MAY 28 1993

INSTITUTE OF MEDICINE
NATIONAL ACADEMY OF SCIENCES
2101 CONSTITUTION AVE. N.W. WASHINGTON, D.C. 20418

COMMITTEE TO REVIEW THE HEALTH EFFECTS IN
VIETNAM VETERANS OF EXPOSURE TO HERBICIDES
MICHAEL A. STOTO, PH.D. STUDY DIRECTOR

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May 26, 1993

E.R. Zumwalt, Jr.
Admiral, U.S. Navy (Ret.)
1500 Wilson Blvd., Suite 641
Arlington, VA 22209

Dear Admiral Zumwalt:

Thank you for your comments on the chapter that discusses U.S. Vietnam veterans and the military use of herbicides in Vietnam. As I mentioned, this chapter will be included in the IOM's report, *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam* prepared by the Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides. Your comments were very helpful and will be considered while revising the draft chapter. Some of your comments may already be addressed in another chapter where the issues are discussed in greater detail, and if not, we will make certain that they are covered in the appropriate section.

The committee appreciates your review of this chapter and thanks you for your effort. The final committee report is scheduled for release to the public on July 27, 1993.

Sincerely,

Michael A. Stoto

Amr
1 cc

AUG 13 1993

VETERANS AND AGENT ORANGE
Health Effects of Herbicides Used in Vietnam

Committee to Review the Health Effects in Vietnam
Veterans of Exposure to Herbicides,
Institute of Medicine

Have U.S. military personnel experienced health problems from being exposed to Agent Orange, its dioxin contaminants, and other herbicides used in Vietnam? This definitive volume summarizes the strength of the evidence associating exposure during Vietnam service with cancer and other health effects and presents conclusions from an expert panel.

Veterans and Agent Orange provides a historical review of the issue, examines studies of populations, in addition to Vietnam veterans, environmentally and occupationally exposed to herbicides and dioxin, and discusses problems in study methodology. The core of the book presents

- What is known about the toxicology of the herbicides used in greatest quantities in Vietnam.
- What is known about assessing exposure to herbicides and dioxin.
- What can be determined from the wide range of epidemiological studies conducted by different authorities.
- What is known about the relationship between exposure to herbicides and dioxin, and cancer, reproductive effects, neurobehavioral disorders, and other health effects.

The book describes research areas of continuing concern and offers recommendations for further research on the health effects of Agent Orange exposure among Vietnam veterans. It will be critically important to both policymakers and physicians in the federal government, Vietnam veterans and their families, veterans organizations, researchers, and health professionals.

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Date: July 28, 1993

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FOR IMMEDIATE RELEASE

REPORT LINKS DISEASE TO HERBICIDES; CALLS FOR NEW STUDIES OF EXPOSED VIETNAM VETERANS

WASHINGTON -- Evidence exists linking three cancers and two other health problems with chemicals used in herbicides in the Vietnam War, a committee of the Institute of Medicine (IOM) has concluded. Those diseases are soft tissue sarcoma, non-Hodgkin's lymphoma, and Hodgkin's disease, as well as the skin diseases chloracne and porphyria cutanea tarda (PCT). The committee also concluded that new studies piecing together different types of information could help determine how much the risk of disease is increased in veterans who were exposed to such herbicides as Agent Orange.

The committee's report* specifically focuses on Agent Orange and other herbicides used in Vietnam, some of which contained dioxin, an unintended byproduct of the manufacturing process.

"Over the years, extreme views have evolved on the issue," said Harold Fallon, IOM committee chair and dean of the School of Medicine at the University of Alabama, Birmingham. "On one extreme is the view that Agent Orange causes a wide range of diseases, and on the other is the suggestion that exposure to Agent Orange has not led to health problems. Our committee has determined through an extensive review of

(MORE)

*Pre-publication copies of ***Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam*** are available from the National Academy Press at the mailing address in the letterhead; tel. (202) 334-3313 or 1-800-624-6242. The cost of the report is $85.00 plus $4.00 shipping. Reporters only may obtain copies from the Office of News and Public Information (contacts listed above).

the scientific literature that indeed, there does appear to be a link between exposure to herbicides and certain diseases."

