Final Regulations Issued for Soft Tissue Sarcomas, Chloracne; Proposed Regulations on Peripheral Neuropathy Under Development

In October 1991, VA issued final regulations governing the adjudication of certain claims for service-connected disability based on exposure to herbicides containing dioxin.

Soft Tissue Sarcomas

On Tuesday, October 15, 1991, the Federal Register published a VA adjudication regulation amendment to establish service connection for soft tissue sarcomas based on exposure to herbicides containing dioxin. Agent Orange is such a herbicide.

Soft tissue sarcomas are a group of different types of malignant tumors which arise from body tissues such as muscle, fat, blood and lymph vessels and connective tissues (that is, distinct from hard tissue such as bone or cartilage). These tumors are relatively rare.

The change was necessary to implement Secretary of Veterans Affairs Edward J. Derwinski’s determination that "it is at least as likely as not that there is a significant statistical association between exposure to herbicides containing dioxin and the subsequent development of soft tissue sarcomas." That determination, based on the advice of the Veterans’ Advisory Committee on Environmental Hazards, was announced in May 1990. Proposed implementing regulations were published in the Federal Register for public comment in February 1991.

While the regulations are expected to primarily affect veterans who served in Vietnam, these regulations apply to all veterans who were exposed to herbicides containing dioxin during military service. Vietnam veterans are presumed to have been exposed to dioxins; veterans who served elsewhere must provide proof of their exposure. The soft tissue sarcomas may be manifested at any time after service.

These regulations implement the provisions of Public Law 98-542, the "Veterans' Dioxin and Radiation Exposure Compensation Standards Act," which requires that determinations as to whether medical conditions are related to dioxin exposure be made by VA after receiving the advice of the Advisory Committee based on its reviews of scientific and medical studies. Since there are significant differences in the eligibility requirements for service connection under these provisions and the presumptions of service connection established under Public Law 102-4, the "Agent Orange Act of 1991," regulations implementing the new statute will be published separately.

Under the final regulations, the term "soft tissue sarcoma" includes adult fibrosarcoma; dermatofibrosarcoma protuberans, malignant fibrous histiocytoma; liposarcoma; leiomyosarcoma; epithelioid leiomyosarcoma (malignant leiomyoblastoma); rhabdomyosarcoma; ectomesenchymoma; angiosarcoma (hemangiosarcoma and lymphangiosarcoma); proliferating (systemic) angioendotheliomatosis; malignant glomus tumor; malignant hemangioendothelioma; synovial sarcoma (malignant synovioma); malignant giant cell tumor of tendon sheath; malignant schwannoma, including malignant schwannoma with rhabdomyoblastic differentiation (malignant Triton tumor); glandular and epithelioid malignant schwannomas; malignant mesenchymoma; malignant granular cell tumor; alveolar soft pan sarcoma; epithelioid sarcoma; and clear cell sarcoma of tendons and aponeuroses.

The effective date of this change is September 25, 1985, which was the effective day of VA's original regulations governing claims based on exposure to herbicides containing dioxin. The original regulations were voided by a court ruling in 1989.

Chloracne, Porphyria Cutanea Tarda

On Monday, October 21, 1991, VA published in the Federal Register additional regulation amendments governing the adjudication of claims for service-connected disability compensation based on exposure to a herbicide containing dioxin. Specifically, these amendments (1) extend, from three to nine months the period during which chloracne must appear following exposure to herbicides containing dioxin to establish service connection, and (2) declare that there is no significant statistical association between exposure to a herbicide containing dioxin and porphyria cutanea tarda.

Chloracne is a skin condition that looks like common forms of acne that affect many teenagers. VA has long recognized that chloracne is caused by exposure to substances containing dioxin. Physicians, even dermatologists, sometime have difficulty in distinguishing chloracne from other more common skin disorders.

Porphyria cutanea tarda (PCT) is a relatively uncommon liver disturbance associated with skin changes. Exposure of some people to certain chemicals can result in the development of PCT.

