenia, pancytopenia.

(4) Endocrine System: Hemorrhage and atrophy of adrenal cortex, hypothyroidism.

(5) Renal: Increase in blood urea nitrogen.

(6) In addition, statistically significant increases in hepatocellular carcinomas (liver) and squamocellular carcinomas of the lung were found.

(b) Studies on the toxic effects of TCDD in man have shown that the following organ systems are damaged:

(1) Skin: Chloracne, hirsutism.

(2) Liver: Porphyria cutanea tarda. Increased levels of transaminase and of GGTP. Enlarged, tender liver, hyperlipidemia.

(3) Renal: Hemorrhagic cystitis, focal Pyelonephritis.

(4) Neuromuscular System: Asthenia, i.e., headache, apathy, fatigue, anorexia, weight loss, sleep disturbances, decreased learning ability, decreased memory, dyspepsia, sweating, muscle pain, joint pain and sexual dysfunction.

(5) Endocrine System: Hypothyroidism.

(c) Based upon the reports of toxic effects in animal and human exposures, the following organ panels were thus recommended:

(1) Hemopoietic

(2) Reticuloendothelial

(3) Renal

(4) Endocrine

(5) Neuromuscular

(d) Hemopoietic screening should include:

(1) Hematocrit

(2) Hemoglobin

(3) RBC indices

(4) Erythrocyte sedimentation rate

(5) Platelet count

(6) Prothrombin time

(e) Reticuloendothelial system:

(1) White blood cell count

(2) Differential

(3) Serum protein electrophoresis

(4) Selective use of immunoelectrophoresis and quantitative immunoglobulin determination

(5) B cell and T cell counts and functions

(f) Hepatic screen:

(1) SGOT

(2) SGPT

(3) GGTP

(4) Bilirubin, Total and Direct

(5) Alkaline phosphatase

(6) LDH

(7) Cholesterol

(8) HDL

(9) Triglyceride

(10) Urine prophyrins

(11) Urine porphobilinogen

(12) Hepatitis B antigens/antibodies

(g) Renal screen:

(1) Urinalysis

(2) BUN

(3) Creatinine

(h) Endocrine screen:

(1) Differential cortisol (0730 and 0930 hours)

(2) Thyroid profile (RIA)

(3) Fasting plasma glucose

(i) Neuromuscular system:

(1) CPK

(j) Elucidation of sympoms of asthenia:

(1) Testosterone

(2) LH

(3) FSH

(k) The following tests should be peformed only as follow-up for abnormalities in the history or physical examination findings:

(1) HAVAB (IgG and IgM)

(2) ANA

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XV. APPENDIX

TABLE A-1	SUMMARY OF 2,4-D, 2,4,5-T AND TCDD ANIMAL STUDIES
TABLE A-2	"SYMPTOM COMPLEX" DERIVED FROM LITERATURE REVIEW OF CASE STUDIES EXPOSED TO 2,4-D, 2,4,5-T AND/OR TCDD
TABLE A-3	DETAILED LISTING OF SYMPTOMS/ SIGNS BY MAJOR CATEGORY FROM LITERATURE REVIEW OF CASE STUDIES EXPOSED TO 2,4-D, 2,4,5-T AND/OR TCDD
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FIGURE A-3	STUDY DESIGN FORMAT

