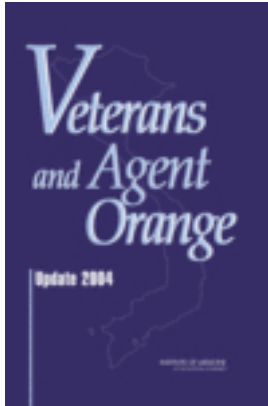


Free Executive Summary

Veterans and Agent Orange: Update 2004



Committee to Review the Health Effects in Vietnam
Veterans of Exposure to Herbicides(Fifth Biennial
Update)

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Executive Summary

From 1962 to 1971, US military forces sprayed 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 grasses and bushes from the perimeters of US base camps and outlying fire-support bases. Mixtures of 2,4-dichlorophenoxyacetic acid (2,4-D), 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), picloram, and cacodylic acid made up the majority of the herbicides sprayed. The herbicide mixtures used were named according to the color of an identification band painted on the storage drums; one main chemical mixture sprayed was Agent Orange (a 50:50 mixture of 2,4-D and 2,4,5-T). At the time of the spraying, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD, one form of dioxin) was an unintended contaminant from the production of 2,4,5-T and was present in Agent Orange and some other formulations sprayed in Vietnam.

In 1991, because of continuing uncertainty about the long-term health effects on Vietnam veterans of the herbicides sprayed, Congress passed Public Law 102-4 (PL 102-4), the Agent Orange Act of 1991. That legislation directed the Secretary of Veterans Affairs to ask the National Academy of Sciences (NAS) to perform a comprehensive evaluation of scientific and medical information regarding the health effects of exposure to Agent Orange, other herbicides used in Vietnam, and the various components of those herbicides, including TCDD. The Secretary was also to ask that NAS conduct updates at least every 2 years for 10 years from the date of the first report to review newly available literature and draw conclusions from the overall evidence. PL 107-103, the Veterans Education and Benefits Expansion Act of 2001, extended the updates until 2014.

In response to the request, the Institute of Medicine (IOM) of NAS convened a committee, whose conclusions IOM published in 1994 in *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam* (hereafter referred to as VAO). The work of later committees resulted in the publication of biennial updates (*Update 1996*, *Update 1998*, *Update 2000*, and *Update 2002*) and in focused reports on the scientific evidence regarding type 2 diabetes (*Type 2 Diabetes*), acute myelogenous leukemia in children (*Acute Myelogenous Leukemia*), and the latency period for respiratory cancer (*Respiratory Cancer*). This report is the fifth review of recently published scientific evidence regarding associations between health outcomes and exposure to TCDD and other chemical compounds in herbicides used in Vietnam.

CHARGE TO THE COMMITTEE

In accordance with PL 102-4, the Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides (Fifth Biennial Update) was asked to “determine (to the extent that available scientific data permit meaningful determinations)” the following regarding associations between specific health outcomes and exposure to TCDD and other chemical compounds in herbicides:

- A) whether a statistical association with herbicide exposure exists, taking into account the strength of the scientific evidence and the appropriateness of the statistical and epidemiological methods used to detect the association;
- B) the increased risk of the disease among those exposed to herbicides during service in the Republic of Vietnam during the Vietnam era; and
- C) whether there exists a plausible biological mechanism or other evidence of a causal relationship between herbicide exposure and the disease.

In conducting its study, this committee operated independently of the Department of Veterans Affairs (VA) and other government agencies. The committee was not asked to and did not make judgments regarding specific cases in which individual Vietnam veterans have claimed injury from herbicide exposure. This report provides scientific information for the Secretary of Veterans Affairs to consider as VA exercises its responsibilities to Vietnam veterans. The committee was not charged to focus on broader issues, such as the potential costs of compensation for veterans or policies regarding such compensation.