The changes are necessary to implement the Secretary's determinations based on reviews of scientific and medical studies by the Veterans’ Advisory on Environmental Hazards. As with the regulations published on October 15, 1991 (described above), these amendments apply to all veterans who were exposed to herbicides containing dioxin during military service.
Regulation Status Report

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Status</th>
<th>Publication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloracne</td>
<td>A skin condition that resembles a common form of teenage acne</td>
<td>Final Rule--(extended period of manifestation from three to nine months)</td>
<td>Federal Register October 21, 1991</td>
</tr>
<tr>
<td>Non-Hodgkin's lymphomas</td>
<td>A group of relatively rare malignant tumors that affect the lymph glands and other lymphatic tissue</td>
<td>Final Rule--Service-connected for Vietnam veterans (not for exposure to herbicides containing dioxin)</td>
<td>Federal Register October 26, 1990</td>
</tr>
<tr>
<td>Porphyria cutanea tarda</td>
<td>A relatively uncommon liver disturbance associated with skin changes</td>
<td>Final Rule--Not Service-connected</td>
<td>Federal Register October 21, 1991</td>
</tr>
<tr>
<td>Soft tissue sarcomas</td>
<td>A group of approximately 25 different types of rare malignant tumors which arise from body tissues such as muscle, fat, blood, and lymph vessels and connective tissues (distinct from hard tissue such as bone or cartilage)</td>
<td>Final Rule</td>
<td>Federal Register October 15, 1991</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>A nervous system condition that causes numbness and tingling and/or weakness</td>
<td>Proposed Rule Pending</td>
<td>None</td>
</tr>
</tbody>
</table>

In March 1991, VA published in the Federal Register for public comment proposed regulations to extend the period during which chloracne must appear following exposure to a herbicide containing dioxin to establish service connection. The proposed regulations also would codify the Secretary's decision that there is no significant statistical association between exposure to a herbicide containing dioxin and PCT. The proposal was adopted without change.

The effective date of the final regulation is September 25, 1985.

For further information regarding the soft tissue sarcoma, chloracne, and PCT regulations, contact the Regulations Staff (211B), Compensation and Pension Service, Veterans Benefits Administration, Department of Veterans Affairs, 810 Vermont Avenue, NW, Washington, DC 20420, or a veterans benefits counselor at the nearest VA regional office or medical center.

Peripheral Neuropathy, Lung Cancer

On July 1, 1991, Secretary Derwinski announced that VA would recognize peripheral neuropathy as service-connected based on exposure to herbicides containing dioxin, provided there is no underlying condition known to cause peripheral neuropathy. Peripheral neuropathy is a nervous system condition that causes numbness and tingling and/or weakness. At the same time, he indicated that VA will propose a rule stating that there is no link between exposure to dioxin and lung cancer.

Officials in the Compensation and Pension Service anticipate that these proposed regulation amendments will be published in the Federal Register for public comment in early 1992. Additional information about this matter will be included in future issues of the "Agent Orange Review."

VA Publishes Literature Review Update and Synopsis

VA recently published Volumes 17 and 18 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 1990. Additional volumes covering more recent publications are planned.

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 8 in the synopsis series corresponds with Volume 17 and 18 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.
Scientific Journals Publish VA Studies

A number of significant scientific studies, conducted by VA scientists, regarding Vietnam veterans have been published in professional journals during the past several months. Several of these research efforts are described below.

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.

This study was authored by Nancy A. Dalager of the VA Environmental Epidemiology Service (EES) in Washington, DC, two other researchers from that office, Dr. Han K. Kang and Vicki L. Burt, and Dr. Lee Weatherbee of the VA Medical Center, Ann Arbor, Michigan. Ms. Butt now works for the National Center for Health Statistics at the Centers for Disease Control in Hyattsville, Maryland.

The study results were published in the *Journal of Occupational Medicine* in July 1991. (The February issue of the "Agent Orange Review" indicated that the investigators had been told that the study would be published in March 1991.)

On March 29, 1990, Secretary Derwinski had announced that VA would recognize non-Hodgkin's lymphomas as service-connected based on service in Vietnam. His announcement was prompted by the release of the Centers for Disease Control Selected Cancers Study, which suggested that Vietnam veterans are at increased risk of developing non-Hodgkin's lymphomas.

