

CHAPTER 1

INTRODUCTION

This chapter briefly describes the background of the Air Force Health Study (AFHS) and provides an overview of the study design, the morbidity component, and the purpose of this report.

BACKGROUND

In January 1962, President John F. Kennedy approved a program of aerial herbicide dissemination, for the purpose of defoliation and crop destruction, in support of tactical military operations in the Republic of Vietnam (RVN). Under this program, code-named Operation Ranch Hand, approximately 19 million gallons of herbicides were dispersed on an estimated 10 to 20 percent of South Vietnam.^{1,2} From 1962 to 1971, approximately 11 million gallons of Herbicide Orange, the primary defoliant of the six herbicides utilized in the program, were disseminated.

Operation Ranch Hand was the subject of intense scrutiny from the start due to the controversial nature of the program and political sensitivity to chemical warfare charges contained in enemy propaganda. The concerns, which were initially based on military, political, and ecological issues, shifted during 1977 to health issues. Numerous claims of exposure to herbicides, particularly Herbicide Orange and its dioxin contaminant, and subsequent adverse health effects among U.S. military service personnel have resulted in class action litigation and substantial controversy. Social concern for the Herbicide Orange issue continues to be manifest by continuing scientific research, media presentations, congressional hearings, and legal action.

The U.S. Air Force Medical Service's concern for the health of Air Force personnel exposed to herbicides was demonstrated in October 1978 when the Air Force Deputy Surgeon General made a commitment to Congress and to the White House to conduct a health study on the Ranch Hand personnel, the men who disseminated the majority of the defoliants in the RVN. The prevailing reasons for the study commitment included the availability of a definitive occupational exposure to herbicides, a sufficient sample size for survey and clinical research, the ability to ascertain the population at risk, and an opportunity for the Air Force Medical Corps to fulfill its adage "we care" to the Air Force community.

The Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas, was tasked by the Surgeon General to develop the Study Protocol. In 1982, after extensive peer review, the epidemiologic study began, and the Protocol was published.

Since 1978, numerous animal and human studies of dioxin effects have been planned or initiated by governmental agencies, universities, and industrial firms. The key scientific issue in these studies was the extent of exposure, e.g., who was exposed and how much each individual was exposed. Unfortunately, population identification and exposure estimation, which are critical for a valid study of ground troops, have been scientifically elusive.

It is believed that of all the military personnel who served in the RVN, the Ranch Hand population was the most highly exposed to herbicides. In 1987, the Air Force initiated a collaborative study with the Centers for Disease Control (CDC) to measure the serum dioxin levels in the AFHS morbidity population. The results of that study clearly demonstrate that substantially elevated levels of dioxin can still be found in the serum of some Ranch Hands, as opposed to the absence of elevated levels found in ground troops by CDC. Based on the principle of dose-response, the Ranch Hands should manifest more and/or earlier evidence of adverse health. Thus, the results of the AFHS should serve as an indicator of herbicide effects in ground personnel.

STUDY DESIGN

The purpose of the study is to determine whether adverse health effects exist and can be attributed to occupational exposure to Herbicide Orange. The study, consisting of mortality and morbidity components, is based on a matched cohort design in a nonconcurrent prospective setting with followup studies. The interwoven study elements of multiple mortality assessments, a Baseline morbidity study, and five followup morbidity studies over 20 years provide a comprehensive approach to the detection of attributable adverse health effects. Complete details on the design are provided in the Study Protocol.

For the Baseline study, the population ascertainment process identified 1,264 Ranch Hand personnel who served in the RVN between 1962 and 1971. By the time the first followup began in 1985, an additional 9 Ranch Hands had been identified. Two years later for the second followup, four additional Ranch Hands were identified. A Comparison group was formed, consisting of individuals assigned to Air Force units operating C-130 cargo aircraft in Southeast Asia. Using a computerized nearest neighbor selection procedure, a maximum of 10 Comparisons was selected for each Ranch Hand, matching on age, race, and military occupation. After personnel record reviews, each Ranch Hand who was determined to be eligible and fully suitable for study had an average of 8.2 Comparison subjects.