Most of the evidence the committee reviewed about adverse health effects came from studies of people who were exposed as a result of their jobs or from industrial accidents. These types of exposures often were at high levels and for long periods of time. Getting a clear picture of the health risks for Vietnam veterans is not so straightforward, the committee said, because the levels of exposure were extremely wide ranging. Indeed, while most veterans probably had lower exposure levels, some may have experienced levels as high as that of occupational or agricultural exposures. What is uncertain is how many veterans may have been exposed to those higher levels and who those individuals are.

"We simply do not know the degree of risk for Vietnam veterans," said committee vice chair David Tollerud, director of occupational and environmental medicine, University of Pittsburgh Graduate School of Public Health. "We do feel, however, that enough information exists to allow studies to be done that would lead to a better understanding of the risk that veterans face for contracting diseases related to herbicide exposure in Vietnam."

ADVERSE HEALTH EFFECTS

The committee examined more than 230 epidemiological studies in detail on a range of health problems and their possible association with herbicides. It found sufficient evidence of a statistical association between exposure to herbicides or dioxin and soft tissue sarcoma, non-Hodgkin's lymphoma, and Hodgkin's disease. The committee also found sufficient evidence of an association between herbicides or dioxin and chloracne and PCT. Chloracne is a specific acne-like skin disorder; PCT is a liver disorder characterized by thinning and blistering of the skin.

The category of sufficient evidence represented the strongest link the committee made between adverse health effects and exposure to herbicides, including Agent Orange or dioxin.

(MORE)

The U.S. Department of Veterans Affairs currently compensates Vietnam veterans for non-Hodgkin's lymphoma, soft tissue sarcoma, and chloracne.

The link between herbicides or dioxin and other adverse health effects the committee studied fell into three remaining categories:

▸ **Limited or Suggestive Evidence.** The committee found limited or suggestive evidence of an association between exposure to herbicides of the kind used in Vietnam and three other cancers: respiratory cancers, prostate cancer, and multiple myeloma.

▸ **Inadequate Evidence.** The scientific data for most cancers and other diseases, such as adverse neurological and reproductive effects, were inadequate or insufficient to determine whether an association exists, the report says (see attached list).

▸ **No Association.** For a small group of cancers, the committee found that a sufficient number and variety of well-designed studies exist to conclude that there is limited or suggestive evidence of *no* association between these cancers and the herbicides or dioxin. This group includes skin cancer, gastrointestinal tumors (colon, rectal, stomach, and pancreatic), bladder cancer, and brain tumors.

NEW MEASURES OF EXPOSURE NEEDED

In reviewing the literature, the committee found that exposure assessment was the weakest element in most epidemiological studies of veterans. While some studies show a link between adverse health effects and herbicides or dioxin, there are few data indicating which individuals may have received high exposures during service in Vietnam.

The evidence about exposure during the war suggests that Vietnam veterans as a group had substantially lower exposure to herbicides and dioxins than the subjects in many occupational studies, the committee said. Veterans who were participants in Operation Ranch Hand -- the extensive spraying of some 19 million gallons of herbicide over 3.6 million acres of South Vietnam from airplanes -- are an exception to this

(MORE)

pattern, however, because of their direct involvement in the spraying missions.

But the committee also said that, among the approximately 3 million Vietnam veterans, there may be some former ground troops not directly involved in the spraying who were exposed to herbicides at levels associated with adverse health effects.

The committee emphasized that it may be possible to develop better exposure measures for Vietnam veterans by relying on "less formal" sources of historical information than have been used in the past. Previous studies have relied primarily on the carefully recorded information on aerial spraying in Operation Ranch Hand and on blood tests for dioxin, but these measures may not reflect the full range of exposures of Vietnam veterans to herbicides.