The final regulations implementing the Secretary's policy determination were published in the Federal Register on October 26, 1990. Public Law 102-4, the "Agent Orange Act of 1991," signed by President Bush on February 6, 1991, codified this decision. The VA study results are not expected to have any impact on VA benefits available to Vietnam veterans with non-Hodgkin's lymphomas or their survivors.

Mortality Among Vietnam Veterans: With Methodological Considerations

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. That EES study indicated that Marine Corps Vietnam veterans appeared to have an increased mortality from lung cancer and Non-Hodgkin's lymphomas. This increase was not seen among Army Vietnam veterans. 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

About the "Review"...

The "Agent Orange Review" is prepared by VA's Environmental Agents Service (EAS). The "Review" is published periodically to provide information on Agent Orange and related matters to Vietnam veterans, their families, and others with concerns about herbicides used in Vietnam. The most recent issue of the "Review" was published in August 1991.

The "Review" is prepared approximately one month prior to the publication date. This issue was written in late October and early November and does not include developments that occurred during the latter part of November or December 1991.

Comments or questions about the content of the "Review" are encouraged. Suggestions and ideas for future issues of the newsletter should be sent to Donald J. Rosenblum, Writer/Editor, Agent Orange Review, Environmental Agents Service (116A), VA Central Office, 810 Vermont Avenue, NW, Washington, DC 20420.

Requests for additional copies of this issue, should also be directed to Mr. Rosenblum. Please specify the number of copies you are requesting. A limited supply of the last six issues (October 1989, May 1990, August 1990, February 1991, April 1991, and August 1991) is also available. VA facilities should order additional copies from the VA Supply Depot.

VA updates the "Review" mailing address listing annually. If you have not been filing Federal income tax annually and have moved to another residence, we may not have the best address for you and may not be able to send you future issues of the "Review." Therefore, if this is your situation, please send your old and new addresses and Social Security number to the Department of Veterans Affairs, Data Processing Center (200/397), 1615 East Woodward Street, Austin, Texas 78772.

If you have questions about your Agent Orange Registry examination, contact the Environmental Physician or Agent Orange Coordinator at the VA medical center where you had the examination. Questions about VA benefit programs, including disability compensation, should be directed to a veterans benefits counselor at the VA facility nearest you. The telephone number can be found in your telephone book under the "U.S. Government" listings.
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 updated study was authored by Kevin K. Watanabe, Dr. Han K. Kang, and Dr. Terry L. Thomas, all of the EES. Dr. Thomas is now with the Office of Epidemiology and Health Surveillance at the U.S. Department of Energy.

The study results were published in the Journal of Occupational Medicine in July 1991. (The February issue of the "Agent Orange Review" reported that publication was anticipated in March 1991.)

Posttraumatic Stress Disorder Among Vietnam Veterans in the Agent Orange Registry -- A Case-Control Analysis

Some of the readjustment problems of Vietnam veterans have been attributed to posttraumatic stress disorder (PTSD). This disorder is described by a host of symptoms associated with exposure to catastrophic stress. Nightmares, flashbacks, anxiety and sudden-startle reactions may occur immediately after exposure to the stress of combat. These difficulties may develop years after the original stress.

This EES case-control study compared demographic and military characteristics of 374 Vietnam veterans who had been diagnosed with PTSD with 373 healthy Vietnam veterans. Veterans were selected from the Agent Orange Registry, a VA computerized database of approximately 200,000 Vietnam veterans who volunteered for a physical examination.

Investigators confirmed that being wounded in Vietnam and having a combat job in Vietnam were risk factors for PTSD. Data analysis also revealed that those who had noncombat jobs but were wounded had the highest risk of PTSD.

The study, authored by Tim A. Bullman, Dr. Han K. Kang, and Dr. Terry L. Thomas, was published in the November 1991 issue of the Annals of Epidemiology.

