

# Characterizing Exposure of Veterans to Agent Orange and Other Herbicides Used in Vietnam

**Final Report** 

Committee on the Assessment of Wartime Exposure to Herbicides in Vietnam Board on Health Promotion and Disease Prevention INSTITUTE OF MEDICINE *oF THE NATIONAL ACADEMIES* 

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"Knowing is not enough; we must apply.

Willing is not enough; we must do." —Goethe

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## REVIEWERS

This report has been reviewed in draft form by persons chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards of objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following for their review of this report:

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by **Jonathan M.Samet**, Johns Hopkins University. Appointed by the National Research Council and Institute of Medicine, he was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the author committee and the institution.

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#### REVIEWERS

## PREFACE

In response to the concerns voiced by Vietnam veterans and their families, Congress called on the National Academy of Sciences (NAS) to review the scientific evidence on the possible health effects of exposure to Agent Orange and other herbicides (Public Law 102–4, enacted on February 6, 1991). The creation, in 1992, of the Institute of Medicine (IOM) committee tasked to conduct the review underscored the critical importance of approaching the question from a nonpartisan scientific standpoint. The study reported here is an outgrowth of that work, focusing on the assessment of wartime exposure to herbicides. The 1994 IOM report *Veterans and Agent Orange* noted that "exposure assessment has been a weak aspect of most epidemiologic studies of Vietnam veterans" (page 18) and recommended that an effort be undertaken to develop exposure reconstruction models. The US Department of Veterans Affairs asked IOM to organize the effort, which led to the formation of the Committee on the Assessment of Wartime Exposure to Herbicides in Vietnam.

As noted in the interim report released in April 2003 (IOM, 2003), the committee commends the work of the team of investigators from the Columbia University Mailman School of Public Health (Jeanne Mager Stellman, PhD, principal investigator) who carried out the exposure-assessment research. Their dogged pursuit of historical records has led to a substantial improvement in the quality and completeness of the information on wartime spraying and the people who may have been exposed to it. The geographic information system they developed is innovative and serves as an exemplar of how this technology can be exploited in exposure-characterization studies. And finally, the spirit of cooperation and collaboration shown by the Columbia University researchers greatly facilitated the committee's job of oversight and made its task enjoyable and intellectually engaging.

David Butler served as the study director for this project. The committee would like to acknowledge the excellent work of IOM staff members Jennifer Cohen, Anna Staton, Elizabeth Albrigo, Joe Esparza, and James Bowers. Kathi Hanna, a consultant to the committee, provided valuable assistance by composing a summary of the Columbia University research effort that served as a foundation for the report text. Thanks are also extended to Melissa French and Jim Banihashemi, who handled the finances for the project; Linda Kilroy, Joan Rodda, Donald Holmes and Robin Cohen, who were responsible for contracting issues; Norman Grossblatt, who edited the manuscript; William McLeod, who conducted database searches; Jennifer Bitticks, who supervised the production of the report; and Rita Gaskins, who provided administrative support to the project.

The committee greatly benefited from the input of scientists, researchers, government employees, veterans service organizations, and other interested persons who generously lent their time and expertise to help give committee members insight on particular issues, provide copies of newly released research, or answer queries concerning their work or experience. We thank them for their contributions.

David G.Hoel, Chair

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#### PREFACE

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## **INTRODUCTION AND BACKGROUND**

#### **ORIGIN OF THE STUDY**

From 1962 to 1971, US military forces sprayed over 19 million gallons of herbicides over Vietnam to strip the thick jungle canopy that helped conceal opposition forces, to destroy crops that enemy forces might depend on, and to clear tall grass and bushes from around the perimeters of US base camps and outlying fire-support bases. Most large-scale spraying operations were conducted from airplanes and helicopters, but herbicides were also sprayed from boats and ground vehicles and by soldiers wearing back-mounted equipment. After a National Institutes of Health report concluded that a contaminant in 2,4,5-trichlorophenoxyacetic acid (2,4,5-T)—one of the primary herbicides used-could cause malformations and stillbirths in mice, US forces suspended its use. All herbicide spraying in Vietnam was halted in 1971.

In response to concerns about the possible health consequences of exposure to the spraying, Congress passed Public Law 102–4, the Agent Orange Act of 1991.<sup>1</sup> The legislation directed the Secretary of Veterans Affairs to ask the National Academy of Sciences (NAS) to conduct a comprehensive review and evaluation of available scientific and medical information regarding the health effects of exposure to Agent Orange<sup>2</sup>, other herbicides used in Vietnam, and their components, including the contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin, informally known as TCDD or dioxin. A committee convened by the Institute of Medicine (IOM) of the National Academies conducted the review and in 1994 published a comprehensive report, Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam (IOM, 1994).

The committee responsible for the 1994 report encountered a severe lack of information about the exposures of individual Vietnam veterans to herbicides. Most studies of veterans had relied on rudimentary measures-selfreports of exposure, service in Vietnam, military occupation, or service in combat zones or in branches of the military responsible for combat

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<sup>&</sup>lt;sup>1</sup> Codified as 38 USC§1116.

<sup>&</sup>lt;sup>2</sup> Agent Orange, the most commonly used herbicide in Vietnam, was a 1:1 mixture of 2,4 dichlorophenoxyacetic acid (2,4-D) and the n-butyl ester of 2,4,5-T.

#### INTRODUCTION AND BACKGROUND

operations—that had limited power to differentiate the intensity and duration of exposure (IOM, 1997). This lack of information had hampered previous attempts to study the effects of herbicide exposure on the health of Vietnam veterans.

That committee felt, however, that it might be possible to develop better methods of determining exposures of individual veterans by drawing on historical reconstructions. The methods might take into account such factors as troop movements, ground and perimeter spraying, herbicide shipments to various military bases, the terrain and foliage typical of the locations sprayed, the military missions of the troops there, and biochemical techniques for detecting low concentrations of dioxin in the blood. If better models of exposure could be developed and validated, a number of important epidemiologic studies of exposure to herbicides and health outcomes might become possible.

The 1994 report offered recommendations concerning additional scientific studies to resolve continuing scientific uncertainty. Three of the recommendations addressed exposure-assessment studies of Vietnam veterans (IOM, 1994):

- A nongovernmental organization with appropriate experience in historical exposure reconstruction should be commissioned to develop and test models of herbicide exposure for use in studies of Vietnam veterans.
- The exposure reconstruction models developed...should be evaluated by an independent, nongovernmental scientific panel established for this purpose.
- If the scientific panel proposed...determines that a valid exposure reconstruction model is feasible, the Department of Veterans Affairs and other government agencies should facilitate additional epidemiologic studies of veterans.

The Department of Veterans Affairs (VA), in response to that report, asked IOM to establish a committee to oversee the development and evaluation of models of herbicide exposure for use in studies of Vietnam veterans. The committee would develop and disseminate a request for

proposals (RFP) consistent with the recommendations, evaluate the proposals received in response to the RFP and select one or more academic or other nongovernment research groups to develop the exposure-reconstruction model, provide scientific and administrative oversight of the work of the researchers, and evaluate the models developed by the researchers in a report to VA, which would be published for a broader audience.

#### CONDUCT OF THE STUDY

The Committee on the Assessment of Wartime Exposure to Herbicides in Vietnam was formed in 1996 to accomplish the model-development tasks. Its initial work resulted in the report *Scientific Considerations Regarding a Request for Proposals for Research Characterizing Exposure of Veterans to Agent Orange and Other Herbicides Used in Vietnam* (IOM, 1997). The report—which comprised a statement of work, criteria for selecting researchers, and an appendix providing background information for potential respondents—was released to the public on March 18, 1997. It summarized the intent of the research as follows (IOM, 1997, p. 3):

1. Develop and document a detailed methodology for retrospectively characterizing the exposure of Vietnam veterans to the major herbicides used by the military in Vietnam— 2,4-D; 2,4,5-T; cacodylic acid; and picloram<sup>3</sup>—and the trace contaminants TCDD and its congeners. The proposal should address how exposure to this array of chemicals will be evaluated. However, the ability to separately identify or quantify exposures to each of these substances is not necessarily a requirement for a successful proposal. The exposure methodology proposed must be applicable to specific types of epidemiologic investigations that could be conducted at a future date under a separate contract or subcontract.

<sup>&</sup>lt;sup>3</sup> These four herbicides were used individually and in combination as the active ingredients of the "Agent" formulations employed during the war: Agents Orange, Orange II, White, Blue, Pink, Purple, and Green.

2. Demonstrate the feasibility and appropriateness of the proposed methodology in sufficient detail to permit the assessment of its potential for use in the conduct of epidemiologic studies.

A formal, complete RFP, including the scientific input and contractual requirements, was developed and was issued on June 30, 1997. It was initially sent to persons and organizations that had requested it or were thought to have an interest in exposure-characterization research. Availability of the RFP was publicized on the Web sites of IOM's Board on Health Promotion and Disease Prevention and the Society for Risk Analysis and was posted to relevant e-mail lists. Members of the veteran community and other interested persons were also informed of the RFP through public events held by IOM committees involved in Vietnam-veteran health research and through contacts made at meetings and conferences attended by committee members and staff.

Three proposals were submitted by the due date of September 4, 1997. Committee members evaluated their technical and scientific merit on the basis of the criteria set forth in the RFP. They concluded unanimously that a proposal submitted by researchers at Columbia University's Mailman School of Public Health (Jeanne Mager Stellman, PhD, principal investigator) merited funding.

