Final Regulations Published on Non-Hodgkin's Lymphoma Claims; Proposed Rule on Soft Tissue Sarcomas, Chloracne, and Porphyria Cutanea Tarda to be Published Soon

On October 26, 1990, VA published in the Federal Register an amendment to adjudication regulations which establishes criteria to be followed in considering claims for service-connection for non-Hodgkin's lymphomas (NHL).

Under the regulations, service in Vietnam includes service in the waters offshore, or service in other locations if the conditions of service involved duty or visitation in Vietnam. Service in Vietnam during the Vietnam Era together with the development of NHL after such service are sufficient, under the regulations, to establish service-connection for that disease. The change is retroactive to August 5, 1964.

The amendment was prompted by the release of results of the Centers for Disease Control (CDC) Selected Cancers Study which indicated that Vietnam veterans are at increased risk of developing NHL. On March 29, 1990, the day the CDC study results were released, Secretary of Veterans Affairs Edward J. Derwinski announced his decision, which he called a "policy determination," that VA would service-connect NHL. (A lengthy article about the study and the Secretary's decision is contained in the May 1990 issue of the "Agent Orange Review.")

On June 21, 1990, VA published in the Federal Register the proposed regulations on NHL. During a 30-day public review period four comments were received. After careful consideration of these comments and suggestions, the proposed regulations were adopted without change.

STS, Chloracne, PCT Regulations

Another amendment to adjudication regulations will soon be published in the Federal Register. A change is required to formally implement the Secretary's decision to recognize soft tissue sarcomas (STS) as service-connected. That decision was announced on May 18, 1990, following a finding by the Veterans' Advisory Committee on Environmental Hazards that it is at least as likely as not that there is a significant statistical association between exposure to a dioxin-containing herbicide and subsequent development of STS.

(For additional information about the Advisory Committee's conclusion and Secretary Derwinski's decision to service-connect STS, see the August 1990 issue of the "Review.")

Draft proposed regulations regarding STS have been reviewed by the Advisory Committee. It is anticipated that proposed regulations regarding this matter will be published for public review in early 1991 in the Federal Register. The regulations should be finalized several months later.

An additional change in regulations involves chloracne and porphyria cutanea tarda (PCT). VA has drafted a proposed regulation amendment that will extend the manifestation period for chloracne following exposure to a herbicide containing dioxin and that will provide that there is no significant statistical association between exposure to a herbicide containing dioxin and PCT. This proposal, like the STS amendment will be published in the Federal Register for a 30-day public review period in early 1991.

The regulations regarding chloracne and PCT reflect advice of the Veterans' Advisory Committee on Environmental Hazards based on its evaluation of 31 scientific or medical documents relating to the association, if any, between exposure to herbicide containing dioxin and either chloracne or PCT considered during a public meeting of August 22-23, 1990.

The Committee concluded that there was no significant statistical association between exposure to a herbicide containing dioxin and the subsequent development of PCT. The Committee recommended that the manifestation period for chloracne following the last date of exposure to a herbicide containing dioxin be extended from three months to nine months.

Further developments regarding regulation changes will be described in future issues of the "Review."

VA Agent Orange Registry Exams To Continue; Rumors of Shutdown Proven False

Widespread reports of an imminent termination of the VA Agent Orange Registry examination program have been repeatedly denied by VA Central Office managers in Washington, DC.

"There is absolutely no basis in fact for this rumor. Unfortunately, such misinformation has unduly alarmed and upset many veterans," declared Lawrence B. Hobson, M.D.,
Priority Medical Treatment Suspended; Prompt Re-establishment Expected

On December 31, 1990, legal authority expired for the VA priority health care program for Vietnam veterans with disabilities possibly, but not necessarily, related to Agent Orange. Health care services under this program were limited to hospital and nursing home care in VA facilities and outpatient care in VA facilities on a pre- or post-hospitalization basis or to prevent a need for hospitalization. Services were provided without regard to the veteran's age, service-connected status, or the veteran's ability to pay the expenses of such care. Veterans (that is, former service personnel who did not receive a dishonorable discharge) receiving outpatient care under this program were given priority ahead of nonservice-connected veterans and equal to former Prisoners of War receiving care for nonservice-connected conditions.