Vietnam veterans who are suffering with PTSD or other readjustment problems are urged to seek help from the nearest VA "vet center" or VA medical center. The location usually can be found in the U.S. Government section of the community telephone directory. Services include individual counseling, group counseling, family counseling, and community outreach and education.

Women Vietnam Veterans Mortality Study

Because of the relatively small number of women who served in the Armed Forces in Vietnam, they were intentionally excluded from the large scale Vietnam veterans mortality study described above. Instead, EES scientists have conducted a separate study of mortality among women Vietnam veterans.

Approximately 4,500 women Vietnam veterans and 6,500 women veterans who never served in Vietnam were identified from military records and followed for vital status on December 31, 1987. Investigators found that women Vietnam veterans had lower than expected mortality from all causes compared to U.S. women and women non-Vietnam veterans. Suicide rates were nearly the same in both cohorts.

There was a slight excess of mortality from external causes among women Vietnam veterans compared with non-Vietnam veterans, primarily due to an excess of motor vehicle accidents. In comparison to U.S. women, mortality from cancers of the pancreas and uterine corpus was elevated among Vietnam veterans but the increase was not statistically significant.

The study was authored by Dr. Terry L. Thomas, Dr. Han K. Kang, and Nancy A. Dalager. The results were published in the American Journal of Epidemiology in November 1991.

Why the Long Delays in Publication of Study Results

It is common that many months, sometimes a year or more, will pass between completion of an important study and the publication of the study results. Some veterans have expressed their understandable impatience, confusion, and frustration with these delays. To better comprehend the reasons for the publication lag, it might be worthwhile to take a look at the procedures generally used by scientific researchers.

When an investigator completes the analysis of the data gathered, a written report is prepared describing the study methodology, findings, and conclusions. Here at VA, and in most large organizations, the report is sent for peer review, both internally and externally. Often the peer review process results in useful comments and suggestions which lead the researchers to reanalyze data and/or perform additional analyses. As a result, the manuscript may be revised.

Some studies are also presented in scientific meetings which add an additional layer of critical scientific scrutiny. Researchers go through this process to ensure that flaws in the design, conduct, or interpretation of their studies are not overlooked.

After these reviews are completed and any necessary manuscript modification accomplished, the study paper is submitted to a scientific journal for publication. Each journal has its own independent review process which delays publication for several months. Occasionally, a journal's review indicates the necessity for manuscript revision. Then there is a lag time between the journal's acceptance of a paper and its actual publication. (If a journal rejects the study paper -- and they sometimes do -- it may be submitted to another journal.)

With all these obstacles and unavoidable delays, some veterans have asked whether they might not be better served if VA (and others conducting research on Agent Orange and Vietnam veterans) would just release a study when completed rather than seek publication in a scientific journal. Unfortunately, there are major drawbacks to this approach as well. Study investigators would not have the benefit of peer criticism and could release data that were based on erroneous assumptions. There might also be faulty analyses. Having a report published in a scientific journal adds credibility and acceptance in the scientific community. It also gives other scientists not involved in the study the opportunity to closely examine the research effort.

Ongoing VA Research Efforts

Several significant EES research projects that have been completed and recently published are described above. EES investigators are currently pursuing a number of other studies related to the possible long-term health consequences of military service in Vietnam and/or exposure to Agent Orange. This research is summarized below.
Hodgkin’s Disease Case Control Study

In light of findings which suggest an increase in the risk for Hodgkin’s disease among men exposed to phenoxy herbicides and concerns among veterans over Agent Orange exposure, EES scientists are conducting a hospital-based case control study to assess the association between Vietnam service and Hodgkin’s disease.

The cases consist of 278 Vietnam-era veteran patients with a diagnosis of Hodgkin’s disease who were treated in one of the 172 VA hospitals. The controls consist of 405 Vietnam-era veterans with a diagnosis other than malignant lymphoma. Cases and controls will be compared with respect to service in Vietnam and surrogate measures of potential Agent Orange exposure. Investigators expect to complete this project in 1992.

