

APPENDIX B

APPENDIX B. PHYSICAL EXAMINATION METHODOLOGY

This appendix contains the following items:

1. The Examiners' Handbook
2. The data collection forms.

ADDENDUM A

STATEMENT OF WORK

FOR THE

AIR FORCE HEALTH STUDY

1997 FOLLOW-UP EXAMINATION

AIR FORCE HEALTH STUDY
EXAMINERS HANDBOOK

3 July 1996
(Statement of Work Updates through 30 April 1999 included)

AIR FORCE HEALTH STUDY EXAMINERS HANDBOOK

A. GENERAL INSTRUCTIONS

The Air Force Health Study is a multiyear prospective study to determine whether Air Force personnel who were engaged with spraying herbicides in Vietnam have developed adverse health effects from exposure to herbicides and their contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). Detailed surveys of the scientific literature have been used to design the questionnaires, the physical examination protocol, and select laboratory tests.

This phase of the study involves a follow-up cross-sectional assessment of each subject's health at the time of the examination. It is important that examiners remain unaware of the subject's exposure status (Ranch Hand, Comparison). The physician examiner is tasked to examine each subject and objectively record findings. The examining physician is not, and cannot be expected, to arrive at any definitive diagnoses, since the full history and physical examination findings and laboratory results will not be available. Medical history, laboratory results, and physical examination findings will be evaluated by an independent diagnostician employed by the contractor. The diagnostician will formulate diagnoses and differential diagnoses, if appropriate. Additional procedures to treat or evaluate emergency or urgent medical conditions will be directed only by the diagnostician. In addition, the diagnostician will present a detailed analysis and debriefing to each study subject and provide a copy of the analysis to the subject's personal physician, if authorized by the subject.

The physicians performing examinations for the study should be aware that the report of the examination will become a permanent record. The report will be referenced not only in the near future as the cross-sectional data is analyzed, but also during future follow-up phases of the study. 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 chronic or latent effects due to exposure. An inaccurate examination may lead to fallacious 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 action.

The examining physician is responsible for recording a complete and detailed report of the physical examination. In this role, the examining physician is tasked with collecting evidence of the presence or absence of physical signs of abnormality only. All items on the physical examination report form must be completed. It is imperative that physicians make such additional remarks as may be required to adequately describe existing physical abnormalities. Since clinical endpoints have not been well defined following exposure to Agent Orange, the examining physician and the diagnostician must not definitively ascribe abnormalities to herbicide exposure during the course of the examination or during the debriefings. If, during the examination, the physician discovers evidence of acute serious illness requiring immediate treatment, the normal emergency or urgent care procedure of the medical facility would apply. The Air Force is not responsible for the cost of such emergency or urgent care.

The debriefing physician shall ask each participant if he received additional testing or additional medical treatment during the physical examination time period and shall annotate any such circumstances or results on the debriefing form. The ultimate value of the study will lie in the collection of complete, accurate and, whenever possible, quantitative data permitting the most stringent and powerful statistical

analysis. For this reason, the physical examination protocol requires, whenever possible, exact measurements and well defined semi-quantitative indicators of abnormalities.

B. CONDUCT OF THE EXAMINATION

1. Overview

Upon arrival at the examining facility, the subject should be briefed by a representative of the contractor on the appointments that have been arranged, their times, and locations. Consent forms covering all examination procedures will be provided to each subject. The subject may decline to participate in any individual portion of the examination, even if he previously signed a consent form.

The examination will be conducted in a manner identical to that used in prior phases of the study and in accord with detail in subsequent sections of this handbook and the Statement of Work.

2. General Physical Examination

The general physical examination shall include an assessment of

1. Appearance (well nourished, obese, under nourished)
2. Appearance relative to stated age (same as, older than, younger than)
3. Appearance of illness or distress (no, yes)
4. Hair distribution (normal, abnormal)
5. Vital signs (height in centimeters, weight undressed in kilograms, oral temperature)
6. Systolic and diastolic blood pressure
7. Pulse rate
8. Premature beats per minute
9. Pulse diagnosis (regular, irregular, irregularly irregular)
10. An eye examination (fundoscopic and external observation)
11. An ENT/neck examination
12. A thorax and lung examination
13. Waist, chest and neck measurements in centimeters
14. A heart examination including an overall diagnosis (normal, abnormal, refused)
15. An examination of the abdomen, extremities and peripheral pulses, musculature and spine
16. An examination of extremities
17. An examination of peripheral pulses
18. An examination of musculature
19. An examination of the spine
20. An examination of the genitourinary system
21. A rectal examination
22. An assessment of the lymph nodes (normal, enlarged, tender, hard, fixed, confluent, other)
23. A summary of follow-up indicated or recommended.