An additional extension was seriously considered as part of a large legislative proposal dealing with various aspects of the Agent Orange issue as well as a number of other VA programs during the latter part of the 101st Congress that adjourned in October 1990. On May 2, 1990, VA Deputy Secretary Anthony J. Principi, testifying before a congressional panel, explained that VA would have "no objection" to a limited extension of this program. Congress adjourned before final action was taken on the extension.

There appears to be continuing and widespread support for an extension of the authority for the priority treatment program within the new Congress. It is anticipated that the action will be taken in early 1991.

Ranch Hand Study Results Published in JAMA

On October 10, 1990, the Journal of the American Medical Association published results of a long-term scientific investigation of mortality rates and physical health of veterans of Operation Ranch Hand, the U.S. Air Force unit responsible for herbicide spraying in Vietnam. Researchers concluded...
Ranch Hand personnel are as healthy as other Air Force veterans assigned to C-130 aircraft during the Vietnam-era.

**Mortality (Death) Assessment**

"An evaluation of cumulative and all-cause mortality revealed no statistically significant differences between Ranch Hands and comparison subjects, after adjustment for rank, occupation, date of birth and calendar time in five-year intervals," wrote principal investigator Col. William H. Wolfe, M.D., of the USAF School of Aerospace Medicine at Brooks Air Force Base in Texas. "These data are not supportive of a hypothesis of increased mortality among Ranch Hands." The mortality rate study looked at all known Ranch Hand veterans (1,261 veterans) and 19,101 other Air Force veterans who served concurrently in Southeast Asia. These data are of cumulative mortality as of December 31, 1987. There were 74 deaths among Ranch Hands and 1,038 among comparison subjects.

Death rates were determined using USAF Military Personnel Center records, the VA Death Beneficiary Identification and Record Location System, and the Internal Revenue Service database of active social security numbers, Death certificates were also ordered.

"Adjusted analyses that contrast Ranch Hands with all comparison subjects on accidental, malignant neoplasm, and circulatory deaths revealed no significant group differences," the investigators wrote. They did find a significant increase in digestive system disease deaths among Ranch Hands. The researchers linked most of this increase to alcoholism.

**Morbidity (Disease) Results**

In addition to the mortality effort, investigators compared the current physical health of 995 Ranch Hand veterans to 1,299 comparison subjects. "The two groups were similar in reported health problems, diagnosed skin conditions, and hepatic, cardiovascular, and immune profiles," according to Dr. Wolfe.

Extensive medical examinations were conducted in 1982 to collect baseline data. Follow-up exams took place in 1985 and 1987.

The physical and dermatologic exams were conducted by board-certified internists and dermatologists. Immunologic tests were carried out on a 39 percent random sample taken from each group.

"We found no overall group differences in the lifetime occurrence of systemic cancer," the authors wrote. "In general, no evidence suggested the Ranch Hands were experiencing significantly increased systemic cancer at any particular site." Ranch Hands did have "significantly more basal cell carcinomas" of the skin than comparison subjects.

"The few positive associations found between physical health and exposure generally are weak and inconsistent," the investigators concluded. "None of the associations reported herein changed significantly with military occupation, currently our best indicator or current TCDD (the dioxin-based poison in the herbicide) body-burden. We are left with the interpretation that the few positive fundings are not supportive of a hypothesis of adverse health effects in Ranch Hands."

**Continuing Research**

The Air Force investigation has been the subject of several articles in previous issues of the "Agent Orange Review." The most recent article appeared in the May 1990 issue. This ongoing research effort is expected to continue into the 21st century.