Marine Corps Vietnam Veterans Mortality Study

This EES study is designed to determine the overall mortality rate as well as the cause-specific mortality rates of about 10,000 Marines who served in Vietnam and an equal number of Marine veterans who served elsewhere. An external comparison to U.S. males adjusted for age, race, and calendar year periods will also be made.

The results of this study will complement the Centers for Disease Control ground troop mortality study which included only Army Vietnam veterans. The study will also help to evaluate findings of the VA Vietnam Veterans Mortality Study. Data collection is underway.

A Review of NVVRS Data for Women Vietnam Veterans

VA, by means of a contract with the Research Triangle Institute (RTI), recently completed the National Vietnam Veterans Readjustment Study (NVVRS). The 3,106 study subjects included 950 women (431 Vietnam veterans, 304 non-Vietnam veterans, and 215 civilians). In addition to a 3-5 hour interview, some Vietnam and non-Vietnam veterans underwent a follow-up clinical interview with an expert mental health clinician. There were 86 women Vietnam veterans and 35 women non-Vietnam veterans in the group that received the follow-up interview. There is already an extensive report on the study design, statistical methods, and results by the RTI.

This follow-up analysis will focus on women veterans, They will be evaluated by military service characteristics, such as occupation (nurse vs. non-nurse), length of service, branch, rank, and career status. Other characteristics, including age, race, substance abuse, and family history of violence will be considered and adjusted for in the analysis.

All the data files, analysis files, and documentation necessary for the project are being obtained from the RTI.


This project is the second update of the Vietnam Veterans Mortality Study. About 11,000 deceased Vietnam-era veterans who served in the Army or Marine Corps were selected from those veterans who died during 1985-1988.

The present study will examine whether the mortality patterns reported in the initial study and first update persist when subsequent deaths are considered and when two additional reference groups are used. Data collection is underway.

Army Chemical Corps Vietnam Veterans Study Update

This study is an update of an investigation published in the American Journal of Industrial Medicine in December 1990. The results were described in the February 1991 issue of the "Agent Orange Review."

The original mortality study was expanded to include Army Vietnam-era veterans who were identified by the Defense Manpower Data Center with a chemical primary military occupational specialty or MOS code and by class rosters (1965-72) obtained from the Army Chemical School of Ft. McClellan.

These additional study subjects will increase the size of the original Vietnam chemical cohort and will provide a comparison group of Army Chemical Corps veterans who never served in Vietnam. Data collection is underway.

Agent Orange Registry Review for Selected Cancers

All men who had their initial Agent Orange Registry examination between 1983 and 1987, and who had a confirmed diagnosis of any of several selected cancers are potential candidates for this project.

Controls will be selected from the Agent Orange Registry group matched to the case group by age, year of initial examination, and race. Military records will be sought for all cases and controls and abstracted to obtain information on dates of military service, dates served in Vietnam, unit addresses, and military occupations in Vietnam.

Case-control analyses will examine the relationship between specific Vietnam service characteristics and the selected cancers. Data collection is underway.

Retrospective Cohort Mortality Study of Army Veterans Who Received Non-Lethal Wounds in Vietnam

This study will examine the effects of combat trauma on the post-Vietnam service mortality of a cohort of Vietnam Army veterans. This cohort or group will be defined as Army veterans who received non-lethal wounds from hostile forces while serving in Vietnam. The mortality experience of these veterans will be compared to that of the U.S. general population adjusting for age at death, calendar year of death, and race.

Based on past research of post-Vietnam health status, investigators hypothesize that Vietnam veterans who were exposed to the trauma of being wounded will have higher than expected rates of suicides and deaths due to accidental poisonings. Data collection is underway.

Retrospective Cohort Mortality Study of Vietnam Veterans with a Diagnosis of Posttraumatic Stress Disorder (PTSD) in the Agent Orange Registry

This study will examine the effects of PTSD on the post-Vietnam service mortality of a cohort of Vietnam veterans. This cohort will be defined as veterans who reported to VA for an Agent Orange Registry examination and were diagnosed by a VA psychologist as having PTSD.

The mortality by specific cause of death among this group will be compared to that of the U.S. general population or veterans on the Agent Orange Registry with no diagnosis indicated adjusting for race, age at death, and calendar year of death.