The committee urged that a non-government organization be commissioned to develop and test new methods of evaluating herbicide exposure in Vietnam veterans. These new methods would draw on historical reconstructions and include information on the spraying that occurred around base camps and other areas which could have led to higher human exposures, the committee said. Important information could be gained from historical records of ground and perimeter spraying, herbicide shipments to various military bases, and knowledge of the type of terrain and foliage typical of the locations sprayed and the military mission of the troops located there. These new methods of measuring exposure should be evaluated by an independent, non-government scientific panel.

If they prove to be valid, a new series of epidemiological studies of veterans should be undertaken to assess the degree to which veterans may be at risk of cancer and other disease as a result of exposure, the committee said.

It also urged continued follow-up of the Ranch Hand veterans and its comparison group, and recommended that members of the Army Chemical Corps also be studied for adverse health effects from exposure. Studies should be done by an independent agency, noting that such an independent body could do much to "satisfy the public's concern about impartiality and scientific credibility."

(MORE)

In addition, the committee recommended that -- for the purpose of facilitating the collection of data for new studies -- the U.S. Department of Defense identify in its computerized index of military service records which veterans served in Vietnam. Currently, this index does not indicate whether an individual served in the Vietnam War. "Lack of an indicator of Vietnam service complicates every epidemiologic study of veterans . . . and leads to methodologic inconsistencies."

HERBICIDE USE IN VIETNAM

Between 1962 and 1971, U.S. military forces sprayed millions of gallons of herbicides over South Vietnam. Agent Orange accounted for much of the total sprayed.

After a scientific report in 1969 concluded that one of the primary chemicals used in Agent Orange could cause birth defects in laboratory animals, use of the herbicide was suspended. All U.S.-authorized herbicide use in Vietnam was halted in 1971. As the decade wore on, concern about possible long-term health consequences of Agent Orange and other herbicides heightened, fueled in part by reports from Vietnam veterans that they had developed cancer or fathered handicapped children. Some veterans attributed these health problems to wartime exposure to herbicides.

Since then, thousands of scientific studies have been conducted. Faced with lingering uncertainty, Congress asked the National Academy of Sciences' Institute of Medicine to conduct a comprehensive review of available scientific information regarding the health effects of exposure to Agent Orange and other herbicides used in Vietnam. The report is the product of the IOM committee's work, begun in 1992.

The study was sponsored by the U.S. Department of Veterans Affairs.

The Institute of Medicine is a private, non-profit organization that provides health policy advice under a congressional charter granted to the National Academy of Sciences. A committee roster is overleaf.

# # #

[NOTE: This news release is available on CompuServe's Journalism Forum, in the NASW Online and SciNews-MedNews libraries.]
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INSTITUTE OF MEDICINE
Division of Health Promotion and Disease Prevention

Committee to Review
The Health Effects in Vietnam Veterans of Exposure to Herbicides

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IOM STAFF

Michael Stoto, project director
Cynthia Abel, research associate

[1] Member, Institute of Medicine

[2] Liaison to the IOM Board on Health Promotion
and Disease Prevention

TABLE 1-1 Summary of Findings in Occupational, Environmental, and Veterans Studies Regarding the Association Between Specific Health Problems and Exposure to Herbicides

Sufficient Evidence of an Association

Evidence is sufficient to conclude that there is a positive association. That is, a positive association has been observed between herbicides and the outcome in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. For example, if several small studies that are free from bias and confounding show an association that is consistent in magnitude and direction, there may be sufficient evidence for an association. There is sufficient evidence of an association between exposure to herbicides and the following health outcomes:

Soft tissue sarcoma
Non-Hodgkin's lymphoma
Hodgkin's disease
Chloracne
Porphyria cutanea tarda (in genetically susceptible individuals)

Limited/Suggestive Evidence of an Association

Evidence is suggestive of an association between herbicides and the outcome but is limited because chance, bias, and confounding could not be ruled out with confidence. For example, at least one high-quality study shows a positive association, but the results of other studies are inconsistent. There is limited/suggestive evidence of an association between exposure to herbicides and the following health outcomes:

Respiratory cancers (lung, larynx, trachea)
Prostate cancer
Multiple myeloma

Inadequate/Insufficient Evidence to Determine Whether an Association Exists

The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association. For example, studies fail to control for confounding, have inadequate exposure assessment, or fail to address latency. There is inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides and the following health outcomes:

Hepatobiliary cancers
Nasal/nasopharyngeal cancer
Bone cancer
Female reproductive cancers (breast, cervical, uterine, ovarian)
Renal cancer
Testicular cancer
Leukemia
Spontaneous abortion
Birth defects
Neonatal/infant death and stillbirths
Low birthweight
Childhood cancer in offspring
Abnormal sperm parameters and infertility

TABLE 1-1 (continued)

Inadequate/Insufficient Evidence to Determine Whether an Association Exists (continued)

Cognitive and neuropsychiatric disorders
Motor/coordination dysfunction
Peripheral nervous system disorders
Metabolic and digestive disorders (diabetes, changes in liver enzymes, lipid abnormalities, ulcers)
Immune system disorders (immune modulation and autoimmunity)
Circulatory disorders
Respiratory disorders

Limited/Suggestive Evidence of No Association

Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter, are mutually consistent in not showing a positive association between exposure to herbicides and the outcome at any level of exposure. A conclusion of "no association" is inevitably limited to the conditions, level of exposure, and length of observation covered by the available studies. *In addition, the possibility of a very small elevation in risk at the levels of exposure studied can never be excluded.* There is limited/suggestive evidence of *no* association between exposure to herbicides and the following health outcomes:

Skin cancer
Gastrointestinal tumors (stomach cancer, pancreatic cancer, colon cancer, rectal cancer)
Bladder cancer
Brain tumors

NOTE: "Herbicides" refers to the major herbicides used in Vietnam: 2,4-D (2,4-dichlorophenoxyacetic acid); 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) and its contaminant TCDD (2,3,7,8-tetrachlorodibenzo-*p*-dioxin); cacodylic acid; and picloram. The evidence regarding association is drawn from occupational and other studies in which subjects were exposed to a variety of herbicides and herbicide components.

E. R. ZUMWALT, JR.
ADMIRAL, U. S. NAVY (RET.)

July 28, 1993

Dr. Leonard T. Kurland
Department of Health Sciences Research
Section of Clinical Epidemiology
Mayo Clinic
Rochester, MN 55905

Dear Len:

I assume you've had a chance to read the Executive Summary of the Institute of Medicine Panel report "Veterans and Agent Orange: Health Effects of Herbicides in Vietnam". With the listing of Non-Hodgkin's Lymphoma, Soft Tissue Sarcoma, Hodgkin's, Chloracne, and PCT for certain and with the probable addition within 60 days of cancers of the lung, larynx, trachea, prostate and multiple myeloma, 7 of the 27 health effects I listed in my study will have been approved for compensation.

The purpose of this letter is merely to point out that my layman's analysis was not as far off the mark as the Committee on Environmental Hazards believed it to be.

I have no doubt that future studies, such as the update on Seveso by Dr. Bertazzi, to be published in the September Epidemiology journal, will add future cancers to the listing.

I remain sufficiently respectful of your distinguished views that I felt the need to do this letter.

All best wishes to you.

Sincerely,

Admiral E.R. Zumwalt, Jr., USN (Ret.)

1500 Wilson Blvd., Suite 641
Arlington, VA 22209
703/527-5380

I still hope to meet with you one of these days

JUL 27 1993

Department of Veterans Affairs

Memorandum

Date: July 26, 1993

From: Executive Secretary, Veterans' Advisory Committee on Environmental Hazards

Subj: Executive Summary

To: All Committee Members

Attached for your information is a copy of the Executive Summary of the report of the National Academy of Sciences "Veterans and Agent Orange: Health Effects of Herbicides in Vietnam".