**CDC Selected Cancers Study Published**

The results of the Centers for Disease Control (CDC) Selected Cancers Study, which prompted Secretary Derwinski's decision to approve service-connection for non-Hodgkin's lymphomas, were published in the December 1990 issue of the Archives of Internal Medicine.

An article about the study results and the Secretary's response was featured on the front page of the May 1990 issue of the "Agent Orange Review." The Archives of Internal Medicine published the findings in three articles, entitled "The Association of Selected Cancers with Service in the U.S. Military in Vietnam," prepared by the investigators. The medical journal also included an editorial by Raymond Suskind, M.D., of the Institute of Environmental Health Kettering Laboratory regarding this research effort.

The first article focused on non-Hodgkin's lymphomas; the second dealt with soft tissue and other sarcomas; and the third concerned Hodgkin's disease, nasal cancer, nasopharyngeal cancer, and primary liver cancer.

Investigators conducted a population-based, case-control study of these six malignant neoplasms between 1984 and 1988. All men born between 1929 and 1953 and diagnosed as having any of these conditions in an area covered by eight cancer registries were considered eligible.

The registries involved are located at Emory University in Atlanta, Georgia; Yale University in New Haven, Connecticut; University of Iowa in Iowa City; University of Kansas in Kansas City; University of Miami in Florida; California Public Health Foundation in San Francisco; Michigan Cancer Foundation in Detroit; and Fred Hutchinson Cancer Research Center in Seattle, Washington.

Control subjects were identified by random-digit dialing from these same regions and were frequency-matched to men with each of these conditions by age. Analyses showed that the risk of non-Hodgkin's lymphomas was approximately 50% higher among Vietnam veterans compared with men who did not serve in Vietnam. Vietnam veterans were also at high risk relative to (1) men who had not served in the military, (2) other veterans, and (3) other veterans who served between 1964 and 1972.

An analysis of military histories suggested that the relative risk of non-Hodgkin's lymphomas (1) increased with length of service in Vietnam, and (2) was higher among men in the sea-based Navy than among other veterans. Little difference in risk of non-Hodgkin's lymphomas, however, was noted by investigators according to dates of service, type of unit, military region, or any other characteristics that may have been associated with the use of Agent Orange.

Investigators concluded that while the cause remains uncertain, this study indicates that the risk of non-Hodgkin's
lymphomas is higher among Vietnam veterans than among other men. Researchers found no evidence of increased risk of soft tissue or other sarcomas, Hodgkin's disease, nasal or nasopharyngeal cancer, or primary liver cancer among Vietnam veterans compared with other veterans or nonveterans.

Edward Brann, M.D., M.P.H., was the principal investigator for the study which was conducted under an interagency agreement with the Department of Veterans Affairs (VA). With VA funding, CDC initiated the Selected Cancers Study in 1983. Requests for reprints of the articles in the Archives of Internal Medicine or for additional information about the Selected Cancers Study should be directed to Dr. Brann at the Center for Environmental Health and Injury Control, Centers for Disease Control, Atlanta, Georgia 30333.

VA Research Update

In recent months, the VA Environmental Epidemiology Service (EES), previously known as the Office of Environmental Epidemiology, has completed and/or has had published in professional journals the results of several important research efforts.

Army I Corps Mortality Study

In October 1990, the American Journal of Epidemiology published the results of the “Proportionate Mortality Among U.S. Army Vietnam Veterans Who Served in I Corps.” This study was designed to determine whether Army veterans stationed in I Corps experience mortality patterns similar to Marines who served there.

The post-service mortality experience of 6,668 Army Vietnam veterans who served in Military Region I (I Corps) was compared to that of 27,917 Army non-Vietnam veterans. Statistically significant excesses of deaths were observed for motor vehicle accidents and accidental poisonings.

Death due to other major disease categories, including malignant neoplasms and suicides, were not more frequent among Army I Corps veterans than their counterparts. No significant excess of deaths due to non-Hodgkin's lymphoma or lung cancer was observed.