The mortality component addresses mortality from the time of the RVN assignment. A Baseline mortality study was conducted in 1982, and the mortality followup consists of annual mortality updates for 20 years. For the Baseline study and the first four updates, five individuals were randomly selected from the matched Comparison set for each Ranch Hand for a 1:5 design. Subsequent to 1987, the design was expanded to include all of the individuals in the Comparison population.

The Baseline morbidity component, begun in 1982, reconstructed the medical history of each participant by reviewing and coding past medical records. A cross-sectional element, designed to assess the participant's current state of mental and physical health, was based on comprehensive questionnaires and physical examinations given to the participants. For this component of the study, each living Ranch Hand and the first living member of his Comparison set were selected to participate in the examination. Sequential questionnaires, medical record reviews, and physical examinations in 1985, 1987, 1992, 1997, and 2002 comprise the morbidity study followup.

MORBIDITY COMPONENT

The Baseline morbidity assessment, conducted in 1982, disclosed some differences between the Ranch Hands and Comparisons, but those differences were generally not traditional indicators of dioxin-related disease. The sustained commitment of Congress and the Air Force to pursue the Agent Orange question to its scientific conclusion was demonstrated by the conduct of the first two morbidity followups in 1985 and 1987. The first (1985) followup provided the first opportunity to confirm or refute some of the Baseline findings and to explore longitudinal changes. For the 1985 followup, the mental and physical health status of the participants during the 3-year interval since the Baseline study was assessed. The results of the 1985 followup approximated those of the Baseline examination; however, the Ranch Hands continued to manifest slightly more adverse health conditions than the Comparisons.

In 1987, the second followup was initiated. During a 2-1/2 year period, the data were collected, automated, and analyzed. The 1987 followup was conducted by Science Applications International Corporation (SAIC) in conjunction with Scripps Clinic and Research Foundation and National Opinion Research Center, working as a team with the Air Force.

PURPOSE

The 1987 morbidity followup is the subject of this report. The objective of the morbidity followup is to continue the investigation of the possible long-term health effects following exposure to herbicides containing 2,3,7,8-tetrachlorodibenzo-p-dioxin (or TCDD). This report describes the procedures and results of the second morbidity followup of the AFHS. Although the blood samples for the measurement of serum dioxin levels were collected during the 1987 followup, the results of this testing were not available for inclusion in this report.

This report is written primarily for clinical epidemiologists, clinicians, and biostatisticians so that they may fully evaluate the data and analytic techniques. Complete familiarity with the Study Protocol and prior mortality and morbidity reports is essential in the full understanding of this report. It should be noted that the intent of the background sections of the clinical chapters is to provide a broad overview of the literature with respect to dioxin endpoints. In addition, statistical analyses in this report were prescribed in an analytic plan developed prior to analysis of the 1987 followup data and are not ad hoc analyses. The report format has been established to be complete, rigorous, and straightforward on all issues. A summary of this report, more suited to the general reader, is available.

This report, prepared by SAIC, is submitted as partial fulfillment of Air Force Contract No. F41689-85-D-0010.

CHAPTER 1

REFERENCES

1. Young, A.L., J.A. Calcagni, C.E. Thalken, and J.W. Tremblay. 1978. The toxicology, environmental fate, and human risk of Herbicide Orange and its associated dioxin. Technical report OEHL-TR-78-92, USAF Occupational and Environmental Health Laboratory, Brooks AFB, Texas. 247 pp.
2. Buckingham, W.A., Jr. 1982. Operation Ranch Hand: The Air Force and herbicides in Southeast Asia, 1961-1971. Office of Air Force History, United States Air Force, Washington, D.C. pp. 9-69, 199-201.
3. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1982. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Study protocol, NTIS: AD A 122 250. USAF School of Aerospace Medicine, Brooks Air Force Base, Texas.
4. Centers for Disease Control. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in Air Force Health Study participants--preliminary report. Morbidity and Mortality Weekly Report 37:309-324.
5. DeStefano, F., O.J. Devine, W.D. Flanders, J.M. Karon, L.L. Needham, D.G. Patterson, and R.M. Worth. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in U.S. Army Vietnam-era veterans. JAMA 260:1249-1254.