The EES researchers hypothesize that PTSD will be associated with higher than expected rates of deaths due to
external causes particularly suicides and accidental poisonings. Data collection is underway.

**Women Vietnam Veterans Reproductive Health Study**

Studies of reproductive outcomes among male veterans have been mostly negative in that service in Vietnam was not associated with the risk of fathering a child with birth defects. Although the results of male Vietnam veterans health studies are useful in assessing the general health of women Vietnam veterans, further investigation may be necessary in the areas of gender specific health outcomes of women and of the birth outcomes of their children. It is generally accepted that maternal exposures are more commonly associated with adverse reproductive outcomes than paternal exposures.

This planned research will compare the reproductive health outcomes of all women Vietnam veterans with those of an equal number of women veterans who did not serve in Vietnam. Information on exposure will be collected from telephone interviews and will be supplemented with and validated by military personnel records. Data on the birth outcomes will also be collected from telephone interviews and validated by reviews of medical and hospital records.

A detailed research design is currently under scientific review.

**International Dioxin Symposium Held in North Carolina**

Approximately 800 scientists from throughout the world participated in the 11th International Symposium on Chlorinated Dioxins and Related Compounds in Research Triangle Park, North Carolina, September 23-27, 1991.

The symposium covered a wide range of topics, including tissue dosimetry, new analytical techniques, bioavailability, atmospheric fate and transport, new emission control technologies, dioxin induced cancers in laboratory animals, tumor promotion and cell proliferation, and induction of cytochrome p450 in humans.

Undoubtedly, the sessions on human exposure and human cancer and on human exposure and other health effects held on September 26 would be of greatest interest to Vietnam veterans and their families. Many important human health research groups were represented at these sessions, including authors of States studies (Michigan, New Jersey, Massachusetts); Seveso, Italy, health studies; U.S. Air Force Health Study (Operation Ranch Hand); NIOSH U.S. Dioxin Registry Studies; New Zealand soft tissue sarcomas, non-Hodgkin's lymphomas, and birth defects studies; Swedish soft tissue sarcomas, non-Hodgkin's lymphomas, and other cancer studies; Centers for Disease Control studies; and VA studies.

Dr. Lawrence B. Hobson, Director, Environmental Agents Service, and Dr. Han K. Kang, Director, Environmental Epidemiology Service, represented VA at the meeting.

The Italian scientists reported that despite the highest dioxin levels measured in humans as a result of an accident in Seveso, Italy, no adverse health effects have been observed in the residents except transient chloracne in some people. There were suggestive associations between exposure to dioxin and certain cancers, especially non-Hodgkin's lymphomas in Seveso males. The audience was cautioned against premature interpretation of these data.

The Ranch Hand Study principal investigator indicated that most health variables in the Air Force project revealed no patterns within or across clinical assessments that were indicative of health detriments due to dioxin. However, a significant association between serum dioxin levels and the following lipid related variables were found: diabetes, body fat, cholesterol, HDL, triglycerides and the cholesterol/HDL ratio. The study results were reported in the August 1991 issue of the "Agent Orange Review."

The author of the NIOSH Dioxin Registry Mortality Study, published early this year, commented that the study's conclusion about an increase in soft tissue sarcomas was limited by the small number of deaths and by misclassification of the cause of death on death certificates.

The principal investigator of the International Dioxin Registry Mortality Study, which included 5,669 sprayers and 8,729 chemical production workers in ten nations, indicated that no statistically significant increased risk of non-Hodgkin's lymphomas or soft tissue sarcomas were observed in this large project. One subgroup of workers that was observed for 10-19 years since their initial exposure showed a significant elevation of soft tissue sarcomas, but no increase in soft tissue sarcomas were seen among groups having 0-9, 20-29, or 30 or more years of follow up.

The author of the New Zealand studies concluded that when cancer epidemiology studies are considered in the light of biological measurements of exposure, no site of human cancer has so far been established to be caused by exposure to TCDD.