COMMITTEE'S APPROACH TO ITS CHARGE

To fulfill its charge of assessing whether specific human health effects are associated with exposure to at least one of the herbicides or TCDD, the committee concentrated its review on epidemiologic studies. The committee also consid-

ered controlled laboratory investigations that provide information on whether it is biologically plausible to suppose that the compounds of interest might be related to a given effect. The committee began its evaluation presuming neither the presence nor the absence of associations.

To obtain all information potentially relevant to the evaluation of health effects related to herbicide exposure, the present committee, in addition to reviewing studies of Vietnam veterans, reviewed studies of other groups potentially exposed to the constituents of the herbicides used in Vietnam (2,4-D, 2,4,5-T, TCDD, cacodylic acid, and picloram). Those groups include chemical production and agricultural workers, people possibly exposed heavily to herbicides or dioxins as a result of residing near the site of an unintended release or areas used to dispose of toxic waste, and residents of Vietnam.

PL 102-4 did not provide a list of specific diseases and conditions suspected of being associated with herbicide exposure. Such a list was developed in VAO on the basis of diseases and conditions that had been mentioned in the scientific literature or in other documents identified through extensive literature searches. The VAO list has been augmented in response to developments in the literature, requests by VA, and concerns of Vietnam veterans.

The information that the present committee reviewed was identified through a comprehensive search of relevant databases, including databases covering biologic, medical, toxicologic, chemical, historical, and regulatory information. Literature identification continued through June 1, 2004. More than 3,000 potentially relevant studies were identified in those searches, and more than 550 were reviewed. Additional information came from veterans and other interested persons who testified at public hearings and offered written submissions.

To determine whether there is an association between exposure and health outcome, epidemiologists estimate the magnitude of an appropriate measure (such as the relative risk or the odds ratio) that describes the relationship between exposure and disease in a defined population or group. In evaluating the strength of the evidence linking herbicide exposure with a particular outcome, the committee considered whether such estimates of risk might be incorrect (the result of confounding, chance, or bias from errors in selection and measurement) or might accurately represent true associations. It has been the practice of all VAO committees to evaluate all studies according to the same criteria whether or not their subjects are Vietnam veterans and then to weight findings of similar strength and validity equivalently when drawing conclusions. The committee recognizes that an absolute conclusion about the absence of association might never be attained, because, as is generally the case in science, studies of health outcomes after herbicide exposure cannot demonstrate that a purported effect is impossible, only that it is statistically improbable.

EVIDENCE REVIEWED BY THE COMMITTEE

Toxicology

Since *Update 2002*, several experimental studies have been published on the chemical compounds of interest. Some examine particular disease outcomes in animals after exposure to the compounds; others focus more on the mechanism or mode of action by which effects are elicited in cells, tissues, or whole animals. Despite extensive study, the exact mechanisms by which the compounds exert their effects are still unclear. Toxicologic information on disease outcomes in animals can, however, support an association seen in an epidemiologic study by providing evidence that an effect is biologically plausible.

Many health effects have been seen in animals after exposure to TCDD or to the herbicides used in Vietnam. Although animal experiments demonstrate that some of the compounds (alone or in conjunction with other treatments) can cause specific cancers, none of the compounds of interest has been shown to act directly by mutating DNA. TCDD is thought to be the most toxic of the compounds, and recent experimental research has shown a great deal about the cellular effects of TCDD. All of the data are consistent with the hypothesis that those effects are mediated by the ability of TCDD to bind a cellular protein, the aryl hydrocarbon receptor, to modulate cell-signaling pathways. However, the exact mechanisms by which those events cause the various effects seen in humans and animals remains unknown.

Relevant effects observed in experimental animals, and their relevance to human health outcomes, are discussed as part of the biologic plausibility section for each outcome.

Exposure Assessment

Assessment of exposure to a toxic substance is an important element in determining whether specific health outcomes are linked to that substance. Under ideal circumstances exposure assessment would quantify the concentration of a substance at its site of action; in human studies that is rarely possible. Exposure estimates, therefore, should be viewed as surrogates for the actual dose.