TABLE A-1

SUMMARY OF 2,4-D, 2,4,5-T, AND TCDD ANIMAL STUDIES

	2,4-D	2,4,5-T	TCDD
LD_{50} RANGE (ACUTE)	100-1000 mg/kg	100-1000 mg/kg	1-1000 g/kg
CHRONIC TOXIC DOSE	APPROACHES ACUTE LEVEL RAPID CLEARANCE	1/2 ACUTE LEVEL; VARIABLE CLEARANCE	MARKEDLY LOWER LEVEL BIOACCUMULATION
SIGNS OF ACUTE/ CHRONIC TOXICITY	ANOREXIA	ANOREXIA	WEIGHT LOSS
	WEIGHT LOSS	ATAXIA	INVOLUTION OF THYMUS
	MUSCULAR WEAKNESS	G.I. INJURY	ALOPECIA
	IRRITATED G.I. TRACT	LIVER CONGESTION	EPITHELIAL CHANGES
	MINOR LIVER INJURY	KIDNEY CONGESTION	LIVER LESIONS (VARIABLE)
	MINOR KIDNEY INJURY		HYPOTHYROIDISM
	MINOR LUNG CONGESTION		
EMBRYOTOXIC DOSE	APPROACHES TOXIC LEVEL	APPROACHES TOXIC LEVEL	MARKEDLY BELOW TOXIC MATERNAL LEVELS
TERATOGENICITY	QUESTIONABLE; WEAK AT BEST	*LOW INCIDENCE ONLY IN MICE (CLEFT PALATES DILATED RENAL PELVIS)	SPECIES VARIATIONS: YES MICE NO RATS
CARCINOGENICITY	QUESTIONABLE; WEAK AT BEST	ONE STUDY: YES NUMEROUS STUDIES: NO	EPITHELIAL CHANGES IN PRIMATES: YES IN RATS

TABLE A-2 "SYMPTOM COMPLEX" DERIVED FROM LITERATURE REVIEW OF CASE STUDIES EXPOSED TO 2,4-D; 2,4,5-T AND/OR TCDD

2,4-D	2,4,5-T (+ TCDD)	TCDD
	CHLORACNE	CHLORACNE
	PORPHYRIA	PORPHYRIA
	HYPERPIGMENTATION	HYPERPIGMENTATION
ASTHENIA	ASTHENIA	ASTHENIA
PERIPHERAL NEUROPATHY	PERIPHERAL NEUROPATHY	PERIPHERAL NEUROPATHY
SWEATING/FEVER		
CARDIAC DISTURBANCE	CARDIAC DISTURBANCE	CARDIAC DISTURBANCE
RENAL DYSFUNCTION		RENAL DYSFUNCTION
LIVER DYSFUNCTION	LIVER DYSFUNCTION	LIVER DYSFUNCTION
GI DISTURBANCE	GI DISTURBANCE	GI DISTURBANCE
HEADACHE		
PNEUMONITIS		
CSF PROTEIN ALTERATIONS		HYPOTHYROIDISM
CONVULSIONS		HEARING/SMELL DISTURBANCES

TABLE A-3 DETAILED LISTING OF SYMPTOMS/SIGNS BY MAJOR CATEGORY FROM LITERATURE REVIEW OF CASE STUDIES EXPOSED TO 2,4-D; 2,4,5-T AND/OR TCDD

NEURO-PSYCHIATRIC ABNORMALITIES

AESTHENIA	PERIPHERAL NEUROPATHY
ANXIETY	HYPOREFLEXIA
DEPRESSION	WEAKNESS
FATIGUE	PARESTHESIAS
APATHY	EXTREMITY NUMBNESS
LOSS OF DRIVE	MYALGIA
DECREASED LIBIDO	GAIT DISTURBANCE
IMPOTENCY	"MILD" PARESIS
SLEEPLESSNESS	
EMOTIONAL INSTABILITY	
ANOREXIA	
DIZZINESS	
DECREASED LEARNING ABILITY	

TABLE A-3 (CONTINUED) DETAILED LISTING OF SYMPTOMS/SIGNS BY MAJOR CATEGORY FROM LITERATURE REVIEW OF CASE STUDIES EXPOSED TO 2,4-D, 2,4,5-T AND/OR TCDD

DERMATOLOGIC DISEASE

CHLORACNE

PORPHYRIA CUTANEA TARDA

HYPERPIGMENTATION

HIRSUITISM (BODY)