Frederic L. Conway

VA FORM MAR 1989 2105

EXECUTIVE SUMMARY
PREPUBLICATION COPY

Veterans and Agent Orange:
Health Effects of Herbicides Used in Vietnam

Committee to Review the Health Effects in
Vietnam Veterans of Exposure to Herbicides

Division of Health Promotion and
Disease Prevention

INSTITUTE OF MEDICINE

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NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

The Institute of Medicine was chartered in 1970 by the National Academy of Sciences to enlist distinguished members of the appropriate professions in the examination of policy matters pertaining to the health of the public. In this, the Institute acts under the Academy's 1863 congressional charter responsibility to be an adviser to the federal government and its own initiative in identifying issues of medical care, research, and education. Dr. Kenneth I. Shine is president of the Institute of Medicine.

Support for this study was provided by the Department of Veterans Affairs (contract no. V101(93)P-1331).

Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam will be available for sale in October from the National Academy Press, 2101 Constitution Avenue, N.W., Box 285, Washington, DC, 20055. Call 800-624-6242 or 202-334-3938 (in the Washington Metropolitan Area).

Printed in the United States of America

The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The image adopted as a logo-type by the Institute of Medicine is based on a relief carving from ancient Greece, now held by the Staatlichemusseen in Berlin.

COMMITTEE TO REVIEW THE HEALTH EFFECTS IN VIETNAM VETERANS OF EXPOSURE TO HERBICIDES

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Foreword

In response to decades of concern surrounding the possible long-term health consequences of exposures to herbicides and the contaminant dioxin, Congress directed the Secretary of Veterans Affairs, in Public Law 102-4 signed on February 6, 1991, to request the National Academy of Sciences (NAS) to conduct a comprehensive review and evaluation of the available scientific and medical information regarding the health effects of exposure to Agent Orange and other herbicides used during the Vietnam conflict. This report from the Institute of Medicine (IOM) Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides is hereby submitted in compliance with Public Law 102-4.

Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam reviews and evaluates the available scientific evidence regarding the association between exposure to dioxin or other chemical compounds in herbicides used in Vietnam and a wide range of health effects, and provides the committee's best assessment of this body of knowledge for the Secretary of Veterans Affairs to consider as the Department of Veterans Affairs exercises its responsibilities to Vietnam veterans. The report also describes areas in which the available scientific data are insufficient to determine whether an association exists and provides the committee's recommendations for areas in which future research is likely to be most productive.

That Congress would ask the NAS--a nongovernmental organization--to conduct this study reflects a time-honored tradition. Created by an act of Congress and signed into law in 1863 by President Abraham Lincoln, the NAS is dedicated to the furtherance of science and technology and to their use for the promotion of general public welfare. A private, nonprofit society of distinguished scholars engaged in scientific and engineering research, the NAS has a mandate to advise the federal government on scientific and technical issues of pressing importance. Its members, drawn from universities and the private sector, are elected by their peers on the basis of exemplary professional achievement. Members, along with other leading experts, voluntarily participate in National Research Council and IOM studies and serve without compensation.

The IOM was chartered by the NAS in 1970 to serve as an adviser to the federal government on issues that affect the public's health, as well as to act independently in identifying important issues of medical care, research, and education. The IOM brings to this mission more than two decades of experience in conducting independent analyses of pressing health problems that involve federal policy decisions.

As described in more detail in Chapter 2 of this report, the NAS has a history of

involvement with the Agent Orange issue. A major study in 1974 focused primarily on the possible ecological consequences of herbicides used in Vietnam, but an individually authored component of that report published eight years later reviewed its possible reproductive effects among the Vietnamese. In the early 1980s, two committees reviewed protocols for large, epidemiologic studies of the health effects in veterans. Between 1986 and 1990, an IOM committee reviewed protocols and the analytical methods of a series of epidemiologic studies of Vietnam veterans carried out by the Centers for Disease Control, though it did not contribute to the final conclusions reached in those studies. Thus, while the NAS and the IOM have been aware of the controversy surrounding the military use of Agent Orange and other herbicides in Vietnam, these past activities are quite different from the current study, of which the primary purpose is to determine whether there are health effects related to exposure to herbicides.