Recent studies of Vietnam veterans, including those of the Ranch Hand and Army Chemical Corps cohorts, have used the measurement of serum blood levels of TCDD as the best available estimator of historical exposures to Agent Orange. This approach has also been used to study health effects in the Seveso population in Italy. Since *Update 2002*, a study of Korean Vietnam veterans developed an exposure index based on duration of service, troop location relative to herbicide spraying, and individual activity data from questionnaires. The investigators attempted to validate this exposure index with serum blood levels of TCDD, but samples were pooled within presumed exposure categories and only a narrow

range of TCDD concentrations was measured across these categories. All concentrations were less than one picogram TCDD per gram of serum (lipid-adjusted).

In 1997, a committee convened by IOM on behalf of the VA requested research proposals designed to reconstruct exposures of US veterans who served as ground troops in Vietnam. This request resulted in a project called “Characterizing Exposure of Veterans to Agent Orange and Other Herbicides in Vietnam”. Since *Update 2002*, a final report of this work has been published by IOM. This report presents an “exposure-opportunity index” based on records of herbicide spraying and troop movements. The IOM committee’s review of the report concluded that the exposure-opportunity index holds promise for epidemiologic investigations of this population.

Epidemiology

The health outcomes reviewed by the committee are categorized as cancer, reproductive and developmental effects, neurologic disorders, and other health effects. This section briefly summarizes the relevant epidemiologic studies published on those health outcomes since *Update 2002*. In the health outcomes chapters, this new literature was evaluated and considered in the context of the previous reviews to derive comprehensive updated conclusions integrating the entire body of information.

Cancer

Since *Update 2002*, several cohort studies were published that investigated multiple cancer outcomes. Cancer incidence and mortality were compared between the Ranch Hand cohort and the Air Force control cohort of Vietnam veterans; an excess incidence of melanoma was observed in some subgroups of the Ranch Hand Air Force veterans, but analyses did not establish this outcome in the entire cohort, and an increase in the incidence of, but not mortality from, prostate cancer was observed. A pilot case-control study of prostate cancer among Vietnam-era veterans found an elevated, but non-significant increase associated with reported Agent Orange exposure. An update of a cohort of Dow Chemical Company workers and a study of pesticide applicators in Iowa and North Carolina both also found an increase in prostate cancer, while a cancer mortality study of Dutch herbicide applicators showed only an increase in “all skin cancers.” An ecological study of Japanese municipalities with and without waste incinerators had negative findings for cancer mortality overall. Case-control studies of soft-tissue sarcoma in Italian and Finnish populations had opposing results concerning residential exposure to the chemicals of interest. No other increases in cancer incidence or mortality were reported in association with the chemicals of interest.

Reproductive and Developmental Effects

Two environmental studies addressed birth defects: One examined proximity to municipal solid waste incinerators in France, and the other reviewed county-wide use of agricultural pesticides in four US states. Neither presented additional information on the occurrence of spina bifida. The French study reported associations with facial clefts and renal abnormalities, and the US study presented results for circulatory and respiratory anomalies; the exposure assessment in each study was ecological. One relatively small study of time-to-conception presented results that suggested a connection with infertility, but the assessment of herbicide exposure was nonspecific. Two ecological studies addressed outcomes that are tangentially related to fertility (sperm quality and regularity of menstrual cycling). One study investigating spontaneous abortion among women exposed during the Seveso accident reported no relationship with serum TCDD concentrations. Studies of birth weight and gestational duration for the pregnancies of Polish farm women and of Seveso residents presented data suggestive of a connection, but compromised by design limitations. A single study of cancers among the offspring of pesticide applicators presented indeterminate results for this quite nonspecific outcome category. One new study of pesticide production workers reported a suggestion of a reduced sex ratio (fewer-than-expected male offspring) for the children of male, but not female, workers.