ALOPECIA OF THE SCALP

OTHER DISORDERS

HEPATIC DYSFUNCTION

INCREASED CHOLESTEROL AND TRIGLYCERIDE

INCREASES IN LIVER FUNCTIONAL TESTS

RENAL DYSFUNCTION

PROTEINURIA

DECREASED OUTPUT

TUBULAR DEGENERATION

GLOMERULAR DEGENERATION

RENAL GLUCOSURIA

GI DISTURBANCE

NAUSEA

VOMITING

DIARRHEA

GASTRITIS

ABDOMINAL PAIN

CARDIAC DISTURBANCE

BRADYCARDIA

TACHYCARDIA

ATRIAL FIBRILLATION

TABLE A-4

AGE COMPARISON OF EXPOSED SUBJECTS AND THEIR MATCHED CONTROLS

	AFSC/Race Strata	Number of Exposed Subjects	Mean Number of Matched Controls	Age Difference Range
Officer:	Pilot/Caucasian	349	9.5	0-60
	/Black	6	2.7	0-57
	Nonpilot/Caucasian	78	10.0	0-07
	/Black	2	10.0	0-36
	Other/Caucasian	25	10.0	0-27
	/Black	1	5.0	0-54
Enlisted:	Flying/Caucasian	187	10.0	0-35
	/Black	15	9.8	0-58
	Nonflying/Caucasian	528	10.0	0-48
	/Black	51	10.0	0-06
Killed in Action				
	Officers/Caucasian	14	--	--
	/Black	1	--	--
	Enlisted/Caucasian	7	--	--
	/Black	0	--	--

TABLE A-5

STATISTICAL DESCRIPTION OF THE MATCHING PROCESS

DIST IN MONTHS	COUNT	DIST IN MONTHS	COUNT	ABSOLUTE DIST IN MONTHS	COUNT	%	CUMULATIVE TOTAL	%
				0	8612	70.6	8612	70.6
- 1	847	1	828	1	1675	13.7	10287	84.3
- 2	231	2	231	2	462	3.8	10749	88.1
- 3	114	3	121	3	235	1.9	10984	90.1
- 4	92	4	91	4	183	1.5	11167	91.6
- 5	88	5	67	5	155	1.3	11322	92.8
- 6	41	6	47	6	88	0.7	11410	93.5
- 7	33	7	39	7	72	0.6	11482	94.1
- 8	28	8	22	8	50	0.4	11532	94.5
- 9	27	9	23	9	50	0.4	11582	95.0
-10	10	10	21	10	31	0.3	11613	95.2
-11	18	11	18	11	36	0.3	11649	95.5
-12	17	12	22	12	39	0.3	11688	95.8
-13	9	13	18	13	27	0.2	11715	96.0
-14	23	14	11	14	34	0.3	11749	96.3
-15	11	15	8	15	19	0.2	11768	96.5
-16	20	16	15	16	35	0.3	11803	96.8
-17	16	17	11	17	27	0.2	11830	97.0
-18	4	18	6	18	10	0.1	11840	97.1
-19	6	19	6	19	12	0.1	11852	97.2
-20	11	20	3	20	14	0.1	11866	97.3
-21	10	21	9	21	19	0.2	11885	97.4
-22	4	22	6	22	10	0.1	11895	97.5
-23	4	23	13	23	17	0.1	11912	97.7
-24	4	24	5	24	9	0.1	11921	97.7
-25	3	25	4	25	7	0.1	11928	97.8
-26	6	26	7	26	13	0.1	11941	97.9
-27	2	27	8	27	10	0.1	11951	98.0
-28	6	28	8	28	14	0.1	11965	98.1
-29	2	29	9	29	11	0.1	11976	98.2
-30	2	30	4	30	6	0.0	11982	98.2
-31	2	31	5	31	7	0.1	11989	98.3
-32	1	32	5	32	6	0.0	11995	98.3
-33	6	33	2	33	8	0.1	12003	98.4
-34	3	34	3	34	6	0.0	12009	98.5
-35	5	35	7	35	12	0.1	12021	98.6
-36	4	36	3	36	7	0.1	12028	98.6
-37	3	37	3	37	6	0.0	12034	98.7
-38	4	38	11	38	15	0.1	12049	99.8
-39	2	39	5	39	7	0.1	12056	99.8
-40	3	40	5	40	8	0.1	12064	99.9
-41	5	41	2	41	7	0.1	12071	99.0
-42	4	42	6	42	10	0.1	12081	99.0
-43	2	43	2	43	4	0.0	12085	99.1
-44	6	44	9	44	15	0.1	12100	99.2
-45	9	45	4	45	13	0.1	12113	99.3
-46	3	46	6	46	9	0.1	12122	99.4
-47	0	47	4	47	4	0.0	12126	99.4
-48	0	48	3	48	3	0.0	12129	99.4
-49	3	49	1	49	4	0.0	12133	99.5
-50	4	50	4	50	8	0.1	12141	99.5
-51	2	51	2	51	4	0.0	12145	99.6
-52	0	52	0	52	0	0.0	12145	99.6
-53	4	53	4	53	8	0.1	12153	99.6
-54	6	54	2	54	8	0.1	12161	99.7
-55	3	55	3	55	6	0.0	12167	99.8
-56	4	56	0	56	4	0.0	12171	99.8
-57	3	57	2	57	5	0.0	12176	99.8
-58	5	58	3	58	8	0.1	12184	99.9
-59	5	59	1	59	6	0.0	12190	99.9
-60	3	60	4	60	7	0.1	12197	100.0