The terms of the contract specified that the researchers were to submit scientific progress reports every 6 months over the length of the contract. The progress reports were to include "a description of the overall progress; descriptions of the specific work accomplished, including problems encountered and corrective actions; pertinent data or other information in sufficient detail to explain significant results achieved and any preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date; and a description of the work to be accomplished over the following six months." Progress reports were presented in public meetings of the committee to disseminate the information to a larger audience and facilitate interaction between the committee and the researchers. The first took place in a November 6, 1998, meeting of the committee, and the last occurred on January 13, 2003. Communication between the Columbia University researchers and the committee was maintained between meetings on a less formal basis.

#### INTRODUCTION AND BACKGROUND

In April 2003, the committee issued an interim report based on the work that had been completed (IOM, 2003). On the basis of a review of the contractor's 6-month update reports and presentations and its published and draft papers, the committee reached the following findings:

- The contractor has developed databases of wartime spraying and accidental dispersion of herbicides, of troop locations and movements, and of land features and soil typology.
- The contractor has developed an effective exposure assessment tool to assign a metric—the E4 Exposure Opportunity Index (EOI)<sup>4</sup>—for herbicide exposure that is based on proximity to spraying in space and time and on the amount and agent sprayed.
- The range of calculated EOIs and information gathered to date on troop locations is sufficient to demonstrate the feasibility of future epidemiologic studies. Additional location data for troops not currently included in present databases appear to be available at the National Archives<sup>5</sup> for abstraction and use by researchers and other interested parties in future studies.
- Given current knowledge and available data, the contractor has adequately demonstrated that the draft model is a valid means of assessing wartime herbicide exposure of Vietnam veterans.

Given those findings, the committee concluded that a valid exposure-reconstruction model for wartime herbicide exposures of US veterans of Vietnam was feasible. It therefore recommended that the VA and other government agencies facilitate additional epidemiologic studies of veterans by nongovernment organizations and independent researchers.

The intent of the present report is to summarize briefly the work done by the contractor over the life of the study and to serve as a vehicle for cataloging and transmitting that work to VA. The sections below delineate the work of the Columbia University researchers as it evolved from proposal through delivery. It is based on the material provided by the Columbia University

 $<sup>^{4}</sup>$  The EOI is not intended for use in evaluating the exposure of groups who were responsible for applying herbicides, although some of the information collected in the research effort may be useful in studies of these groups.

<sup>&</sup>lt;sup>5</sup> Formally, the US National Archives and Records Administration (NARA).

researchers in their 6-month progress reports, presentations, draft materials, and final report; and it quotes freely and extensively from these materials. A complete list of the materials produced by the contractor in the course of its work is given in Appendix A; these materials are the definitive references for the research summarized here.

The committee concludes here, on the basis of its review of the contractor's final report and all previous work, that the Columbia University researchers have satisfactorily completed the research project as defined in their proposal and modified in consultation with the committee. It also affirms all the findings and conclusions reached in its own Interim Report (IOM, 2003).

The Interim Report details the reasoning that underlies the committee's conclusions regarding the scientific quality of the contractor's work. As detailed in that earlier report, a central issue was the demonstration that the draft model was a valid means of assessing the wartime herbicide exposure of Vietnam veterans. The Columbia University researchers implemented extensive quality control measures to assure the precision and completeness of their data, and offered both qualitative and quantitative validation information for their model. Considered together, this material led the committee to conclude that the exposure assessment model was feasible.

The committee also notes that the Columbia University researchers' work has been subjected to additional peer review as part of the processes that lead to the papers they have published in *Environmental Health Perspectives* (Stellman JM et al., 2003) and *Nature* (Stellman SD et al., 2003) and that they will soon publish in *Journal of Clinical and Consulting Psychology* and *Journal of Exposure Analysis and Environmental Epidemiology*. Appendix A of this report notes other papers that are presently under preparation and submission.

## **CONTRACT SUMMARY**

The overall goal of the Columbia University research effort was to determine whether a valid and useful method could be developed for estimating Vietnam veterans' opportunity to be exposed to herbicides on the basis of historical reconstruction of relevant military records. The conceptual framework for the overall project included research on and quality control for the identification and reconstruction of military records, development and testing of exposure-opportunity models that used those records, and research on selected Vietnam veterans to understand the extent to which covariates or confounders need to be taken into account in epidemiologic studies of the health effects of herbicides on Vietnam veterans.

The goal was to elucidate the basic determinants of exposure: person, place, and time. With regard to person, the aim was to identify the specific locations of a veteran's military unit<sup>6</sup> and the specific tasks that may have resulted in exposure to herbicides. The Columbia University researchers were also interested in elucidating inservice and post-service experiences that might have affected any potential response to herbicide exposure so that they could be controlled for in future epidemiologic studies. They aimed to determine the extent to which the long period since the end of the spraying activities could affect a veteran's recall and the researchers' ability to identify and locate potential epidemiologic cohort members.<sup>7</sup> With respect to place and time, the researchers' goals were to optimize the quality of the data available on herbicide spraying and to develop statistically robust models for herbicide-exposure opportunity for the entire period of the Vietnam War.

Another research aim was to provide guidance for future epidemiologic studies on the degree to which important confounders and covariates might influence the outcome of epidemiologic health studies with respect to herbicide exposures. On the basis of previous studies of veterans'

<sup>&</sup>lt;sup>6</sup> Several terms are used to specify the organizational position and size of a military unit. The primary terms used in the US Army during the war were corps, division, brigade, battalion, company, platoon and squadron. Other services used different designations.

<sup>&</sup>lt;sup>7</sup> All protocols involving human subjects were submitted to the Columbia University Institutional Review Board and were approved. They included procedures and systems for preventing records access by persons who were not members of the study team.

health, including their own published work (Stellman SD et al., 1988a, 1988b; Stellman JM et al., 1988; Snow et al., 1988), the contractors hypothesized that the experience of combat might have a profound effect both on subsequent health and on such important lifestyle factors as smoking and drinking, which, in turn, heavily influence disease outcomes. They thus undertook a large-scale survey of veterans to gather and evaluate the association among demographic, socio-economic status and behavior variables; military service history; self-reported exposures to herbicides and to combat; measures of post-traumatic stress disorder (PTSD) and other psychiatric symptoms; and numerous health outcomes. A focused study of women veterans was also conducted and an outreach effort was conducted to involve black and Hispanic veterans in order to evaluate the generalizability of such measures.

The working plan proposed by the contractor consisted of five<sup>8</sup> interrelated projects on various methodologic aspects of characterizing herbicide exposures of American troops who served in Vietnam. Each project was related to an aspect of the historical reconstruction of exposure to herbicides. The projects were as follows:

#### Project 1: Military Unit and Herbicide Spraying Databases, and Exposure Assessment Model Development

- Compilation and assessment of data on troop locations.
- Collection of data on the application of herbicides in the wartime aerial spraying program and other releases such as perimeter spraying.
- Analysis of the database contents to evaluate their suitability for use in the historical reconstruction of exposure to herbicides.
- Development and refinement of a means of characterizing wartime exposure of US veterans to herbicides.

<sup>&</sup>lt;sup>8</sup> A sixth proposed project would have developed priorities and methods for epidemiologic research based on the findings of Projects 1–5, other available health-outcome databases, and additional technical and pragmatic considerations. This project was not included in the final contract, because a decision was made to focus on activities related to the development of an exposure-assessment model.

• Creation of a user-friendly software system to facilitate the estimation of exposure.

#### Project 2: Covariates, Confounders, and Consistency: Characterizing the Vietnam Veteran for Epidemiologic Studies

- Examination of self-reports of military service, exposure to herbicides, and confounders and covariates of methodologic interest (such as combat experience).
- Evaluation of validity of veteran recall and various approaches to obtaining self-reported data.

#### Project 3: Evaluation and Standardization of Military Records for Use in Epidemiologic Studies<sup>9</sup>

- Identification of the Vietnam-era military personnel and other records that contain information potential relevant to epidemiologic studies.
- Development and testing of a standardized means to abstract records data needed to determine a veteran's dates of service in-country, military unit(s), occupation(s), and other service-related information potentially relevant to epidemiologic studies.
- Evaluation of the consistency of the records data with self-reports of military service and experience.
- Development of a guide to obtaining and abstracting military records for use in epidemiologic research.

#### Project 4: Biomarkers of TCDD (Dioxin) Exposure in Vietnam Veterans

<sup>&</sup>lt;sup>9</sup> This project was entitled *Evaluation and Standardization of Military Personnel Records for Epidemiologic Studies* in the contractor's proposal. It is revised here to clarify that both personnel and other records were examined.

- Evaluation of TCDD in blood serum samples from selected veterans likely to have been heavily exposed and of an appropriate selection of Vietnam-era veteran controls using high-resolution gas chromatography/high-resolution mass spectrometry analysis.
  - Examination of the utility of chemical-activated luciferase gene expression (CALUX) analysis as a lower-cost method of screening for TCDD exposure in studies of Vietnam veterans.

#### Project 5: Analysis of International Agency for Research on Cancer (IARC) Tissue Samples of Selected Vietnamese for Dioxin and Dibenzofuran Levels in Archived Adipose Tissues

• Evaluation of the correlation between levels of TCDD and dioxin- and dibenzofuran congeners in adipose tissue collected from Vietnamese citizens as part of an IARC case-control study tissue archive with lifetime residence-history data and herbicide-spray records, on the basis of the exposure-opportunity index developed in Project 1.

#### EVOLUTION OF PROJECT DEVELOPMENT AND IMPLEMENTATION

In the course of the study, the Columbia University researchers entered considerable amounts of data into new composite databases, creating, cleaning, and expanding archives for use in future epidemiologic studies. They also refined their computational approaches and developed new approaches to classifying and analyzing existing data. The researchers conducted two large surveys to elucidate the extent to which covariates and confounders must be considered in designing and executing studies of the effects of herbicide exposure on Vietnam veterans. In the course of seeking access to military personnel records for research purposes, they documented gaps and flaws in the data and identified potential barriers to conducting new studies of veterans' health.