The 16-members of the Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides represent a wide range of expertise including occupational and environmental medicine, toxicology, epidemiology, pathology, clinical oncology, psychology, neurology, and biostatistics. The committee was chaired by Harold Fallon, M.D., Dean of the Medical School at the University of Alabama, Birmingham, and a member of the IOM. David Tollerud, M.D., M.P.H., Director of Occupational and Environmental Medicine at the University of Pittsburgh, served as vice-chair. Committee member Norman Breslow, Professor of the Department of Biostatistics of the University of Washington and also a member of the IOM, served as a liaison to the IOM Board on Health Promotion and Disease Prevention, which was responsible for overseeing this study. Biographical sketches of the other committee members and the professional staff appear in Appendix D.

All committee members were selected because they are leading authorities in their scientific fields, are well-respected by their colleagues and peers, have no conflicts of interest with regard to the matters under study, and, indeed, have taken no public positions concerning the potential health effects of herbicides in Vietnam veterans or related aspects of herbicide or dioxin exposure. The committee thus has provided a fresh analysis of this issue–which is both scientifically complex and emotionally charged–and this report reflects the committee's thorough and unbiased scientific judgments. As with all reports from the IOM, the committee's work was reviewed by an independent panel of distinguished experts.

Kenneth I. Shine
President, Institute of Medicine

Preface

The use of Agent Orange and other herbicides in Vietnam has stimulated concern and controversy ever since the U.S. began the military herbicide program in 1962. Questions regarding the effects of herbicides on health and the environment have persisted over several decades. Many veterans, who served their country in Vietnam at great personal sacrifice and hardship, face continuing uncertainty about whether a myriad of diseases and health effects are associated with exposure to the herbicides used in Vietnam. Some of these veterans and their families feel that their pain and suffering have been ignored and that these questions have not been adequately addressed.

In response to the concerns voiced by Vietnam veterans and their families, Congress called upon the National Academy of Sciences (NAS) to review the scientific evidence on the possible health effects of exposure to herbicides. The creation of the NAS Institute of Medicine's committee underscores the critical importance of approaching these questions from a scientific standpoint, yet the committee realized from the beginning that it could not conduct a credible scientific review without a full understanding of the experiences and perspectives of veterans. Thus, to supplement its standard scientific process, the committee opened several of its meetings to the public to allow veterans and other interested individuals to voice their concerns and opinions, to provide personal information about individual exposure to herbicides and associated health effects, and to educate the committee on recent research results and studies still under way. This information provided a meaningful backdrop for the numerous scientific articles that the committee reviewed and evaluated. The committee appreciates the efforts of everyone who presented information to it and acknowledges this valuable addition to the study process.

As the study progressed, two separate but interdependent themes became evident to the committee. First, this report is a scientific investigation of the potential health effects of exposure to the herbicides that were used in Vietnam and to dioxin (2,3,7,8-tetrachlorodibenzo-*para*-dioxin; TCDD), an unintentional contaminant of some of those herbicides. This theme is discussed first in Chapter 2, which provides a context for the investigation by relating the history of national concern about TCDD and herbicides and of efforts to address this concern. Chapter 4 reviews the toxicological data (based on laboratory studies and animal investigations) on these chemicals, with a focus on the TCDD contaminant because this area has been the object of more substantial scientific research. Most of the committee's work, however, focused on the review of epidemiologic studies. Chapters 8 through 11 analyze and present the committee's conclusions regarding the relationship between herbicide/TCDD exposure and 44 specific diseases and disorders. These diseases and disorders include different forms of cancer,

reproductive and developmental effects, neurobehavioral disorders, and other health effects, including chloracne and porphyria cutanea tarda. In order to understand the committee's approach to these reviews, Chapter 5 lays out the general methodological considerations that the committee used in evaluating this evidence, and Chapter 6 addresses the question of how to assess the nature of exposure to the substances in question, a critical element in evaluating the epidemiologic studies that were reviewed. Many of these studies addressed the health effects of people who were occupationally or environmentally exposed to TCDD or the herbicides in question, and many of the studies investigated more than one health outcome. Rather than summarize the methods of these studies each time they are considered, the committee's review and summary of the health effects are preceded by a complete and thorough methodologic description of all the studies under review--organized by the nature of the population exposed and by study methods--in Chapter 7.