Army Chemical Corps Study

This investigation examined health effects of chemical exposures during military service in Vietnam among men who served in the Army Chemical Corps. Because they were involved in the mixing and application of herbicides these men were likely to have had heavier exposure than others.

Nearly 1,000 Army Chemical Corps veterans who served in Vietnam between 1965 and 1971 were identified from unit morning reports. Fifty-three deaths were observed through December 1987. Based on rates for U.S. men adjusted for race, age, and calendar period, there were statistically significant excesses of digestive disease deaths, primarily alcohol-related, and from motor vehicle accidents. Two deaths were observed from leukemia (with 0.5 expected) and two from brain cancer (0.4 expected).

A total of 257 of the veterans had received VA inpatient care and/or the VA Agent Orange Registry medical examination during the study period. Two veterans had confirmed diagnoses of Hodgkin's disease (0.7 expected).

Investigators concluded that because of the small study group size and the lack of specificity of information regarding exposure, these results cannot be attributed to any single chemical agent. The study results were published in the American Journal of Industrial Medicine in December 1990.

Adipose Tissue Study

EES, in collaboration with the Environmental Protection Agency (EPA), completed a very detailed analysis of adipose tissue specimens taken from 200 men of the Vietnam-era age group. The specimens were analyzed for 2,3,7,8-TCDD, the contaminant found in one of the ingredients (2,4,5-T) of Agent Orange, and sixteen other related dioxins and dibenzofurans.

Researchers used adipose tissue collected for the EPA's National Human Adipose Tissue Survey.

A total of 40 Vietnam veterans, 80 veterans who did not serve in Vietnam, and 80 civilians were selected for this study and their archived tissues analyzed. Investigators found that the average level of 2,3,7,8-TCDD in the adipose tissue of Vietnam veterans was not significantly different from that of the non-Vietnam veterans or the civilians. This was the case both with and without adjustment for several demographic variables.

The study results indicated no association between TCDD levels and Agent Orange exposure opportunity estimations based on military records.

The study was published in February 1991 in the American Journal of Public Health. The Journal also included an editorial about the study results and its significance.

Non-Hodgkin's Lymphoma Among Vietnam-era Veterans

This hospital-based case control study examined the association between military service in Vietnam and non-Hodgkin's lymphoma. The case group of 201 Vietnam-era veterans who were treated in VA medical centers between 1969 and 1985 with a diagnosis of non-Hodgkin's lymphoma was compared with 358 Vietnam-era veterans with a diagnosis other than malignant lymphoma.

Investigators found that military service in Vietnam did not increase the risk of non-Hodgkin's lymphoma either in general or with increased latency period (defined as the duration in years from the first service in Vietnam to hospital discharge date). Service in a specific military branch, a specific region of Vietnam, or in a combat role (as determined by military occupational specialty) were not associated with any increased risk of non-Hodgkin's lymphoma.

The investigators have been told that the study results will be published in the Journal of Occupational Medicine in March 1991.

Mortality Study Update

In May 1988, the Journal of Occupational Medicine published the results of a large scale mortality study of Army and Marine Corps Vietnam veterans who died during the 1965-82 period. This EES study indicated that Marine Corps Vietnam veterans appeared to have an increased mortality from lung cancer and non-Hodgkin's lymphomas. Army Vietnam veterans did not. Statistically significant excess deaths were
observed among Army Vietnam veterans for motor vehicle accidents, non-motor vehicle accidents and accidental poisonings. The study compared the mortality patterns and specific causes of death among 24,235 Vietnam veterans and 26,685 veterans without Vietnam service.

EES has updated these data by including deaths through 1984. The update includes a total of 62,068 deaths. Compared to non-Vietnam veterans, Army and Marine veterans who served in Vietnam had a small but statistically significant excess of deaths from external causes. Army Vietnam veterans had small excesses of laryngeal cancer and lung cancer. The role of known causes of these types of cancer, smoking and drinking, could not be determined.