The Swedish investigators are the only group of researchers repeatedly publishing reports of statistically significant positive association between phenoxy herbicide exposure and the risk of soft tissue sarcomas. At the symposium they reviewed several papers that focused on exposure to dioxins as a risk factor for soft tissue sarcomas.

An official from the Centers for Disease Control outlined how epidemiologic studies can be incorporated in health risk assessments.

A senior VA scientist described "meta-analysis," a technique that can help researchers to overcome the lack of statistical power of individual studies and to resolve controversies between apparently contradictory results of different studies. Meta-analysis provides a quantitative statistical method for combining results from different studies.

While there is no single correct method to perform a meta-analysis, once agreement is reached on various items (which studies should be included or excluded, relative weight assigned based on exposure uncertainty and strength of study design, etc.), a meta-analysis can provide a quantitative means to synthesize all available data.

A fair amount of new data was presented at the symposium. Researchers from different perspectives found data to support their own views. There was, however, no conclusive resolution to the issues faced by Vietnam veterans and their families. It was clear at the end of the meeting that the scientific debate on dioxin and its health effects will continue.
Q's and A's

Editor's Note: The "Agent Orange Review" exists to serve the needs of its readers. Following publication of the April 1991 issue, several veterans commented that some of the terms used in the newsletter were unfamiliar to them and that they were having difficulty understanding medical and technical language often used in discussions of Agent Orange-related matters. We responded by adding a "Terminology" feature in the August 1991 issue. Eighteen frequently used terms were defined in the glossary published in that issue. We noted that other words may be defined in future issues.

In early October, we received a letter from a veterans contact representative at the Philadelphia Veterans Multi-Service Center suggesting "discussion in future issues as to the impact on offspring of Vietnam Veterans exposed to Agent Orange." In response, we have decided to include a "Q's and A's" (Questions and Answers) feature in the "Review." In this issue, we respond to the suggestion from Philadelphia and several other inquiries we have received in recent months.

We hope this new feature is helpful. Questions for future issues should be sent to Donald J. Rosenblum, Writer/Editor, Environmental Agents Service (116A), VA Central Office, 810 Vermont Avenue, NW, Washington, DC 20420. We cannot promise that all questions will be published, but writers can be assured that all inquiries will be considered.

What is the impact on the offspring of Vietnam veterans exposed to Agent Orange?

Clearly, one of the most emotional aspects of the Agent Orange issue is the concern that exposure to herbicides in Vietnam may have caused or contributed to the risks of having children with birth defects or other serious medical problems. Literally thousands of Vietnam veterans have fathered children with abnormalities. It is natural for these veterans to search for answers to these problems.

Approximately 2.6 million veterans served in Vietnam and many of them have multiple children. It has been estimated that 3-6 percent of all children are born with some kind of birth defects. Thus, scientists expect to see many thousands of children with abnormalities among the offspring of Vietnam veterans.

This certainly is unfortunate. This situation is worsened by the fact that in many instances scientists cannot explain what caused these difficulties.

Important research has been conducted to determine whether exposure to Agent Orange or military service in Vietnam may have increased the risk of fathering children with birth defects or other problems. While all of this research has not yet been completed, a considerable amount of information on this subject has been gathered.

At present, there is no conclusive medical or scientific evidence that Agent Orange has adversely affected the children of Vietnam veterans. Obviously, no one knows what ongoing or future research will reveal.

Vietnam veterans with possible Agent Orange-related medical problems are eligible for priority medical treatment from VA. Can veterans who were exposed to Agent Orange elsewhere also get this treatment?

No. This priority treatment authority, established in 1981, by Public Law 97-72, is limited to veterans of the Vietnam era (August 5, 1964 - May 7, 1975) who may have been exposed to dioxin in a herbicide used for military purposes during their active duty military service in Vietnam. Since its establishment, this authority was extended by Congress three times (Public Laws 99-166, 100-687, and 102-4), but the restriction to military service in Vietnam has remained.

There is no doubt that a very small number of veterans had exposure to Agent Orange outside Vietnam. Some of these veterans may be eligible for VA health care services under other programs or provisions of law.