As it became apparent that some tasks were larger and more time-consuming than originally thought or it became obvious that some records or databases could not be used for the intended purposes of the research, the proposed projects were modified, augmented, or partly abandoned.

This report chronicles some of the activities undertaken by the Columbia University researchers as they met the various challenges posed by the study and in response to continuing communication with the IOM committee.

## **PROJECT 1:**

## MILITARY UNIT AND HERBICIDE SPRAYING DATABASES, AND EXPOSURE ASSESSMENT MODEL DEVELOPMENT

The goal of Project 1—the primary task in the research effort—was to construct a transportable system for evaluating herbicide exposure of veterans who served in Vietnam. The purpose of the system was to provide data for use in epidemiologic studies. The Columbia University researchers outlined the following specific aims in their proposal:

- 1. Identify and fill in remaining gaps in the Military Unit Database-Vietnam (MUD-V) by retrieving, evaluating, and abstracting primary source materials.
- 2. Develop additional mathematical models for use as exposure opportunity indices (EOIs).
- 3. Carry out sensitivity analyses of models to characterize the robustness of exposure indices to inaccuracies in the locations of the troops.
- 4. Where inaccuracies or inconsistencies are found, attempt to obtain and incorporate additional or alternative troop-location data from primary sources.
- 5. Create a final database of troop locations that contains alternative exposure estimates from a variety of models and their reliabilities.

- 6. Incorporate the final database into user-friendly software that will permit future investigators to use the models to assign exposures or to propose their own models.
- Interview Division Chemical Officers who served in Vietnam and served as principal advisers to division commanders on the use of all chemicals to complete to the extent possible the record of known spraying missions.

Thus, the central goal of the project was to develop a comprehensive database that contained all known information on the military herbicide spraying that had been carried out under Air Force Operation Ranch Hand; by the US Army for perimeter defense and other smaller localized purposes; and in other, unintentional releases. An additional database was planned to contain locations and dates of "residence" of US military units stationed in Vietnam.

#### CONSOLIDATION, QUALITY CONTROL, AND STANDARDIZATION OF DATABASES

Before the initiation of the contract, a set of individual geographic locations of military units assigned to Vietnam were collected by Columbia University investigators Jeanne Mager Stellman and Steven D.Stellman for use in the Agent Orange Veterans Payment Program (AOVPP), in collaboration with Lt. Col. Richard Christian (ret.). The Drs. Stellman were consultants to the special master presiding over this program, which resulted from the Agent Orange Product Liability Litigation—a class-action lawsuit brought by Vietnam veterans and their families regarding injuries allegedly incurred as a result of the veterans' exposure to chemical herbicides during the Vietnam war. In that effort, the Columbia University researchers created a military-unit database for claim evaluation. The database contained about 500,000 records, each of which provided an exposure opportunity index<sup>10</sup> for one military unit during a discrete period. The exposure of any individual claimant was calculated by summing the tabled exposures for his or her unit(s) during service in Vietnam. The database, the "Military Unit

<sup>&</sup>lt;sup>10</sup> This exposure opportunity index (EOI) is an earlier formulation of the E4 EOI that was developed under the contract. In general, an EOI may be defined as an estimate of the possibility that a person will come into contact with a toxic chemical without regard to route of entry or later metabolism.

Database-Vietnam (MUD-V)," although not intended for epidemiologic purposes, was viewed as a prototype for the present study.

The Columbia University researchers undertook to examine the extent of coverage of the MUD-V database, evaluate gaps in the data, assess the implications of misclassification of exposure, and—given all these considerations—ascertain how much usable information remained for epidemiologic investigations. One aim of Project 1 was to carry out a sensitivity analysis of the data in MUD-V to determine the extent to which it could satisfactorily produce a rank-ordered exposure rating for the military units.

On the basis of their previous experiences, the Columbia University researchers concluded that many socalled gaps or inconsistencies in the secondary data sources were minor and would not seriously affect the accuracy of epidemiologic studies. Indeed, they had developed methods in the AOVPP for imputing reasonable locations and exposure scores where data were missing, such as substituting average battalion locations for companies or using the highest computed exposure among companies with known locations for a company whose location during a particular period was not known. Nonetheless, one of the immediate tasks undertaken in this contract was to re-examine the database and remove all imputed data. To accomplish that, the researchers returned to the original troop-movement data that had been collected by the US Army and Joint Services Environmental Services Group (ESG), now known as the US Joint Services Center for Research of Unit Records.

#### **Restoring the Troop-Movement Database**

The original troop-movement database was stored on 9-in. magnetic reels in virtual address extension (VAX) backup format, which is no longer manufactured. Recovery entailed first locating a working Digital Equipment Corporation VAX and obtaining licenses for appropriate operating systems and other software. Eventually, the original data and directory structure were restored, original research notebooks were located, and data were made compatible with current

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software systems. The data library was documented and written to CD-ROM. All programs and databases are now VAX-independent.

The AOVPP database exposures were calculated by using 1-month periods. However, the original data sources contain considerably finer time detail for many military units; in many instances, biweekly data exist; and in a few cases, daily coordinates were abstracted. The researchers went back to the original tapes to make the more detailed data available. All data were converted from the Universal Transverse Mercator (UTM) coordinate system used by the US military to a Cartesian<sup>11</sup> system more amenable to the required modeling. The researchers also appended the Department of Defenses (DOD) uniform unit-identification system designation, the Unit Identification Code (UIC), to the information in the files.

#### Identifying Units That Served in Vietnam

In addition to reconstructing the existing troop-movement databases and determining where gaps or inconsistencies existed, the researchers updated the UIC LIST, a compilation of all the unit-identification numbers developed by ESG for military units with service in Vietnam. The UIC LIST had not been designed to be a comprehensive catalog of the units but rather was developed by ESG for its work in support of VA and the Centers for Disease Control<sup>12</sup> (CDC), as a recordkeeping system. It thus represented, to a large extent, units to which a VA or CDC study subject may have been assigned and units that had been identified for other study-specific purposes. The Columbia University researchers systematically examined the UIC LIST, compared and combined it with other data sources on military units, and created a master list.

The master list is the first easily accessible and cross-referenced comprehensive list of all Army units that were stationed in Vietnam and the numbers of troops assigned to them in Vietnam. Where possible, the database also includes the identification of the next-higher command to which a unit was assigned. The next-higher command provides important

<sup>&</sup>lt;sup>11</sup> The Cartesian system expresses coordinates in terms of latitude and longitude.

<sup>&</sup>lt;sup>12</sup> Now called the Centers for Disease Control and Prevention.

information about unit location and enables researchers to locate military records more easily at the National Archives and in other reference materials.

#### Classifying and Modeling the Mobility of Military Units

The Columbia University researchers developed a new concept for studying troop movement for use in reconstructing herbicide-exposure histories based on a concept they called the mobility factor. The mobility factor is a three-part classification system for characterizing the location and movement of military units in Vietnam. It comprises a mobility designation (stable, S; mobile, M; or elements mobile, E), a distance designation (usually in a range of kilometers) to indicate how far the unit might travel in a day, and a notation of the modes of travel available to the unit (air; ground—truck, tank, or armored personnel carrier; or water). They then assigned a mobility factor to every unit that served in Vietnam. The mobility-factor concept simplifies the task of characterizing exposure of military personnel to hazardous substances and conditions during the course of military conflict.

The mission of the organization had to be considered in conjunction with the organizational structure when mobility factors were being assigned. For example, if the mission was transportation, the mobility of the unit would vary with the command. In some cases, the mobility factor was determined in whole or in part by the type of installation to which it was assigned (for example, an airfield or a fire-support base).

Not all stable units remained in the same location throughout the war. The researchers wrote a program that provides a list of all stable units that "moved", according to the database. In assessing the data, they found that in most cases the "move" was real—a unit was reassigned to a different location. In some cases, however, typographic errors were responsible for the ostensible movement. In other cases, units were reclassified because some elements were, indeed, mobile. Because the mobility factor was a new concept, the researchers assembled a panel of military experts to review the concept itself and to examine the designations given to the military units stationed in Vietnam. In general, the concept was strongly endorsed by the panel, and the mobility assignments given to particular units were approved.

**Stable Units** An important distinction made by the researchers was that the great majority of military units assigned to Vietnam were "stable"; that is, their missions did not require routine movement around Vietnam, and they were assigned to a specific base-camp location. Thus, the military-occupancy probability assigned to these units would be 100% for the grids that they occupied.

Initially, the Columbia University researchers made a rough working estimate of the exposure-opportunity scores for the stable units. Most units were in the low-exposure category for aerial applications because the strategy underlying the herbicide projects was to defoliate or destroy crops in areas away from the main support-troop locations. However, some stable units were in heavily sprayed areas, and the perimeters of the base camps were also subject to backpack and other, more poorly documented spraying.

In investigating the issue further, the researchers identified a previously unrecognized source of supplementary data in the National Archives. From those data, they deduced that each time an installation or base camp was built or occupied by American forces, a formal land-transfer agreement was executed between the governments of South Vietnam and the United States. These agreements contained specific maps and descriptions of, for example, base camps and power stations. The researchers reviewed those documents and extracted extensive quantitative data, including complete dimensions of about 200 base camps, locations of airfields, water supplies, and hospitals. In addition, they were able to identify the precise locations of 36 military units that were stationed in those installations. They also obtained coordinates for a large number of perimeters of U.S. installations. The data were used for additional quality control of the stable-units database.

The stable-units database of base-camp locations and dates of residence created by the researchers covers about 80% of the troops stationed in Vietnam.

**Mobile-Troop Location Modeling** The Columbia University researchers developed and tested algorithms and programs for describing and analyzing the movement of mobile battalions and their elements to further the goal of developing models of troop movement and unit dispersion. The ultimate aim was to assign militaryoccupancy probabilities to specific grids in the map of Vietnam for every military unit, down to the company level, for the duration of its assignment in South Vietnam.