3. Dermatologic Examination And Biopsy

The examination shall include

1. An examination of the skin
2. Skin biopsy, if indicated
3. Physical features
4. Mapping of lesions on an anatomical chart.

4. Neurological Examination

The examination shall include

1. An examination of the head and neck
2. An examination of motor systems
3. An examination of muscle status
4. An assessment of abnormal movements
5. An assessment of tremors
6. An assessment of coordination
7. An assessment of deep tendon reflexes
8. An assessment of cranial nerves and mental status
9. An assessment of meningeal irritation and sensory system
10. An examination of cranial nerves (I, VII)
11. An examination of cranial nerves (II)
12. An examination of cranial nerves (III, IV, VI)
13. An examination of cranial nerves (V, IX, XI, XII)
14. An impression of the entire neurological examination.

5. Psychological Testing

The Symptom Check List-90-Revised (SCL-90-R) will be given to all study subjects. This self-administered test was chosen to ensure adequate analysis of alleged psychological manifestations of herbicide toxicity. The psychologist in charge will interpret the results of the test, record those interpretations on a form, and provide them to the debriefing physician. The contractor shall forward all test materials as scored with annotations, interpretations, and impressions to the diagnostician for inclusion in the subject's file.

6. Electrocardiogram

A standard 12-lead scalar electrocardiogram is required. If an arrhythmia is observed, a 1-minute rhythm strip is additionally requested. This electrocardiogram will be accomplished after a minimum 4-hour abstinence from smoking, food, and liquid intake. The tracing should be mounted in the usual manner of the laboratory for the recorder used. The electrocardiograms will be interpreted by cardiologists at the examination facility. Forward the mounted tracing and rhythm strip, if obtained, to the diagnostician.

7. Pulmonary Function Testing

Standard evaluation of pulmonary function will be conducted on each subject following at least 4 hours abstention from the use of tobacco products and will include, as minimum, forced expiratory volume at 1 second, total vital capacity, and the ratio of the two measurements.

8. Automated Blood Pressure Determination

An electronic device will be used to measure blood pressure. The device to be used will be selected by the contractor, subject to approval by the Air Force.

9. Stool Examination For Occult Blood

Three stool smears from each subject will be tested for the presence of occult blood. Subjects with positive tests will be advised and appropriate follow-up will be arranged.

10. Radiographic Examination

A standard 14×17 inch, standing, roentgenogram in the posterior-anterior (PA) position will be administered to all subjects. A board-certified radiologist at the examining facility will interpret the roentgenogram, record the results, and forward them to the diagnostician.

11. Doppler Testing Of Peripheral Pulses

A Doppler device shall be used to quantitatively measure peripheral pulses. This procedure shall be conducted after a minimum of 4 hours abstinence from smoking.

12. Measurement Of Height And Weight

The contractor shall determine the height in meters and weight in kilograms following a standard protocol on each subject. The contractor also shall measure the circumference of the waist at the navel and the circumference of the neck in centimeters.

13. Adipose Tissue Samples

The contractor shall:

1. Collect 10–15 gm fat tissue by liposuction procedure or any other alternative method.
2. Rinse one time with ice-cold normal phosphate-buffered saline (PBS).
3. Remove any excess of PBS solution from the tissue using paper towel.
4. Either snap freeze immediately in liquid nitrogen or keep it on ice until snap freezing (no longer than 30 minutes).
5. Store at –80 °C until delivery to Brooks Air Force Base.

14. Laboratory Procedures – General Instructions

On the first day, the subject should report in the morning in a fasting state having had only water after midnight. Blood for the serum dioxin measurement will be drawn on 650 selected subjects who consent to this procedure. Sufficient blood for the dioxin measurement will be drawn to bring the total volume collected over the 2 days to not more than 450 cc from these volunteers.