Marine Vietnam veterans, when compared to their non-Vietnam counterparts, still showed an excess of deaths due to lung cancer and non-Hodgkin's lymphomas. However, when the Marine Vietnam veteran group was compared to the combined Army and Marine non-Vietnam veteran group, the excess became smaller and was not statistically significant.

The results of the update should be published in the Journal of Occupational Medicine in March 1991.

Other Research Efforts

In addition to the studies described above, EES is pursuing many other related research projects. Several of these investigations are nearing completion; other studies are ongoing and will not be published for two or three years.

Dr. Han K. Kang is the Director of EES. He leads a staff of ten. Requests for additional information or study reprints should be sent to the VA Environmental Epidemiology Service, 1825 K Street, NW, Room 322, Washington, DC 20006.

Environmental Hazards Committee Maintains Active Meeting Schedule

The Veterans' Advisory Committee on Environmental Hazards, established in 1985 in accordance with Public Law 98-542, is continuing to meet frequently to advise the Secretary on Agent Orange/dioxin matters and on ionizing radiation.

Under the law the Committee is charged with responsibility for advising VA on guidelines and standards and criteria for the resolution of claims for VA benefits where the criteria for eligibility include a requirement that a death or disability be service-connected and the claim of service-connection is based on a veteran's exposure during service in Vietnam to a herbicide containing dioxin. The Committee has similar responsibility with regard to veterans' participation in atmospheric nuclear tests or with the American occupation of Hiroshima or Nagasaki, Japan, to ionizing radiation from the detonation of a nuclear device.

Recent Committee meetings have been held in May 1990, July 1990, August 1990, and October 1990. The January 29-31, 1991 meeting had not occurred when this edition of the "Agent Orange Review" was prepared. While several of these meetings have dealt with radiation concerns, much of the Committee's focus during the past year has been on the Agent Orange/dioxin issue.

Secretary Derwinski's announcement of May 18, 1990, that VA would recognize, as service-connected, soft tissue sarcomas based on exposure to dioxin-containing herbicides was the direct and immediate result of a Committee finding at the May 1990 meeting. (The August 1990 issue of the "Review" has a front page article about the May meeting and its aftermath.)

The July meeting focused on procedural matters, with the Committee trying to establish a more effective mechanism for assessing scientific evidence in very different studies, weighing this evidence, considering significant confounding and other factors, and determining the relative strengths and weaknesses of a given research effort.

In its August 1990 meeting, the Committee reviewed the appropriateness of the manifestation period for chloracne, a skin disorder that has been recognized for many years as related to dioxin exposure. The Committee recommended that VA adopt a nine-month maximum manifestation period.

The Committee also carefully examined a number of research efforts to determine whether there is a significant statistical association between dioxin exposure and the development of porphyria cutanea tarda. The Committee found no such association, although one member, a lay member, dissented. The Committee is composed of eleven scientists and four non-technical members. The Committee also made recommendations regarding draft VA regulations on soft tissue sarcomas.

In October 1990, the Committee reviewed a number of scientific papers relating to the effects of exposure to Agent Orange or its components. It also discussed several approaches it might employ in assessing the relative weights of the various positive, negative, and inconclusive studies it had reviewed.

Mr. Frederic L. Conway, III, a VA attorney, manages the Committee's operations.

VA Publishes Herbicide Literature Review Update; Volumes 15-16 Cover 1989 Studies; Non-Technical Summary Released

VA recently published Volumes 15 and 16 of the Review of Literature on Herbicides, Including Phenoxy Herbicides and Associated Dioxins. The report consists of an analysis and annotated bibliography of literature produced worldwide regarding Agent Orange and other herbicides. The comprehensive technical document is prepared primarily for researchers, physicians, scientists, and others with similar backgrounds.

The initial two volumes of the literature review, mandated by Public Law 96-151, were released in 1981. The latest issues describe herbicide literature that became available in 1989. Additional volumes covering more recent publications are under consideration.