The primary problem in characterizing mobile units' locations was incomplete data. A critical issue was to determine whether data on a unit for particular dates were missing simply because the unit did not move and therefore did not report its continued residence at one location or whether the gaps are missing data. To develop statistical methods that could be used to evaluate the data in the entire database, the researchers studied patterns of movement of units on which substantial data already existed. That exercise yielded criteria for identifying data that indicated "short-term location stability" (where there may not have been consistent recording of location but there were not data gaps), which in turn helped to identify units for which "true" gaps existed. The researchers could then more reliably impute missing locations for these units.

A preliminary cleaning and analysis of a large dataset of troop locations of Army combat battalions assigned to Military Region III<sup>13</sup> suggested that data sources available in the National Archives (including Daily Journals, After-Action Reports, and Operation Reports-Lessons Learned) could be used to resolve most of the data problems encountered. That indicated to the researchers that it should be possible to assemble location databases for other mobile units—an important finding because such units are likely to have been among the most heavily exposed to herbicides.

#### Herbicide Dispersion Data

The Columbia University researchers determined that a major aspect of linking a military location with an exposure opportunity rests in the computerized records of herbicide application commonly known as the HERBS files. Records indicate that 95% of all herbicide used during the war were dispersed under Operation Ranch Hand, the US Air Force aerial spraying program (Stellman JM et al., 2003). Those records, although incomplete, are by far the most important

<sup>&</sup>lt;sup>13</sup> Military Region III, also known as the III Corps Tactical Zone (III CTZ), comprises a large area in the south of Vietnam surrounding Ho Chi Minh City (formerly Saigon). It was an area of heavy combat and wartime spraying.

records available for exposure-assessment purposes. In 1974, the National Research Council organized data into a file, known as the HERBS tape, that contained coordinate points for more than 6,200 missions flown by fixedwing aircraft and included date, type of herbicide, gallons applied (gallonage), and purpose of mission (NAS, 1974). The data in the HERBS file are given in UTM coordinates; a mission is recorded as a series of turning points in the flight path. Algorithms were written to translate from UTM to Cartesian coordinates so that spraymission data could be integrated with other geographic information. Other programs transformed the discrete turning points into continuous flight paths so that exposure potential could be evaluated over complete spray routes.

Although herbicide operations in Vietnam began in August 1961, the HERBS file contains data only from 1965 on. During the course of their work, the researchers found additional information on pre-HERBS-file spraying in a variety of sources, including two early Air Force documents (Buckingham, 1982; CHECO, 1967), the Air Force Herbicide Project folders housed at the National Archives (which contain detailed information on the planning and execution of most Air Force herbicide missions), publications produced by the US Military Assistance Command, and information retrieved from the government of South Vietnam "202 Tasks Realized" report.

In the early 1980s, ESG assembled a tape to supplement HERBS—the Services-HERBS tape—consisting of helicopter, backpack, truck, and other smaller-scale spraying data. The database also included some information on aborted spray missions, leaks, and other unintentional releases. The combined data from those two sources comprised over 8,800 individual military spray missions. However, several discrepancies existed between the two files. Many could be resolved by a careful comparison between consecutive legs with cross-referencing to the map of Vietnam or by reference to the Daily Air Activity Reports (DAARS). When discrepancies could not be resolved, a panel of military experts assembled by the contractor reviewed the missions and determined whether it was clear that the error was typographic and whether it was possible to resolve the differences. If it was impossible to resolve

a difference, the mission was flagged as questionable in the database so that it could be included or excluded at the discretion of the user.

As a result of that exercise, the researchers developed a composite HERBS file that contains the date of spraying, coordinates of the spray mission, type of herbicide, number of gallons, mode of application, type of aircraft (if appropriate), and-where available-area sprayed. For missions flown with aircraft, the file also contains connectivity indicators that enable one to trace the path of spraying.

During the researchers' reinspection of the DAARS, it became clear that individual missions were associated with particular targets and that identifying numbers (project numbers) were assigned to the targets. An earlier NAS report (1974) described how herbicide operations were organized into projects to be approved by various committees. In re-examining the original HERBS file obtained from NARA and ESG, the researchers found a field that could be related to the project numbers on the DAARS. When the HERBS file was grouped according to this field, all the Ranch Hand missions fell into specific projects. That was a major breakthrough in understanding the herbicide-spraying program because it allowed several thousand spray missions to be rationalized into a few hundred projects for analysis purposes. It is described in greater detail in a paper by the researchers that was featured on the cover of Nature on April 17, 2003 (Stellman JM et al., 2003).

Combining and validating data from all those sources produced a final composite spraymission database that comprised 9,141 missions (19,977 sorties<sup>14</sup>) that dispersed 19,491,090 gal of herbicide in 1961–1971 (Stellman and Stellman, 2003). Depending on the assumptions used, the researchers estimate that the herbicides contained 487-807 lb (221-336 kg) of TCDD (Stellman JM et al., 2003).

attribution

<sup>&</sup>lt;sup>14</sup> A mission was executed by one to four aircraft. Each aircraft's flight was considered a sortie.

#### **Approach to Exposure Assessment**

The Columbia University researchers proposed the EOI as a useful alternative to such traditional toxicologybased measures as blood or adipose-tissue concentrations. It was not meant to be a substitute; neither method is perfect, and both can yield valuable information about potential exposure. The EOI method used in this project was originally developed and published by the researchers during the 1980s (Stellman and Stellman, 1986). Its central feature is the comparison of the geographic location of a potentially-exposed military unit with all known locations of herbicide release. Total exposure opportunity for the unit is the sum of the EOI estimates for all temporally-appropriate<sup>15</sup> data in the database.

Four models to quantitatively assess exposure opportunity were developed by the Columbia University researchers in the course of this and previous work. They incorporate increasingly realistic (and more complex) exposure concepts of distance and time of potential exposure to herbicide application. The simplest, E1 (the "hit" model), simply counts the instances in which a person was within a specified distance of a known spray. The second, E2, also counts hits but makes close hits count more by weighting each hit according to inverse distance from the spray. The third model, E3, begins with distance-weighted hits and factors in the total time during which the person is considered to have been exposed. E1 and E2 can be regarded as representing acute or direct exposures, since no allowance is made for exposure engendered by entering a sprayed area after the spraying has occurred or for the length of time spent in the sprayed area. E3 is analogous to acute followed by chronic exposure.

Time is an essential characteristic of the current, E4 EOI model. Any person or entity that is present on the day of spray would be considered to have "direct exposure". Those entering a sprayed location after that time and those remaining in the location after having been directly exposed would be considered to have "indirect exposure", that is, exposure to any residual

<sup>&</sup>lt;sup>15</sup> The exposure assessment software that implements the model allows the user to set the time period over which potential exposure should be factored. This may be relatively short if the user is examining herbicide ingredients that break down in sunlight or extremely long for a chemically-stable compound like dioxin.

herbicide or dioxin that is present. The E4 EOI may be expressed mathematically as a product of three factors:

- Concentration of the toxicologically active substance in the herbicide mixture.
- A person's distance from spray paths.
- Residence time at an exposed location.

Thus, E4 EOI=concentration factor×distance factor×time factor. The E4 EOI for a given mission is calculated as the sum of the component E4 values for all its legs.

The researchers expanded the scope of assessment for the models in three important ways: by giving greater consideration to the questions of dispersion of individual troops than to reported locations of their units, using nonlinear error methods; by carrying out sensitivity analyses to account for spray-coordinate errors introduced by deviation of aircraft from flight paths and wind dispersion of herbicides; and by investigating other exposure models as extensions of or alternatives to the above. Two elements needed improvement for exposure-opportunity models: incorporation of gallonage of herbicide and consideration of connectivity of fixed-wing aircraft flight paths.

The intent of this work was thus to attempt to improve the modeling of herbicide dispersal by creating a mathematical means of estimating the herbicide release along the entirety of flight paths rather than at points along flight paths.

#### **Modeling Herbicide Exposure**

As the project evolved, the Columbia University researchers refined their approach to calculating the EOI. Rather than estimating it directly for a military unit on the basis of its location, they chose to calculate an exposure score for a series of contiguous grids that cover Vietnam and a military-unit occupancy probability, which represents the likelihood that an individual military unit will occupy any specific grid. These grids are  $0.01^{\circ} \times 0.01^{\circ}$ , which is

equal to ~1.2 km<sup>2</sup> on average. The gridding concept permits use of statistical methods to evaluate exposure of units whose locations are known only probabilistically. It also makes it possible to superimpose contours of exposure on maps of Vietnam to visualize regions of especially high and low exposure. Finally, it permits more rigorous treatment of the various geophysical characteristics that may affect exposure to and bioavailability of herbicides (soil type, presence of water, and the like). The geographic information system (GIS) developed by the researchers transforms exposure estimation into a more efficient process.

The researchers digitized an existing soil map of the former Republic of Vietnam that was incorporated into the GIS to extend exposure modeling to account for differential environmental decay of herbicides (or dioxin) that may depend on soil typology. The map was derived from a 1961 field survey that was carried out by the UN Food and Agricultural Organization (FAO) for the Vietnam Ministry of Agriculture (Moormann, 1961). The original FAO map was scanned, and each of the 925 contours was traced manually. A point-in-polygon algorithm was used to assign to each of the GIS grids an integer corresponding to the soil contour in which it fell. This allows the EOI for a grid to be computed by using a half-life appropriate to the soil type.