Neurologic Disorders

Since *Update 2002*, cognitive outcomes have been investigated in a study of elderly residents of Bordeaux, France; in an updated cohort of Czech workers; in an ecological study of a community adjacent to a wood treatment plant; and in two studies of Vietnam veterans, one of US Ranch Hands and one of Korean veterans. Only the Bordeaux study reported an increase in cognitive disorders, but it did not implicate the compounds of interest to this report.

Three publications examined possible associations with Parkinson's disease. Although some associations were reported, the limitations of those studies (particularly the lack of information on the compounds of interest) do not permit conclusive interpretation.

One study reported a higher rate of peripheral neuropathy among Korean Vietnam veterans than was found among veterans who did not serve in Vietnam, but the results were unrelated to estimated dioxin exposures. Although the committee carefully reviewed the available literature on peripheral neuropathy, neither the new report nor the previous epidemiologic literature convincingly indicates an association between exposure and persistent neuropathy in veterans who do not have diabetes. Peripheral neuropathy is seen secondary to diabetes, for which an association with the compounds of interest has been noted. It is not possible to determine from the available literature whether observed increases in peripheral neuropathy are primary effects from dioxin exposure or secondary to diabetes.

Other Health Effects

Several studies have investigated health effects other than those classified as cancer, reproductive and developmental effects, or neurological disorders. The incidence of chloracne; increases in uroporphyrins; changes in immune parameters; and increased hypertension, valvular heart disease, and ischemic heart disease were observed to be higher in Korean Vietnam veterans who served in Vietnam than in those who did not. The study's limitations, however, do not permit conclusions to be drawn based only on its data. Changes in immune parameters also were seen in studies of residents of Seveso. Some respiratory effects were suggested by a study of people living near a wood treatment plant, but there was no evidence that those effects were specifically related to the compounds of interest. Several other studies presented evidence of additional effects, but none was of high enough quality or sufficiently relevant to the compounds of interest to affect the conclusions of previous reviews.

COMMITTEE'S CONCLUSIONS

Health Outcomes

The present committee weighed the strengths and limitations of the epidemiologic evidence reviewed in this report and in previous *Veterans and Agent Orange* reports. Its conclusions were drawn from the new evidence in the context of the entire body of literature. It assigned each health outcome to one of four categories on the basis of the evidence. Table ES-1 defines these categories and gives criteria for assigning a health outcome to each of them. Based on the committee's evaluation of occupational, environmental, and veterans studies, this table also lists the relative weight of evidence for association between particular health outcomes and exposure to the herbicides that were used in Vietnam or to any of their components or contaminants (with no intention of specifying a particular chemical). After careful consideration, the present committee did not change the categorization of health outcomes in this report from *Update 2002*. It did, however, modify the previous terminology of "acute and subacute" transient peripheral neuropathy to "early-onset" transient peripheral neuropathy as being more reflective of the intended properties of the condition's symptoms, rather than suggesting the conditions of exposure.

As mandated by PL 102-4, the distinctions among categories are based on statistical association, not on causality. The committee was directed to review the scientific data, not to recommend VA policy; therefore, conclusions reported in Table ES-1 are not intended to imply or suggest policy decisions. The conclusions are related to associations between exposure and outcomes in human populations, not to the likelihood that any individual's health problem is associated with or caused by the herbicides in question.

TABLE ES-1 Summary of Findings in Occupational, Environmental, and Veterans' Studies Regarding the Association Between Specific Health Outcomes and Exposure to Herbicides^a

Sufficient Evidence of an Association

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

- Chronic lymphocytic leukemia (CLL)
- Soft-tissue sarcoma
- Non-Hodgkin's lymphoma
- Hodgkin's disease
- Chloracne

Limited or Suggestive Evidence of an Association

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

- Respiratory cancer (lung and bronchus, larynx, and trachea)
- Prostate cancer
- Multiple myeloma
- Early-onset transient peripheral neuropathy^b
- Porphyria cutanea tarda
- Type 2 diabetes (mellitis)
- Spina bifida in offspring of exposed individuals