Copies of all volumes are maintained at VA medical center libraries. The report has also been distributed to researchers throughout the world. The reviews are prepared by independent contractors.

To assist non-technical readers in understanding the complex scientific issues involving Agent Orange and other herbicides, VA also publishes a series of "lay language"
summaries, entitled *Synopsis of Scientific Literature on Phenoxy Herbicides and Associated Dioxins*.

Number 7 in the synopsis series corresponds with Volume 15 and 16 of the literature review. The summaries, published as booklets, were prepared by the same contractors who produced the literature review. Copies of the synopses have been sent to all VA medical center libraries.

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**Class Action Lawsuit Referral Information**

The Department of Veterans Affairs (VA) has received a large number of inquiries regarding the status of claims for compensation from the Agent Orange Settlement Fund, established as a result of the settlement of a class action lawsuit ("Agent Orange" Product Liability Litigation) brought by Vietnam veterans and their families against the manufacturers of Agent Orange.

Neither VA nor any other Federal department or agency is directly involved in the distribution of the settlement funds. Information on this matter can be obtained by calling, toll-free 1-800-225-4712, or writing to the Agent Orange Veteran Payment Program, P.O. Box I10, Hartford, Connecticut 06104.

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**Revised "Agent Orange Brief" Fact Sheet Series Issued in September 1990**

The Environmental Agents Service in VA headquarters in Washington, DC, has revised and released a series of Agent Orange fact sheets, known as "Agent Orange Briefs."

The updated "Briefs," dated September 1990, describe a wide range of Agent Orange-related matters. The following "Briefs" are currently available:

1. Agent Orange--General Information
2. Agent Orange Registry
3. Agent Orange Class Action Lawsuit
4. Agent Orange--The Problem Encountered in Research
5. Agent Orange--Priority Treatment Program
6. Agent Orange and Birth Defects
7. Agent Orange and Chloracne
8. Agent Orange and VA Disability Compensation
9. Agent Orange and Soft Tissue Sarcoma
10. Agent Orange and Vietnam Related Research
11. Agent Orange and Vietnam Related Research--VA Efforts
12. Agent Orange and Non-Hodgkin's Lymphoma
13. VA Information Resources on Agent Orange and Related Matters

The "Briefs" were distributed widely throughout the VA system and to various State offices. Earlier versions of the "Briefs" were released in October 1988 and October 1989.

For additional information or a copy of the revised fact sheets, contact the Agent Orange Coordinator at the nearest VA medical center or write to the Environmental Agents Service (146A), VA Central Office, 810 Vermont Avenue, NW, Washington, DC 20420.

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**VA Central Office Realigned; Agent Orange Office Renamed, Relocated**

In July 1990, Department of Veterans Affairs (VA) Central Office underwent a major realignment of program elements within the Veterans Health Services and Research Administration (VHS&RA), the VA medical agency. The Environmental Medicine Office, previously known as the Agent Orange Projects Office, was renamed the Environmental Agents Service (EAS). The EAS continues to have responsibility for the VHS&RA national Agent Orange and low level ionizing radiation programs.

Correspondence with EAS should be addressed to Lawrence B. Hobson, M.D., Ph.D., Director, Environmental Agents Service (146A), VA Central Office, 810 Vermont Avenue, NW, Washington, DC 20420. The telephone number is (202) 233-4117. Dr. Hobson reports to the Assistant Chief Medical Director for Environmental Medicine. That office also oversees the AIDS, Women's, and Smoking programs in VHS&RA.

In February or March 1990, several VA Central Office components, including VHS&RA, will be temporarily relocated to TechWorld, an office complex approximately one mile east of the Vermont Avenue building. This will allow for the extensive renovation, expected to be completed in about four years, of VA headquarters. The mailing address will not be affected. The telephone numbers for some offices will be changed. No disruption in the Agent Orange program is anticipated.

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**Agent Orange Review**

*Information for Veterans Who Served in Vietnam*

February 1991