To make the GIS more easily accessible to researchers, the contractors developed a userfriendly software interface called "Herbicide Exposure Assessment-Vietnam" (HEA-V). The HEA-V employs information from various components of the database—flight paths of aerial spray missions, number of gallons sprayed (gallonage), and chemical agents; documented spraymission targets; herbicide storage, transport, and unplanned-dispersal information; military-unit identification codes; locations of military units, bases, structures, air fields, and landing zones; movements of combat troops; land features<sup>16</sup>; soil typology; and locations of civilian populations—to calculate exposure opportunity. A paper published in the March 2003 edition of the journal *Environmental Health Perspectives* details the development and application of the GIS and associated software system (Stellman SD et al., 2003).

<sup>&</sup>lt;sup>16</sup> Including coordinates of a variety of: elevations and land contours, rivers and streams, mountains and highlands, coastal areas and mangrove forests, bays and estuaries, and such structures as roadways and utilities.

While the research effort was directed at characterizing the exposures of US veterans of Vietnam, the databases and model created by the Columbia University researchers could be adapted for use in studies of other countries' veterans and of Vietnam residents.

#### EXPANDING PERIMETER SPRAYING DATABASE

Seven Army divisions served in Vietnam during the years in which herbicide spraying took place (1965– 1970). A Division Chemical Officer, who generally held the rank of lieutenant colonel or major, served in each division. Each officer served for a 1-year tour of duty, although some may have served for shorter periods and some for more than one tour. An objective of this Project 1 task was to attempt to learn how much perimeter spraying and local spraying took place during the Vietnam War for which no records exist on the Services-HERBS tape.

The researchers intended to identify Division Chemical Officers from available military records, such as the Daily Journals and the Morning Reports, and interview them. They also anticipated retrieving further data on people in the Chemical Corps from the National Personnel Records Center (NPRC) in St. Louis, which holds all military records for the armed services and Coast Guard. An exchange of correspondence occurred among the investigators, NPRC, representatives of the individual branches of the services, the DOD Privacy Board, the Secretary of Defense, and the Defense Manpower Data Center (DMDC) (which maintains the Vietnam file) to secure more information. The records requested—unit assignments, military occupational specialties, and awards won—are releasable public records, in contrast with medical records and Social Security numbers, which are considered private records. The armed services have set up "routine-use" mechanisms by which private records may be released to federal contractors but have not established routine-use mechanisms for the release of releasable records. After negotiations among VA, NPRC, and DOD, it was agreed that a contract would be drawn between VA and NPRC for finding Social Security numbers of the chemical officers. The results of the search would be given to NAS, the VA contractor, and then to Columbia University, the NAS subcontractor.

A text file containing 983 records of Chemical Corps officers and enlisted personnel was given to NAS to transfer to VA for transfer to NPRC. Each record contained either Army serial number or Social Security number. Of the 983 records, NPRC was able to match 218, 160 of them officers. Social Security numbers—the most straightforward means of tracing the veterans—were available for just 29 of these officers. Given the additional challenges of locating the surviving veterans in this truncated cohort and the fact that only some of them would have been involved in herbicide spraying operations, the researchers concluded that this approach was unlikely to yield enough data to warrant its pursuit. In consultation with the committee, the task was abandoned.

#### **CONTINUING WORK**

The researchers have indicated that they hope to pursue further information-gathering and analysis of veterans' exposure to herbicides, using funding from other sources. Among the materials submitted in fulfillment of the contract with NAS (listed in Appendix A) is a draft Web site and its associated documentation. The intent of the Web site is to gather voluntarily submitted information on the locations of military units that served in Vietnam directly from individuals or organizations. That would be used to fill gaps in data on the highly mobile combat units that served in Vietnam.

#### ACCOMPLISHMENTS

- Expansion and cleaning of an archive of previously tracked locations of combat battalions.
- Development of an approach to classifying military units so that they can be broken down by the degree to which their mission required frequent changes in location. The approach has permitted the development of a database of locations of about 80% of all Army troops, most Air Force personnel, and Navy personnel assigned to construction battalions or permanent installations and calculation of exposure opportunity and hit scores for them.

- Expansion and cleaning of herbicide-spray data (the HERBS and Service-HERBS files) that had been used extensively by the researchers and others in the past. That work has led to a substantially expanded inventory of spraying and to a higher estimate of the amount of dioxin likely to have been deposited in the Republic of Vietnam during the war.
- Refinement of the computational approach of a previously developed EOI and refinement of the model itself to account for gallonage and direct-hit exposures better.
- Development of a GIS for Vietnam into which were placed extensive databases, such as the HERBS file
  of spraying missions, an exposure table of hits and exposure-opportunity scores, military-unit
  identification codes, and military locations.
- Design and development of a unique user-friendly software system—the Herbicide Exposure Assessment-Vietnam—that implements the GIS and may serve as an archetype for other epidemiologic software for GIS-based analyses.

Exploiting the National Archives data resulted in a revision of both the tasks and the timetable for the Columbia University researchers' work. The committee, who were consulted on the changes, felt that they were appropriate and desirable. It should be noted that although these data have substantially expanded knowledge about spray activities, they do not constitute a complete accounting of all herbicide releases. Indeed, it is not possible to document the myriad opportunities for in-country exposure. The best that any database of wartime herbicide exposures can do is to provide a basis for better-informed epidemiologic studies of veterans.

## **PROJECT 2:**

## COVARIATES, CONFOUNDERS, AND CONSISTENCY: CHARACTERIZING THE VIETNAM VETERAN FOR EPIDEMIOLOGIC STUDIES

The Columbia University researchers' proposal indicated that the primary aim of Project 2 was to identify and evaluate key variables and other aspects of military experience in Vietnam, such as herbicide handling and exposure to combat stress, that need to be taken into account in future epidemiologic studies of Vietnam veterans. Such knowledge will be essential in developing the conceptual framework and design of future studies.

A second, equally important goal was to examine and evaluate the quality of methods of military-unit identification for individual veterans, because it is through the military unit that linkage with the herbicide-exposure database is effected. One aspect of reaching this goal was to assess the reliability of veterans' recall and of various approaches to obtaining military-unit data on people who may be enrolled in epidemiologic studies.

A third goal was to address issues of generalizability by carrying out surveys in different populations of veterans with a focus on assessment of exposure to herbicides, military combat, and physical and mental-health outcomes that are likely to be relevant to future Vietnam-veteran studies.

To accomplish those objectives, the researchers designed and conducted three substudies:

- A follow-up study of members of the American Legion who were originally surveyed in 1984–1985 and who made up the study population in previously published epidemiologic work (Stellman SD et al., 1988a, 1988b; Stellman JM et al., 1988; Snow et al., 1988),
- A survey of veterans in minority groups (blacks and Latinos) that may have been underrepresented in previous studies,

#### FOLLOW-UP OF THE AMERICAN LEGION SURVEY

#### **Enduring Effects of Vietnam Service**

The researchers recovered the original data files and identified the earlier cohort of 12,748 men who were randomly sampled from the American Legion membership for a 1984 survey (the Wave 1 survey). The American Legion membership department was able to trace about 60% of them from current membership roles. An additional 12% were then located by attending Legion state conventions, networking with attendees, and circulating lists of "missing" Legionnaires to individual legion posts (organizational units). Some remaining veterans were found through online searches and use of a commercial credit-rating service that maintains an extensive name and address database. Of the 72% found, a follow-up determined that some were deceased and a small number were not eligible for participation because their service did not meet the study requirements. In total, 63% of the original cohort was sent questionnaires.

A survey nearly identical with that used in 1984 was reviewed and slightly amended after discussions with VA and American Legion officials, subjected to institutional review board approval at Columbia University, and mailed to nearly 9,000 Legionnaires in 1998 (the Wave 2 survey).

Investigation of the data on respondent characteristics and the response rate yielded some interesting results that are potentially important for future epidemiologic studies. Those with the highest posttraumatic stress disorder (PTSD) scores and those in the poorest health were much more likely to be lost to followup. It has been found that PTSD is highly correlated with combat and combat with Agent Orange exposure scores, so special care must be taken in the design of study populations and the execution of epidemiologic studies to ensure that one does not miss precisely the groups one is most interested in studying. Papers addressing the survey methods and results in greater detail are listed in Appendix A.

Among the items assessed in the survey discussed above were the test-retest reliability and internal consistency of responses. Both demographic and health-outcome variables were evaluated. Earlier work by the researchers had found remarkable consistency in reports of combat experience in this cohort (Stellman SD et al., 1988a). In the present work, they found that respondents were largely consistent in self-reports of physical and mental health between the two waves of the survey. That suggests that surveys are a valid means of gathering data from this population.

#### **OUTREACH TO BLACK AND LATINO VETERANS**

Although it represents a wide range of educational and income levels, the original American Legion cohort is predominantly white, so there were concerns over the generalizability of results. Furthermore, the National Vietnam Veterans Readjustment Study (NVVRS) suggested that black and Latino veterans are particularly at risk for negative outcomes related to service in Southeast Asia (Kulka et al., 1990; Stellman SD et al, 1988a). Given the documented association between combat and Agent Orange exposure, that suggests that veterans from those groups might have been at higher risk for exposure to herbicides than white veterans (Bullman et al., 1990; Breslin et al., 1988).

The investigators consulted with the American Legion leadership and identified several posts in Ohio and Maryland that participated in the original study and had large numbers of black members. In addition, they identified posts in New Mexico and Texas with large numbers of Hispanic members and enlisted the cooperation of the American Legion in Puerto Rico.

Questions regarding perceptions of discrimination in the military were adapted from those included in the NVVRS and were added to the survey. The wording of the questions was changed so that respondents of any race or ethnic group could answer them in as much as none of the posts in the outreach was segregated by race or ethnicity and white veterans would thus be expected among the respondents. The outreach sample comprised 1,230 respondents from all the

regions listed above. Approximately 26% of the cohort identified themselves as black; about 52% as Hispanic (white). The results of the effort are described in the contractor's final report (Stellman and Stellman, 2003).