Inadequate or Insufficient Evidence to Determine Whether an Association Exists

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

- Hepatobiliary cancer
- Oral, nasal, and pharyngeal cancer
- Bone and joint cancer
- Skin cancers (melanoma, basal cell, and squamous cell)
- Breast cancer
- Female reproductive cancer (cervix, uterus, ovary)
- Testicular cancer
- Urinary bladder cancer
- Renal cancer
- Leukemia (other than CLL)
- Abnormal sperm characteristics and infertility
- Spontaneous abortion
- Neonatal or infant death and stillbirth in offspring of exposed individuals

TABLE ES-1 *Continued*

Low birthweight in offspring of exposed individuals
Birth defects (other than spina bifida) in offspring of exposed individuals
Childhood cancer (including acute myelogenous leukemia) in offspring of exposed individuals
Neurobehavioral disorders (cognitive and neuropsychiatric)
Movement disorders, including Parkinson's disease and amyotrophic lateral sclerosis (ALS)
Chronic peripheral nervous system disorders
Respiratory disorders
Gastrointestinal, metabolic, and digestive disorders (changes in liver enzymes, lipid abnormalities, ulcers)
Immune system disorders (immune suppression, autoimmunity)
Circulatory disorders
AL amyloidosis
Endometriosis
Effects on thyroid homeostasis

Limited or Suggestive Evidence of No Association

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

Gastrointestinal tumors (esophagus, stomach, pancreas, colon, rectum)
Brain tumors

^a *Herbicides* indicates the following chemicals of interest: 2,4-dichlorophenoxyacetic acid (2,4-D), 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and its contaminant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD, or dioxin), cacodylic acid, and picloram. The evidence regarding association was drawn from occupational, environmental, and veterans studies in which individuals were exposed to the herbicides used in Vietnam, to their components, or to their contaminants.

^b For clarity, this committee has changed the nomenclature from "acute and subacute" to "early-onset" transient peripheral neuropathy.

Risk in Vietnam Veterans

There have been numerous health studies of Vietnam veterans, but most have been hampered by relatively poor measures of exposure to herbicides or TCDD and by other methodologic problems. In light of those problems, many conclusions regarding associations between exposure to the chemicals of interest and disease are based on studies of people exposed in various occupational and environmental settings rather than on studies of Vietnam veterans. The committee believes that there is sufficient evidence to reach general conclusions about asso-

ciations between herbicide exposure and the health outcomes, but the lack of adequate exposure data on Vietnam veterans themselves makes it difficult to estimate the degree of increased risk of disease in Vietnam veterans, as a group or individually. Thus, quantification of the actual risks experienced by veterans exposed to the compounds of interest during the Vietnam War is not possible.

Because of those limitations, only general assertions can be made about risks to Vietnam veterans, depending upon which category of the association has been attributed to a given health outcome. When there is “limited or suggestive evidence of *no* association” between herbicide exposure and a health outcome, the evidence suggests that there is no increased risk of the outcome among Vietnam veterans that is attributable to exposure to the compounds of interest, but that conclusion is limited to the conditions, exposures, and lengths of observation covered by the studies reviewed by the committee. Even qualitative estimates are not possible when there is “inadequate or insufficient” evidence of an association. For outcomes categorized as having “sufficient” or “limited or suggestive” evidence of an association with herbicide exposure, the lack of exposure information for Vietnam veterans prevents calculation of precise risk estimates.

RESEARCH RECOMMENDATIONS

IOM has been asked to make recommendations concerning the need, if any, for additional scientific studies to resolve continuing scientific uncertainties about the health effects of the herbicides and their contaminants used in Vietnam.

Great strides have been made over the past several years in understanding the health effects of exposure to TCDD and to the herbicides used in Vietnam and in elucidating the mechanisms that underlie those effects, but there are still important gaps in our knowledge. On the basis of its review of the epidemiologic evidence and consideration of the quality of exposure information available in existing studies, especially of Vietnam veterans, the present committee concludes that continuation of epidemiologic studies of veterans could yield valuable information.