The second theme in this report relates to the use of herbicides in Vietnam, the effects of exposure on Vietnam veterans, and the direction of future research efforts toward learning more than is currently known about these issues. The discussion of this theme also begins in Chapter 2, but the history of military operations in Vietnam, with a special focus on the herbicide program, is described in detail in Chapter 3. In addition to addressing exposure assessment in general, Chapter 6 discusses the methods that have been used to assess exposure to herbicides in studies of Vietnam veterans and summarizes what is currently known about the nature and extent of that exposure. Chapter 6 also proposes a new method of historical exposure reconstruction in studies of Vietnam veterans, a topic that is the focus for the committee's research recommendations in Chapter 12. In addition, Chapter 12 comments on existing studies of Vietnam veterans and makes recommendations about four specific programs mandated in Public Law 102-4.

CONDUCT OF THE STUDY

The committee worked on several fronts in conducting this study, always with the goal of seeking the most accurate information and advice from the widest possible range of knowledgeable sources. Consistent with procedures of the Institute of Medicine (IOM), the committee met in a series of closed sessions and working group meetings in which members could freely examine, characterize, and weigh the strengths and limitations of the available evidence. Given the nature of the controversy surrounding this issue, the committee deemed it vital to convene open meetings as well. Three public meetings were held during the course of the study, which provided timely forums for veterans and veterans service organizations, researchers, policymakers, and other interested parties to present their concerns, review their research, and exchange information directly with the committee members.

The first open meeting was held in September 1992. To solicit broad participation, the IOM committee sent announcements to nearly 1,000 persons known to have an interest in this issue. Names were gathered from veterans service organizations, scientific organizations, labor unions, environmental groups, government agencies, and numerous other sources, and news of

the meeting was circulated to approximately 1,500 media outlets nationwide. During this day-long public meeting, 25 persons made oral presentations. Because some individuals were unable to attend the public meeting, written statements were given equal weight to oral presentations; by April 15, 1993, 28 additional individuals had submitted written statements. Besides these statements, the committee received specially prepared analyses from several groups. All of this material was carefully considered by the committee over the course of the study. The oral presentations and written statements submitted to the committee are described in detail in Appendix B.

The second public meeting, a "Scientific Workshop on Exposure Assessment," took place in December 1992. The committee assembled 17 experts in various scientific fields--drawn from universities, veterans service organizations, federal agencies, and health groups--to discuss how exposure to Agent Orange, other herbicides, and TCDD is assessed in epidemiologic studies. Participants discussed records-based methods, as well as more recent biomedical research in which current dioxin levels are measured in the blood and tissue of individuals to estimate previous levels of exposure to TCDD (see Appendix B).

A third public meeting, held in February 1993, focused on the "Vietnam Experience." The committee heard from veterans who had served in the U.S. Marines, Navy, Army, and Air Force. Some of these individuals experienced extensive combat, frequently in areas sprayed with herbicides. Others had been directly involved in spraying herbicides from aircraft or "brown water" river patrol boats. The committee also heard from the Vietnam Veterans of America on the wartime experiences of women, thousands of whom served in Vietnam, primarily as military nurses.

In addition to its formal meetings, the committee actively and continuously sought information from, and explained its mission to, a broad array of individuals and organizations with interest or expertise in assessing the effects of exposure to herbicides. These interactions included frequent meetings with representatives of veterans service organizations, congressional committees, federal agencies, and scientific organizations. The committee heard from the public through several hundred telephone calls and letters, each of which received a response from the IOM staff.