The Columbia University researchers have prepared papers intended for publication in peer-reviewed journals regarding both the enduring effect of combat exposure with respect to PTSD and the more general health and well-being effects of combat exposure among American Legion members. They assessed the validity of veteran recall in this longitudinal cohort and have found a high level of agreement between questionnaires responses from 1984 and 1998. The work is described in their final report (Stellman and Stellman, 2003).

#### STUDY OF WOMEN VETERANS

In response to the committee's request that the researchers study the generalizability of their survey and conclusions, the researchers also constructed a study of women veterans. Women shared some stressors with men but were also exposed to unique stressors related either to their occupational assignments or to their sex, and these stressors could have had a lasting effect on their physical and mental health.

The researchers were provided with an unexpected opportunity by the Vietnam Women's Memorial Foundation (VWMF)<sup>17</sup> to use its membership database to carry out an extensive study of nearly 2,500 military and civilian women who served in Vietnam. To obtain wartime location data on the respondents, a comprehensive list was developed containing military units in which large numbers of women were known to have served; a large proportion of women veterans served as nurses or in other medical roles, so many of the locations were hospitals and other medical facilities. The researchers also used focus groups to ensure that they covered subjects of relevance and concern to women veterans, and they included questions that were relevant to the experiences of nonmilitary women who served with the Red Cross and other nongovernment

<sup>&</sup>lt;sup>17</sup> VWMF (previously called the Vietnam Women's Memorial Project) is a nonprofit organization that, among other missions, is seeking to identify the military and civilian women who served during the Vietnam War, to educate the public about their role, and to facilitate research on the physiologic, psychological, and sociologic issues correlated to their service.

organizations. As a result, a number of changes were made in the American Legion questionnaire to accommodate the experiences of women in Vietnam; for example, the researchers expanded coverage of issues related to sexual harassment.

In brief, the researchers found that previously developed measures of stressors (Wolfe et al, 1993) were reliable for women who served in Vietnam and that future epidemiologic studies of women veterans need to take such measures into account when assessing health risks related to their service in Vietnam. The results are discussed in the contractor's final report (Stellman and Stellman, 2003) and will be addressed in future papers to be submitted to peer-reviewed journals.

#### **CONTINUING WORK**

In addition to the papers cited above, the researchers indicate that they have several manuscripts regarding topics related to covariates, confounders and consistency in preparation or in early stages of submission. They will elaborate on information contained in the final report and disseminate it in the peer-reviewed literature.

#### ACCOMPLISHMENTS

- Design and implementation of three studies examining self-reports of military service, physical and mental health, and other potential confounders and covariates of methodologic interest (for example, combat experience): a followup survey of a large cohort of Vietnam veterans who are members of the American Legion, a new survey of black and Latino Legionnaires who are veterans of Vietnam, and a new study of women veterans and civilians who were stationed in Vietnam during the conflict.
- An empirical evaluation of the validity of veterans' recall.

## **PROJECT 3:**

## **EVALUATION AND STANDARDIZATION OF MILITARY RECORDS FOR USE IN EPIDEMIOLOGIC STUDIES**

Military records contain information useful to epidemiologic studies that involve exposure assessment. However, few researchers are familiar with the disparate record forms produced by the various branches of the military over the course of the war or have experience working with the bureaucracy that maintains them. The aim of Project 3 was to evaluate military personnel records to determine whether data relevant to examining potential exposure to herbicides could be found and extracted. The data obtained from the records were to be compared against self-reports of military service and experience in order to evaluate the consistency between these two sources of information. A guide to using military records in epidemiologic research would also be produced.

As noted in the discussion of Project 1 tasks, the investigators encountered a series of roadblocks to accessing the nonprivate sections of the military personnel record that engendered an extended delay in obtaining military records from NPRC. Eventually, the records were retrieved by NPRC staff working at the instruction of VA. That change in the work plan delayed progress because all the record transmissions were manual and involved the reentry of data, reproofreading, and then matching the entries to an electronic database system.

About 9% of the records retrieved had missing fields or internally-inconsistent data. In addition, some records were identified in which tour of duty dates were entered but the dates associated with each unit in which the individual served were not delineated. The researchers were thus prevented from carrying out quality-control checks to ensure that they had units for a veteran's full tour and that there were no conflicts in reporting.

Concerns with the abstracted data led the researchers to conclude that a comparison of it with self-reports would be problematic and was unlikely to generate useful information. These

concerns also foreclosed reliable identification of individual veterans who might be interviewed or tested for specific biomarkers (Project 4).

The project therefore did not identify or validate a standardized means of extracting data from military personnel records for use in epidemiologic studies. The contractor did note that if subjects are available to complete and sign an SF180 (Request for Military Records), researchers could obtain copies of their personnel records. This would allow them to control how data were abstracted.

The exercise was useful, however, because it brought to light this possible impediment to veteran studies. It also yielded valuable practical experience that has been encapsulated in the contractor's report *Characterizing Exposure to Agent Orange and Other Herbicides Used in Vietnam: An Epidemiologist's Guide to Useful Military Records* (version 1.1, June 26, 2003), which appears as an appendix to its final report.

In brief, the *Guide* divides military records that document details of wartime service into two primary categories:

- 1. records that provide data on the location, mission, conditions and events of military units to which the soldiers had been assigned; and
- 2. records that provide information on the individual soldier's military assignments and experiences, and some personal pre-enlistment characteristics.

The first category of records includes Daily Journals, Situation Reports, "Operational Reports-Lessons Learned", Combat Operations After Action Reports, Command Reports, Intelligence Summaries, and Morning Reports.<sup>18</sup> These records may be found in the National Archives. They are accessible by the general public, although not always in an easily available or usable form. The second category of records—military personnel records—are housed in the National Personnel Records Center, a separate part of the National Archives. Personnel records

<sup>&</sup>lt;sup>18</sup> These are the standard Army nomenclature for the records; other services used different names to label accounts of locations and actions.

are subject to privacy restrictions and, as noted here, it may be difficult to both access them and use the data contained within them.

The *Guide* provides a table delineating available records by the branch of the service that produced them, the record's formal name, and the data available in them. It also suggests a hierarchical order in which to access them, based on the quality and level of detail of the information.

#### ACCOMPLISHMENTS

• Creation of *Characterizing Exposure to Agent Orange and Other Herbicides Used in Vietnam: An Epidemiologist's Guide to Useful Military Records,* a lessons-learned guide to the design and execution of future studies of veterans.

## **PROJECT 4:**

## BIOMARKERS OF TCDD (DIOXIN) EXPOSURE IN VIETNAM VETERANS

The focus of this project was the extent to which biologic samples from people are a useful tool in quantifying exposure to herbicides some 25 or more years earlier. The original intent was to analyze the dioxin content of samples drawn from veterans identified through E4 EOI estimates as representing a range of possible exposures, with an oversampling of heavily exposed veterans. The association between the measurements and EOI estimates was to be evaluated, as was the correspondence between these data and self-reports of herbicide exposure. The researchers intended to use a screening test based on a recombinant cell-bioassay system (CALUX) (Garrison et al., 1996; Murk et al., 1997). The assay would be run on split samples that represented an appropriate range of concentrations and of dioxin congeners to test the sensitivity and specificity of the screening method in this application.

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# It became evident during the conduct of the study that the project would not be possible, because of the difficulty of identifying specific people for study. As delineated in the discussion of Projects 1 and 3, initial attempts to use NPRC uncovered substantial barriers to data access and poor-quality data. The Columbia University researchers concluded that those problems could not be resolved soon enough to pursue this project, and—with the assent of the committee—it was abandoned.

The researchers concluded, more generally, that it was unlikely that such biomarkers as TCDD will play a major role as quantitative exposure surrogates in future studies of the health of Vietnam veterans. They stated that the most important reason is that the time that has elapsed since spraying is many multiples of the half-life of dioxin in human serum or adipose tissue; any future assays will thus almost certainly be dominated by false negatives. Additional constraints include high cost, lack of biomarkers for non-TCDD-contaminated herbicides, and the potential for selection bias. A more detailed discussion of the issue of using biomarkers in validating exposure-assessment models is in the committee's interim report (IOM, 2003).

## **PROJECT 5:**

## ANALYSIS OF IARC TISSUE SAMPLES OF SELECTED VIETNAMESE FOR DIOXIN AND DIBENZOFURAN LEVELS IN ARCHIVED ADIPOSE TISSUE

This project was intended to assess the correlation between the exposure opportunity index (the E4 EOI) developed in Project 1 and a direct measurement of dioxin in the adipose tissue of Vietnamese. It was suspected that this population might have higher body burdens of dioxin than US Vietnam veterans by virtue of having lived for long periods in areas that were sprayed.

The project was carried out in collaboration with the World Health Organization's International Agency for Research on Cancer in Lyon, France. Since 1993, IARC has been carrying out a case-control study of soft-tissue sarcoma and non-Hodgkin lymphoma in Ho Chi

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Minh City (formerly Saigon). The study is hospital-based at the Oncology Centre of Ho Chi Minh City, which treats 5,000 inpatients per year, one-third of whom are residents of Ho Chi Minh City and the remainder from elsewhere in Southern Vietnam. Steven Stellman was collaborating with the IARC researchers on this study before the start of the exposure-assessment research effort.

IARC researchers have published two papers addressing the research (Verger, et al., 1994; Kramárová, et al., 1998). Exposure-opportunity scores used in those papers were calculated by using an earlier formulation of the EOI developed by the Columbia University researchers (Stellman and Stellman, 1986).