Another population that has been understudied is the Vietnamese, including those who served in the military during the war and civilians. Anecdotal evidence and studies published in non-English-language journals suggest an array of long-term health effects that could potentially be related to the chemicals used by US troops in Vietnam. Although the explicit purpose of the newly established exposure database was to determine exposures of US service personnel who spent time in Vietnam, the possibility of using it to identify study populations among Vietnamese residents should be considered.

Veterans and Agent Orange

Update 2004

Committee to Review the Health Effects in
Vietnam Veterans of Exposure to Herbicides
(Fifth Biennial Update)

Board on Health Promotion and Disease Prevention

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*“Knowing is not enough; we must apply.
Willing is not enough; we must do.”*

—Goethe



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**COMMITTEE TO REVIEW THE HEALTH EFFECTS IN
VIETNAM VETERANS OF EXPOSURE TO HERBICIDES
(FIFTH BIENNIAL UPDATE)**

JOHN J. STEGEMAN, (Chair), Senior Scientist, Woods Hole Oceanographic Institution, Department of Biology, Woods Hole, Massachusetts

KIROS T. BERHANE, Associate Professor, Department of Preventive Medicine, University of Southern California, Los Angeles, California

PAUL F. ENGSTROM, Senior Vice President and Medical Director, Fox Chase Network, Philadelphia, Pennsylvania

RICHARD A. FENSKE, Professor of Environmental and Occupational Health Sciences and Director of the Pacific Northwest Agricultural Safety and Health Center, University of Washington, Seattle, Washington

JORDAN FIRESTONE, Assistant Professor of Neurology, Clinic Director of Occupational and Environmental Medicine, University of Washington, Seattle, Washington

THOMAS A. GASIEWICZ, Professor and Chair of Environmental Medicine and Director of the Environmental Health Sciences Center, University of Rochester, Rochester, New York

CLAUDIA HOPENHAYN, Assistant Professor, College of Public Health, University of Kentucky, Lexington, Kentucky

LOREN D. KOLLER, Consultant, Environmental Health and Toxicology, Corvallis, Oregon

NANCY I. KERKVLIT, Professor, Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, Oregon

JOEL MCCULLOUGH, Medical Director of Environmental Health, Chicago Department of Health, Chicago, Illinois

DAVID S. STROGATZ, Associate Professor and Chair of Epidemiology, School of Public Health, State University of New York at Albany, New York

Staff

Michelle C. Catlin, Study Director (through October 2004)

Mary Burr Paxton, Study Director (as of November 2004)

Jennifer A. Cohen, Senior Program Associate

Rose Marie Martinez, Director, Board on Health Promotion and Disease Prevention

David Butler, Senior Program Officer

Sonia J. Cheruvillil, Senior Program Assistant (as of October 2004)

Joseph A. Esparza, Senior Program Assistant (through May 2004)

Peter James, Senior Program Assistant

Kate Kelly, Senior Editor

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:

Hans Berkel, President and CEO, Cancer Prevention Institute, Dayton, Ohio

Linda S. Birnbaum, Director, National Health and Environmental Effects Research Laboratory, US Environmental Protection Agency, Research Triangle Park, North Carolina

Margit L. Bleecker, Director, Center for Occupational and Environmental Neurology, Baltimore, Maryland

Norman Breslow, Professor, Department of Biostatistics, University of Washington, Seattle, Washington

Mark R. Cullen, Professor, Occupational and Environmental Medicine Program, Yale University School of Medicine, New Haven, Connecticut

Chris Gennings, Professor, Department of Biostatistics, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia

Russ B. Hauser, Associate Professor, Occupational Health Program, Harvard School of Public Health, Boston, Massachusetts

Robert F. Herrick, Senior Lecturer on Industrial Hygiene, Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts

Howard M. Kipen, Director, Occupational Health Division, Environmental and Occupational Health Sciences Institute, Rutgers University, Piscataway, New Jersey

Stephen H. Safe, Professor, Texas A&M Institute for Biosciences and Technology, College Station, Texas

Herbert H. Schaumburg, Professor, Albert Einstein College of Medicine, Yeshiva University, Bronx, New York

Bailus Walker, Jr., Professor, Howard University Cancer Center, Washington DC

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 **Dan Blazer**, Duke University Medical Center, Durham, North Carolina. Appointed by the 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.