How can a Vietnam veteran get compensated for Agent Orange exposure?

Vietnam veterans are not compensated for being exposed to Agent Orange (or any other substances). VA provides disability compensation to veterans who have injuries or illnesses that were incurred or aggravated during active service in the line of duty during wartime or peacetime service and discharged or separated under other than dishonorable conditions.

As noted earlier in the "Review," VA has recognized soft tissue sarcomas, chloracne, and peripheral neuropathy as service-connected based on exposure to herbicides containing dioxin. Veterans with these conditions may be eligible for compensation from VA.

Veterans who have medical problems they think may be related to their military service are encouraged to file a claim for disability compensation. For information or assistance in applying, veterans can write, call, or visit a veterans benefits counselor at the nearest VA regional office or VA medical center. Veterans service organizations (such as the American Legion, Veterans of Foreign Wars, Disabled American Veterans, etc.) may also be helpful.

Completion of an Agent Orange Registry examination does not automatically make a veteran eligible for disability compensation. Veterans who wish to be considered for disability compensation must file a claim for that benefit.

Veterans who are seeking benefits from the Agent Orange Veteran Payment Program, a non-VA program, should call 1-800-225-4712, or write to the Agent Orange Veteran Payment Program, P.O. Box 110, Hartford, Connecticut 06104.

Will we ever have conclusive answers to the many questions raised about the medical consequences of exposure to Agent Orange?

Extensive Agent Orange-related research has been conducted during the past decade. While scientists have gained a substantial amount of knowledge about this subject, not all of the questions raised have been satisfactorily answered to date. This is a frustrating situation for scientists as well as Vietnam veterans and their families. However, research is ongoing, and
we expect it to continue for at least another decade. Every year researchers learn more about this matter and are closer to the elusive answers that veterans deserve.

**Agent Orange Registry Serves as Model for Atomic Vets, Persian Gulf Vets**

The VA Agent Orange Registry, established in mid-1978 and refined in the early 1980’s to identify and assist Vietnam veterans concerned about exposure to herbicides, is serving as a model for VA registries for veterans exposed to ionizing radiation and veterans who served in the recent Persian Gulf conflict.

Several years ago the existing VA Ionizing Radiation Registry was modified and significantly improved when the Environmental Agents Service (EAS) altered the program to closely parallel the policies and procedures governing the Agent Orange Registry. "The Agent Orange Registry has been very effective, and we felt it would serve as an excellent model for the radiation program," declared Layne A. Drash, EAS Deputy Director.

The Ionizing Radiation Registry is available to veterans who may have been exposed to ionizing radiation while on active military duty, either at the testing of a nuclear device between 1945 and 1962, or during the American occupation of Hiroshima or Nagasaki, Japan, between September 11, 1945 and July 1, 1946.

As with the Agent Orange Registry, eligible veterans who participate in the Ionizing Radiation Registry program are provided with a comprehensive medical examination at the nearest VA medical center. A medical history is taken, physical examination is performed, and a series of basic laboratory tests are done. If the examining physician thinks that consultations with specialists are indicated, arrangements are made for additional examinations. Data gathered at each medical center is consolidated at the VA Data Processing Center in Austin, Texas, the same facility that handles the data from the Agent Orange Registry examinations.

A Persian Gulf Registry is now being designed to help meet the needs of veterans returning from the recent mideast conflict. It has been estimated that tens of thousands of U.S. troops in the Kuwait Theater of Operation during "Operation Desert Storm" were exposed to unignited petroleum and/or copious smoke from sabotaged Kuwaiti oil wells. Such experiences and other aspects of this military operation may have long-term health consequences on these veterans.

According to Mr. Drash, this new registry also is being modeled after the Agent Orange program. Mr. Drash recently reported that the Persian Gulf Registry should be fully operational by late 1992.

**Class Action Lawsuit Referral information**

The Department of Veterans Affairs (VA) has received many inquiries regarding the status of claims lot compensation from the Agent Orange Settlement Fund. This fund was established by a Federal court 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 Executive Branch 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 110, Hartford, Connecticut 06104.