In March 1999, the IARC study manager visited Vietnam to attempt to resolve some of the data-quality issues that had arisen in the work. Her trip report raised questions for the Columbia University researchers regarding the reliability of some subjects' residence data. The database was reviewed, and the researchers chose to analyze data on 266 subjects whose residential data appeared most reliable. Those data were geocoded,<sup>19</sup> EOIs were estimated, and the subjects were rank-ordered from highest to lowest putative exposure.

IARC shipped two batches of 25 adipose tissue samples each—chosen randomly from among the highest and lowest EOI estimates-to the Midwest Research Institute, a US analytic testing laboratory. However, the laboratory received only one batch; the other was lost in transit and could not be relocated by the shipper. On arrival, sample identifications were verified against the chain of custody and stored. Standard laboratory quality control and sample blinding were applied. Dioxin congeners in all samples were found to be below the limit of detection or at background concentrations.

The residential coding problems and the preliminary experience with dioxin testing suggested to the researchers that further testing of samples from the IARC archive was unlikely to generate informative results. In consultation with the committee, they chose to end the project.

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<sup>&</sup>lt;sup>19</sup> That is, the location in geographic space was converted into computer-readable form.

#### ACCOMPLISHMENT

 Analysis, in collaboration with IARC and the Midwest Research Institute, of tissue samples from Vietnam residents and comparison of the results with EOIs calculated for the subjects.

## FINDINGS, CONCLUSIONS, AND RECOMMENDATIONS

Over the life of the study, the Columbia University researchers encountered unexpected sources of data and barriers to data access. The opportunities and challenges shaped the execution of their initial proposal for research. In consultation with the committee, tasks were expanded, modified, and in some cases abandoned to take advantage of some circumstances and adapt to the realities of others. However, the underlying goal of the work— creation of a herbicide-exposure assessment model for use in epidemiologic studies of Vietnam veterans— remained the same.

The committee finds, on the basis of its oversight and evaluation of the work, that Jeanne Mager Stellman, principal investigator, and her research colleagues and collaborators have fulfilled the study goals set forth in the request for proposals (IOM, 1997) and have thus:

- Developed and documented a detailed method for retrospectively characterizing the exposure of Vietnam veterans to the major herbicides used by the military in Vietnam—2,4-D; 2,4,5-T; cacodylic acid; and picloram—and the trace contaminants TCDD and its congeners.
- Demonstrated the feasibility and appropriateness of the proposed method in sufficient detail to permit the
  assessment of its potential for use in the conduct of epidemiologic studies.

The committee therefore concludes that that the Columbia University researchers have satisfactorily completed the research project as defined in their proposal and modified in consultation with the committee.

The committee also affirms all the findings and conclusions reached in its interim report released in April 2003:

- The contractor has developed databases of wartime spraying and accidental dispersion of herbicides, of troop locations and movements, and of land features and soil typology.
- The contractor has developed an effective exposure assessment tool to assign a metric—the E4 exposure-opportunity index (EOI)—for herbicide exposure that is based on proximity to spraying in space and time and on the amount and agent sprayed.
- The range of calculated EOIs and information gathered to date on troop locations is sufficient to demonstrate the feasibility of future epidemiologic studies. Additional location data on troops not included in present databases appear to be available at the National Archives for abstraction and use by researchers and other interested parties in future studies.
- Given current knowledge and available data, the contractor has adequately demonstrated that the draft model is a valid means of assessing wartime herbicide exposure of Vietnam veterans.

On the basis of those findings, the committee concludes that a valid exposure-reconstruction model for wartime herbicide exposures of US veterans of Vietnam is feasible. It therefore continues to recommend that the Department of Veterans Affairs and other government agencies facilitate additional epidemiologic studies of veterans by nongovernment organizations and independent researchers.

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## Appendix A

## Papers, Reports, and Other Materials Prepared Under the Contract with the Columbia University Researchers

#### PUBLISHED PAPERS

- Stellman JM, Stellman SD, Christian R, Weber T, Tomasallo, C. 2003. The extent and patterns of usage of Agent Orange and other herbicides in Vietnam. Nature 422(6933):681–687.
- Stellman SD, Stellman JM, Weber T, Tomasallo C, Stellman AB, Christian R. 2003. A geographic information system for characterizing exposure to Agent Orange and other herbicides in Vietnam. Environmental Health Perspectives. 111(3):321–328.

#### MANUSCRIPTS IN-PRESS OR ACCEPTED FOR PUBLICATION

- Koenen KC, Stellman JM, Stellman SD, Sommer JF Jr. 2003. Risk factors for course of PTSD among Vietnam veterans: a 14-year follow-up of American Legionnaires. Journal of Consulting and Clinical Psychology 71 (6):[in press].
- Stellman SD, Stellman JM. 2003 Exposure opportunity models for Agent Orange, dioxin, and other military herbicides used in Vietnam, 1961–1971. Journal of Exposure Analysis and Environmental Epidemiology (accepted for publication).
- Koenen KC, Stellman JM, Stellman SD, Sommer JF. Persistence of posttraumatic stress disorder symptoms among Vietnam Veterans. American Journal of Psychiatry (revision submitted)
  - Additional papers addressing topics discussed in the Contractor's Final Report are under preparation.

#### **OTHER REPORTS**

- Stellman JM, Stellman SD. 2003. Contractor's Final Report: Characterizing Exposure of Veterans to Agent Orange and Other Herbicides in Vietnam. Submitted to the National Academy of Sciences, Institute of Medicine, in fulfillment of Subcontract VA-5124–98–0019, June 30, 2003.
- Characterizing Exposure to Agent Orange and other Herbicides Used in Vietnam: An Epidemiologist's Guide to Useful Military Records Version 1.1, June 26, 2003. 13 pages, (available as Appendix C of the Contractor's Final Report...).

#### PRESENTATIONS (PARTIAL LISTING)

- Stellman JM. Agent Orange: geographical distribution, fate and transport. NIEHS Ad Hoc Panel, Monterey, CA. August 18, 2000
- Stellman SD, Koenen K, Stellman JM. Enduring consequences of exposure to combat in Vietnam. American College of Epidemiology, Atlanta, GA. September 20, 2000.
- Stellman SD, Stellman JM, Christian R. Modeling veterans' exposure opportunity for herbicides in Vietnam using expanded and cleaned HERBS data files. Symposium on assessing military exposures: methods And lessons learned from the Vietnam and Gulf Wars. International Society for Exposure Assessment, Monterey, CA. October 20, 2000.
- Koenen K, Stellman JM, Stellman SD, Sommer JF Jr. Social stress factors: essential components of military environmental modeling. Symposium on assessing military Exposures: Methods and lessons learned from the Vietnam and Gulf Wars. International Society for Exposure Assessment, Monterey, CA. October 20, 2000.
- Koenen KC, Stellman JM, Stellman SD, Sommer JF. Course and risk factors for PTSD in Vietnam veterans. 16th Annual Meeting of the International Society of Traumatic Stress Studies, San Antonio, Texas. November, 2000.

#### APPENDIX A

- Stellman JM, Stellman SD, Koenen KC, Sommer JF. Persisting social and behavioral effects of exposure to combat in Vietnam veterans. 16th Annual Meeting of the International Society of Traumatic Stress Studies, San Antonio, Texas. November, 2000.
- Stellman JM, Stellman SD, Koenen KC, Sommer JF. Experiences of Vietnam era veterans with VA health care facilities. 16th Annual Meeting of the International Society of Traumatic Stress Studies, San Antonio, Texas. November, 2000.
- Stellman SD, Stellman JM, Koenen KC, Sommer JF Jr. Long-term smoking patterns in relation to military combat in a cohort of Vietnam veterans. American Society of Preventive Oncology, New York. March 12, 2001.
- Stellman JM, Stellman SD, Christian R, Weber T. A comprehensive view of herbicide spray projects in the Vietnam War. International Society of Exposure Analysis, Charleston, SC. November 5, 2001.
- Stellman JM, Stellman SD, Christian R, Weber T. Influence of soil-specific dioxin decay rates on estimates of exposure to residual phenoxy herbicides in Vietnam. International Society of Exposure Analysis, Charleston, SC. November 5, 2001. Also presented at: US-Vietnam Scientific Conference on Agent Orange/Dioxin, Hanoi, Vietnam. March 3–6, 2002.
- Stellman JM, Stellman SD, Christian R, Weber T, Tomasallo C, Stellman A. The extent and usage patterns of military herbicides in Vietnam, 1961–1971: a reanalysis based on examination of newly analyzed primary source materials. US-Vietnam Scientific Conference on Agent Orange/Dioxin, Hanoi, Vietnam. March 3–6, 2002.
- Stellman JM, Stellman SD, Christian R, Tomasallo C, Weber T. Visualization of US Army military unit locations in relation to herbicide spraying during the Vietnam War. International Society of Exposure Analysis, Vancouver, BC. August, 2002.
- Stellman JM. Panel Presentation. Ecological and Health Effects of the Vietnam War Symposium . Yale University School of Nursing, New Haven. September 13–15, 2002.

#### SOFTWARE AND ASSOCIATED DOCUMENTATION

- Herbicide Exposure Assessment Vietnam (HEA-V) software. Version 1.0.2. April 25, 2003.
- HEA–V Manual (.PDF file). PDF dated June 24, 2003. 29 pages.
- Analyzing the HERBS table (.PDF file) PDF dated June 24, 2003. 6 pages.
- Database Used by the Herbicide Exposure Program (.PDF file) date June 24, 2003. 6 pages.