Preface

In 1991, because of continuing uncertainty about the long-term health effects on Vietnam veterans who were exposed to herbicides during their service in Vietnam (mixtures of 2,4-dichlorophenoxyacetic acid [2,4-D], 2,4,5-trichlorophenoxyacetic acid [2,4,5-T], and its contaminant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin [TCDD], picloram, and cacodylic acid), Congress passed Public Law 102-4, the Agent Orange Act of 1991. That legislation directed the Secretary of Veterans Affairs to ask the National Academy of Sciences (NAS) to perform a comprehensive evaluation of scientific and medical information regarding the health effects of exposure to Agent Orange, other herbicides used in Vietnam, and the various chemical components of those herbicides, including TCDD. The resulting report, *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam* (VAO) was published by the NAS Institute of Medicine (IOM) in 1994. The Secretary also asked that NAS conduct updates at least every 2 years for 10 years from the date of the first report to review newly available literature and draw conclusions from the overall evidence. PL 107-103, The Veterans Education and Benefits Expansion Act of 2001, extended the updates until 2014.

The first report in the resulting series was *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam* (abbreviated as VAO in this report). It evaluated and integrated the scientific evidence regarding statistical associations between health outcomes and exposure to TCDD or other compounds in these herbicides that had accumulated prior to 1994. Public Law 102-4 also required the NAS to conduct biennial updates that would review newly published scientific literature regarding such associations. The first of these, *Veterans and Agent Orange: Update 1996* (*Update 1996*) was published in March of that year. The second, *Veterans and Agent Orange: Update 1998* (*Update 1998*) was pub-

lished in 1999. The third, *Veterans and Agent Orange: Update 2000 (Update 2000)* was published in 2001. The fourth, *Veterans and Agent Orange: Update 2002 (Update 2002)* was published in 2003.

The focus of this fifth updated review is on scientific studies published since the release of *Update 2002*. To conduct the review, the IOM established a committee of 11 members representing a wide range of expertise to take a fresh look at the studies reviewed in *VAO, Update 1996, Update 1998, Update 2000, and Update 2002*, along with the newest scientific evidence. To provide a link to the experience and expertise developed by the previous committees, seven of the members of the committee responsible for this report were recruited from the committee responsible for *Update 2002*. All committee members were selected because they are leading experts in their fields, have no conflicts of interest with regard to the matter under study, and have taken no public positions concerning the potential health effects of herbicides in Vietnam veterans or related aspects of herbicide or TCDD exposure. Biographical sketches of committee members and staff appear in Appendix D.

The committee worked on several fronts in conducting this updated review, always with the goal of seeking the most accurate information and advice from the widest possible range of knowledgeable sources. Consistent with NAS procedures, the committee met in a series of closed sessions in which members could freely examine, characterize, and weigh the strengths and limitations of the evidence. It also convened open meetings in May and July 2004 to provide the opportunity for veterans and veterans' service organizations, researchers, policymakers, and other interested parties to present their concerns, review their research, and exchange information directly with committee members. The oral presentations and written statements submitted to the committee are listed in Appendix B. The committee thanks the individuals who provided valuable insights into the health problems experienced by Vietnam veterans.

The committee is grateful to Michelle Catlin and Mary Paxton, who skillfully served as study directors for this project. The committee would also like to acknowledge the excellent work of IOM staff members Jennifer Cohen, Joe Esparza, Peter James, Sonia Cheruvillil, and David Butler. Thanks are also extended to Jim Banihashemi and Christie Bell, who handled the finances for the project; Kate Kelly, who provided editorial skills; and William McLeod, who conducted database searches.

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John Stegeman, *Chair*

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