The committee also benefited from the expert advice and reviews of consultants in toxicology, environmental health, neurotoxicology, autoimmune disorders, reproductive effects, and dermatological disorders, including porphyria cutanea tarda. A list of the background papers, their authors, and the experts consulted appears in Appendix B.

During the course of the committee's work, the Environmental Protection Agency (EPA) has been in the process of carrying out an open scientific reassessment of the health risks of dioxin to guide its regulatory policy. The committee has benefited from this effort by being able to read and consider draft scientific reports prepared for the EPA by independent scientists as part of this process, and by IOM committee members' and staff's attendance at the EPA's public meetings. However, the congressional charge to the IOM committee is substantially different than the EPA's review in at least two important ways: (1) the EPA is concerned only with dioxin, whereas the IOM is concerned with all of the herbicides used in Vietnam, and (2)

because of its regulatory focus, the EPA is more concerned with defining a dose-response relationship than the IOM committee felt was either necessary or feasible for Vietnam veterans.

The value of this continued, open, and wide-ranging dialogue between the IOM committee and the scientific community, veterans, policymakers, and citizens proved itself many times over and ultimately contributed to a more comprehensive report.

Most of the committee's work involved reviewing the scientific literature bearing on the association between herbicides or dioxin and various health outcomes. The committee or its staff read approximately 6,420 abstracts of scientific or medical articles which were then entered into a computerized bibliographic data base. From these, approximately 230 epidemiologic studies were chosen for detailed review and analysis. These included studies of people exposed to the herbicides in question in occupational and environmental settings, as well as studies of Vietnam veterans. The committee relied on the original publications themselves rather than on summaries or commentaries. Such secondary sources were used to check the completeness of the review. The committee also reviewed the primary and secondary literature on basic toxicological and animal studies related to dioxin and other herbicides in question. Appendix A describes the committee's literature review strategy in detail.

Controversy has surrounded the study of Agent Orange since the first questions of herbicide-related health effects in Vietnam veterans were raised more than 20 years ago. In the course of its work, the committee heard allegations of scientific misconduct and claims of a government conspiracy to suppress information on health effects, as well as serious disagreements among scientists about the interpretation of laboratory and clinical data. The committee was not charged with investigating or resolving these controversies, and it did not attempt to do so. The committee took these issues into consideration only to the extent that they had a direct bearing on the scientific results that are the subject of this review.

We believe that the committee has produced a comprehensive, unbiased scientific review of the available evidence regarding potential health effects of exposure to herbicides in Vietnam veterans. Although the conclusions and recommendations presented here will not end the controversy surrounding this issue, it is the committee's hope that this report will crystallize the current scientific information on this important topic and prompt further research to answer the remaining questions being asked by veterans and their families, the Department of Veterans Affairs, and Congress.

The committee wishes to acknowledge that this study could not have been done without the assistance of a number of people, many of whom are listed in Appendix B. A special acknowledgement is extended to Donald Whorton and Albert Munson, both of whom served for a brief period with the committee. The work of the Institute of Medicine staff deserves high praise. Thanks are extended to the professional staff, Susan Rogers, Diane Mundt, Cynthia Abel, Catharyn Liverman, Gail Charnely, and Jane Durch, for their input, advice, and support. Thanks are also extended to Catherine Wesner, the study's project assistant, who planned travel and meeting arrangements and provided assistance with editorial changes to the manuscript; Jana Katz, the committee's student intern, who assisted with literature searches and in compiling the literature data base; Thomas Burroughs, who worked with IOM staff members in drafting several sections of the report; Zoe Schneider who aided in the preparation of the final

manuscript; Andrea Posner, who proofread the final changes in the manuscript; and Florence Poillon, who provided excellent editorial skills. Finally, the committee wishes to recognize the major contributions of the study director, Michael Stoto. It is through his expert leadership that this report has come to fruition.

Harold Fallon, Chairman
David Tollerud, Vice-chairman

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