#### DATABASES AND ASSOCIATED DOCUMENTATION

- Herbicidal spraying records (HERBS table in HEA.mdb in HEA-V software)
- Modeled exposure opportunity scores (EXPOSURE\_MASTER contained in HEA.mdb in HEA-V software)
- Spray targets (TARGETS.MDB)
- Comprehensive Lists and coding system of military units assigned to Vietnam (UICLISTS.MDB)
- Locations of US Army combat support and support military units (STABLE UNITS.MDB)
- Digitized Soil Typology Map of Vietnam (SOIL.MDB)
- Locations of Army combat battalions operating in III Corps Tactical Zone, Vietnam, 1967–1969 (BNTRAK.MDB)

#### WEBSITES AND ASSOCIATED DOCUMENTATION

- AO PARTICIPATORY RESEARCH WEBSITE.HTM (draft—for validating military locations through prospective veterans' participatory research project) (available from the contractor)
- Systems Requirements Specifications—Agent Orange-Vietnam Website. Last revised June 30, 2003. 9 pages, (available as Appendix D of the Contractor's Final Report...).

#### SURVEY INSTRUMENTS

- American Legion—Columbia University Vietnam Veterans Study ("Wave 2" survey) (available from the contractor)
- La Legión Americana—La Universidad de Columbia Estudio sobre los Veteranos de Vietnam ("Wave 2" survey, Spanish) (available from the contractor)
- Women in the Vietnam Era (available from the contractor)

## **Committee and Staff Biographies**

## COMMITTEE ON THE ASSESSMENT OF WARTIME EXPOSURE TO HERBICIDES IN VIETNAM

**David G.Hoel,** PhD (Chair), is Distinguished University Professor at the Medical University of South Carolina. Dr. Hoel received his AB in mathematics and statistics from the University of California, Berkeley and his PhD from the University of North Carolina at Chapel Hill. He is the author or coauthor of over 150 journal articles and coeditor of several books and journals. Dr. Hoel serves on a variety of national advisory committees and panels, including National Research Council and Institute of Medicine (IOM) committees and the Environmental Protection Agency's Science Advisory Board. He is a member of IOM, a National Associate of the National Academy of Sciences, and a Fellow of the American Association for the Advancement of Science. Before joining the faculty at the Medical University, Dr. Hoel was director of the division of the National Institute of Environmental Health Sciences with responsibility for the institute's program in biostatistics, epidemiology, and biochemical and toxicologic risk assessment.

**Loren D.Koller,** DVM, PhD, served in academe for nearly 30 years, the last 16 as professor in the College of Veterinary Medicine of Oregon State University, Corvallis. For 10 of those years, he served as dean of the college. He operates a business in environmental health and toxicology. Dr. Koller pioneered the discipline now known as immunotoxicology with a research focus also in toxicology, pathology, carcinogenesis, and risk assessment. He served for 6 years as a member of the National Research Council Committee on Toxicology. He also served as a member of the Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides (third biennial update).

**S.Katharine Hammond,** PhD, CIH, is professor of environmental health sciences in the School of Public Health, University of California, Berkeley. Dr. Hammond is a certified industrial hygienist, and her research is focused on exposure characterization. She previously served on the Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides.

**Dana Loomis,** PhD, is professor of epidemiology and environmental sciences in the School of Public Health, University of North Carolina at Chapel Hill. His work centers on environmental and occupational epidemiology, and he has published extensively on the characterization of exposure to and risk posed by nonionizing radiation and other physical and chemical agents.

**David J.Tollerud,** MD, MPH, is professor and chair of the Department of Environmental and Occupational Health Sciences, School of Public Health and Information Sciences, University of

Louisville, Kentucky. He has extensive clinical training, with specialty-board certifications in internal medicine, pulmonary and critical-care medicine, and occupational medicine. Dr. Tollerud has research expertise in environmental and occupational health, epidemiology, and immunology and consulting experience in occupational and environmental respiratory disease, medical surveillance, and workplace-injury prevention programs. He has served on a number of other Institute of Medicine committees since 1992. He served in leadership roles on committees responsible for the original (1994) and updated (1996 and 1998) Agent Orange reports.

**Thomas Smith,** PhD, is professor of industrial hygiene in the Department of Environmental Health at the Harvard School of Public Health and director of the school's industrial-hygiene program. Dr. Smith's primary research interest is in the characterization of environmental exposures for studies of health effects. He has developed a toxicokinetic modeling approach for integrating the health effects of toxic substances into epidemiologic studies.

**Lauren Zeise,** PhD, is chief of the Reproductive and Cancer Hazard Assessment Section in the Office of Environmental Health Hazard Assessment of the California Environmental Protection Agency. Dr. Zeise is a toxicologist who has published extensively in exposure assessment and cancer risk assessment.

#### STAFF

**Rose Marie Martinez,** ScD, is director of the Institute of Medicine (IOM) Board on Health Promotion and Disease Prevention. Before joining IOM, she was a senior health researcher at Mathematica Policy Research, where she conducted research on the impact of health-system change on the public-health infrastructure, access to care for vulnerable populations, managed care, and the health-care workforce. Dr. Martinez is a former assistant director for health financing and policy in the US General Accounting Office, where she directed evaluations and policy analysis in national and public-health issues. Dr. Martinez received her doctorate from the Johns Hopkins School of Hygiene and Public Health.

**Kathleen Stratton,** PhD, was acting director of the Board on Health Promotion and Disease Prevention of the Institute of Medicine (IOM) from 1997 to 1999. She received a BA in natural sciences from Johns Hopkins University and a PhD from the University of Maryland at Baltimore. After completing a postdoctoral fellowship in the neuropharmacology of phencyclidine compounds at the University of Maryland School of Medicine, she joined the staff of IOM in 1990. Dr. Stratton has worked on projects in environmental risk assessment, neurotoxicology, the organization of research and services in the Public Health Service, vaccine safety, fetal alcohol syndrome, and vaccine development. She has had primary responsibility for the reports *Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality; DPT Vaccine and Chronic Nervous System Dysfunction; Fetal* 

Alcohol Syndrome: Diagnosis, Epidemiology, Prevention, and Treatment; and Vaccines for the 21st Century: An Analytic Tool for Prioritization.

**David A.Butler,** PhD, is senior program officer in the Institute of Medicine (IOM) Board on Health Promotion and Disease Prevention. He received a BS and an MS in engineering from the University of Rochester and a PhD in public-policy analysis from Carnegie-Mellon University. Before joining IOM, Dr. Butler served as an analyst for the US Congress Office of Technology Assessment and was a research associate in the Department of Environmental Health at the Harvard School of Public Health. He has directed several National Academies studies on environmental-health and risk-assessment topics, including studies that resulted in the reports *Veterans and Agent Orange: Update 1998; Veterans and Agent Orange: Update 2000; Clearing the Air: Asthma and Indoor Air Exposures;* and Escherichia coli *O157:H7 in Ground Beef: Review of a Risk Assessment.* He is directing a study on damp indoor spaces and health—a review of the literature regarding the health consequences of mold and related microbial exposures.

Jennifer A.Cohen is a research associate in the Institute of Medicine (IOM) Board on Health Promotion and Disease Prevention. She received her undergraduate degree in art history from the University of Maryland. She has also been involved with the IOM committees that produced *Clearing the Air: Asthma and Indoor Air Exposures;* Escherichia coli 0157:H7 in Ground Beef: Review of a Risk Assessment; Organ Procurement and Transplantation; Veterans and Agent Orange: Herbicide/Dioxin Exposure and Type 2 Diabetes; Veterans and Agent Orange: Herbicide/Dioxin Exposure and Acute Myelogenous Leukemia in the Children of Vietnam Veterans; and Veterans and Agent Orange: Update 2002.

**Anna B.Staton,** MPA, was a research assistant in the Institute of Medicine (IOM) Board on Health Promotion and Disease Prevention through October 2002. Ms. Staton joined IOM in December 1999 and worked with the committees that produced *No Time to Lose: Getting More from HIV Prevention; Veterans and Agent Orange: Update 2000;* and Escherichia coli O157:H7 *in Ground Beef: Review of a Risk Assessment.* Before joining IOM, she worked at the Baltimore Women's Health Study. Ms. Staton graduated from the University of Maryland Baltimore County with a BA in visual arts (major) and women's studies (minor). She earned her MPA in nonprofit management at the George Washington University School of Business and Public Management.

**Elizabeth J.Albrigo** is a project assistant in the Institute of Medicine (IOM) Board on Health Promotion and Disease Prevention. She received her undergraduate degree in psychology from the Virginia Polytechnic Institute and State University. She is involved with the IOM Committee on Damp Indoor Spaces and Health. She also helped to facilitate the production of the reports *Veterans and Agent Orange: Update 2002; Veterans and Agent Orange: Herbicide/Dioxin Exposure and Acute Myelogenous Leukemia in the Children of Vietnam Veterans;* and Escherichia coli O157:H7 *in Ground Beef: Review of a Risk Assessment.* 

Joe A.Esparza is a project assistant in the Institute of Medicine (IOM) Board on Health Promotion and Disease Prevention. He attended Columbia University, where he studied biochemistry. Before joining IOM, he worked with the Board on Agriculture and Natural Resources (BANR) of the National Research Council. While with BANR, he was involved with the committees that produced *Frontiers in Agricultural Research: Food, Health, Environment, and Communities; Air Emissions from Animal Feeding Operations: Current Knowledge, Future Needs;* and Publicly Funded Agricultural Research and the Changing Structure of US Agriculture. Att IOM, he assisted on the report Veterans and Agent Orange: Update 2002.

James A.Bowers through July 2000 was a project assistant and, later, research assistant in the Institute of Medicine (IOM) Board on Health Promotion and Disease Prevention. He received his undergraduate degree in environmental studies from Binghamton University. He has also been involved with the IOM committees that produced *Characterizing Exposure of Veterans to Agent Orange and Other Herbicides Used in Vietnam;* Adequacy of the Comprehensive Clinical Evaluation Program: Nerve Agents; Clearing the Air: Asthma and Indoor Air Exposures; and Veterans and Agent Orange: Herbicide/Dioxin Exposure and Type 2 Diabetes.