Table A-6
SPECIFIC RULES FOR ENTRY INTO THE MORBIDITY STUDY

CIRCUMSTANCES	RULES
RANCH HANDER (RH) DIES FOLLOWING INITIAL DATA COLLECTION	CONTROL FOLLOWED THROUGHOUT AND REPLACED AS NECESSARY
RH DIES OF COMBAT CAUSE	MEDICAL RECORDS REVIEWED; NO CONTROL SET FORMED
RH DIES OF NONCOMBAT CAUSE PRIOR TO INITIAL DATA COLLECTION	1ST ORDER SURROGATE INTERVIEW ACCOMPLISHED; CONTROL SELECTED AND FOLLOWED THROUGHOUT; AS NECESSARY
RH NONCOMPLIANT FOR BASELINE QUESTIONNAIRE AND PHYSICAL	CONTROL FOLLOWED THROUGHOUT THE STUDY; REPLACED AS NECESSARY
RH COMPLIANT FOR QUESTIONNAIRE; NONCOMPLIANT FOR BASELINE PHYSICAL EXAMINATION	CONTROL FOLLOWED THROUGHOUT THE STUDY; REPLACED AS NECESSARY
RH NONCOMPLIANT DURING FOLLOWUP	CONTROL FOLLOWED THOUGHOUT THE STUDY; REPLACED AS NECESSARY
CONTROL DIES FOLLOWING INITIAL DATA COLLECTION	NOT REPLACED IN THE PROSPECTIVE STUDY OF MORBIDITY
CONTROL DIES OF COMBAT CAUSE	MEDICAL RECORDS REVIEWED; EXCLUDED FROM FURTHER STUDY
CONTROL DIES OF NONCOMBAT CAUSE PRIOR TO INITAL DATA COLLECTION	INCLUDED IN MORTALITY AND RETROSPECTIVE MORBIDITY STUDIES; SURROGATE INTERVIEW ACCOMPLISHED. NOT INCLUDED IN PROSPECTIVE MORBIDITY STUDY AND REPLACED BY A LIVING COMPLIANT CONTROL.
CONTROL NONCOMPLIANT FOR BASELINE PHYSICAL EXAMINATION	CONTROL FOLLOWED THROUGHOUT STUDY REPLACE AS NECESSARY
CONTROL NONCOMPLIANT DURING FOLLOWUP	CONTROL FOLLOWED THROUGHOUT STUDY REPLACE AS NECESSARY
NONCOMPLIANT CONTROL RETURNS TO STUDY	BOTH PRIMARY AND REPLACEMENT CONTROLS WILL BE CONTINUED IN STUDY

Table A-7

SCHEDULE AND MODE OF CONTACTS WITH

STUDY SUBJECTS

STUDY PHASE	CONTACT MADE	TIME
Morbidity Study	Introductory Letters	Oct 81
Morbidity Study	Comprehensive Questionnaire	Oct 81-Mar 82
	Baseline Physical Exam	Dec 81-Sep 82
Follow-up Study	Adaptive Questionnaire	Oct 83-Mar 84
	Adaptive Physical Examination	Dec 84-Jun 85
	Adaptive Questionnaire	Oct 86-Mar 87
	Adaptive Physical Examination	Dec 86-Jun 87
	Adaptive Questionnaire	Oct 91-Mar 92
	Adaptive Physical Examination	Dec 91-Jun 92
	Adaptive Questionnaire	Oct 96-Mar 97
	Adaptive Physical Examination	Dec 96-Jun 97
	Adaptive Questionnaire	Oct 2001-Mar 2002
	Adaptive Physical Examination	Dec 2001-Jun 2002