All study subjects should be informed that they should abstain from alcohol for 24 hours prior to the start of the physical examination.

15. Laboratory Procedures - Specific Tests To Be Performed

1. Erythrocyte sedimentation rate (mm/hr)
2. Prostate specific antigen (ng/ml)
3. AST (U/L)
4. ALT (U/L)
5. GGT (U/L)
6. Alkaline phosphatase (U/L)
7. Total bilirubin (mg/dl)
8. Direct bilirubin (mg/dl)
9. Lactic dehydrogenase (U/L)
10. Cholesterol (mg/dl)
11. HDL cholesterol (mg/dl)
12. Triglycerides (mg/dl)
13. Creatine phosphokinase (U/L)
14. Serum amylase (U/L)
15. Antibodies for hepatitis A, B, C and D
16. Serological evidence of prior hepatitis B infection (positive anti-HB_s or anti-HB_c)
17. Protein profile: pre-albumin (mg/dl)
18. Protein profile: albumin (mg/dl)
19. Protein profile: α -1-glycoprotein (mg/dl)
20. Protein profile: α -1-antitrypsin (mg/dl)
21. Protein profile: α -2-macroglobulin (mg/dl)
22. Protein profile: apolipoprotein (mg/dl)
23. Protein profile: C3 complement (mg/dl)
24. Protein profile: C4 complement (mg/dl)
25. Protein profile: haptoglobin (mg/dl)
26. Protein profile: transferrin (mg/dl)
27. Red blood cell count (million/cu mm)
28. White blood cell count (thousand/cu mm)
29. Hemoglobin (gm/dl)
30. Hematocrit (percent)
31. Platelet count (thousand/cu mm)
32. Prothrombin time (seconds)
33. RBC morphology (abnormal, normal)
34. Absolute neutrophils (segs) (million/cu mm)
35. Absolute neutrophils (bands) (million/cu mm)
36. Absolute lymphocytes (million/cu mm)
37. Absolute monocytes (million/cu mm)
38. Absolute eosinophils (million/cu mm)
39. Absolute basophils (million/cu mm)
40. Urinary occult blood (RBC/HPF)
41. Urinary protein (present, absent)
42. Urine white blood cell count (WBC/HPF)
43. Serum creatinine (mg/dl)
44. Urine specific gravity
45. Anti-thyroid antibodies (present, absent)
46. Thyroid stimulating hormone (μ IU/ml)
47. T₄ (μ g/dl)

48. Fasting glucose (mg/dl)
49. Fasting urinary glucose (present, absent)
50. Serum insulin (μ IU/ml)
51. α -1-C hemoglobin (percent)
52. Luteinizing hormone (mIU/ml)
53. Follicle stimulating hormone (mIU/ml)
54. Total testosterone (ng/dl)
55. Free testosterone (pg/ml)
56. Estradiol (pg/ml)
57. Two-hour postprandial glucose (mg/dl) (non-diabetics only)
58. Two-hour postprandial urinary glucose (present, absent) (non-diabetics only)
59. CD3+ (T Cells) (cells/cu mm and percent)
60. CD4+ (Helper T Cells) (cells/cu mm and percent)
61. CD8+ (Suppressor T Cells) (cells/cu mm and percent)
62. CD3+CD8+ (Suppressor T Cells) (cells/cu mm and percent)
63. CD16+56+(CD3-) (Natural Killer Cells) (cells/cu mm and percent)
64. CD20+ (B Cells) (cells/cu mm and percent)
65. CD3+CD4+ (Helper T Cells) (cells/cu mm and percent)
66. CD45+(CD14-) (used as quality control marker)
67. Absolute lymphocytes (cells/cu mm)
68. IgG (mg/dl)
69. IgM (mg/dl)
70. IgA (mg/dl)
71. Lupus panel: ANA test (present, absent)
72. Lupus panel: ANA thyroid microsomal antibody (present, absent)
73. Lupus panel: MSK smooth muscle antibody (present, absent)
74. Lupus panel: MSK mitochondrial antibody (present, absent)
75. Lupus panel: MSK parietal antibody (present, absent)
76. Lupus panel: Rheumatoid factor (present, absent)