The National Academy of Sciences (NAS) is making substantial progress on the Agent Orange project undertaken on behalf of VA early this year. NAS officials have been gathering herbicide literature from VA (including VA’s 18-volume literature review) and other sources, making contact with scientists and other interested parties throughout the country, and assembling a committee of experts to complete the project envisaged by Congress in Public Law 102-4, the "Agent Orange Act of 1991."

Initial Committee Meeting

The NAS Institute of Medicine's Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides held its first meeting on June 26, in Washington, DC. The morning session, which was opened to invited guests and speakers, was devoted to providing Committee members with expectations, interpretations of the congressional charge, and essential background information. Invited speakers included officials from the following government entities: VA, the Senate and House Committees on Veterans' Affairs, the Office of Technology Assessment, and the Environmental Protection Agency. Comments were also received from individuals not affiliated with the government.

Much of the initial meeting was spent planning the Committee's efforts in the remaining period of the study. A public meeting on the project is scheduled for early September 1992, in Washington, DC. Announcements will be sent to veterans’ organizations and to scientists and others known to have an interest in Agent Orange and dioxin. This will be followed by a Committee meeting on the next day.

Another two-day meeting is planned for December 1992. One of these days will be devoted to an open scientific meeting to allow the Committee to meet with scientists with expertise in various areas. The final Committee meetings will be held in February and April 1993.

The Committee has approved a working outline for the final report. Assignments for reviewing the literature and drafting the report have been made. A preliminary plan has been developed for assessing the literature and summarizing the information.

Committee Membership

The Committee is chaired by Harold Fallon, M.D., Chair of the Department of Medicine of the Medical College of Virginia in Richmond, Virginia. M. Donald Whorton, M.D., Vice President, ENSR Health Sciences, Alameda, California, is vice-chair. Norman Breslow, Ph.D., Professor and Chairman of the University of Washington's Department of Biostatistics is the liaison between the Committee and the Institute of Medicine's Board on Health Promotion and Disease Prevention. All three are members of the Institute of Medicine.

Committee members represent a wide range of expertise in environmental and occupational medicine, toxicology, pathology, genetics, clinical oncology, psychology, epidemiology, and biostatistics.

Individuals seeking information regarding the Committee can contact Ms. Cynthia Abel, Research Associate, Committee to Review the Health Effects of Vietnam Veterans of Exposure to Herbicides, Institute of Medicine, National Academy of Sciences, 2101 Constitution Avenue, NW, Washington, DC 20418. Her telephone number is (202) 334-2357.

Legal Requirements

Section 3 of Public Law 102-4 required VA to seek to enter into a contract with the NAS (or should NAS decline, another non-government not-for-profit scientific entity) to review scientific and medical information regarding the health effects of exposure to Agent Orange and other herbicides used in Vietnam. The contract with the NAS was signed on January 31, 1992.
For each disease suspected of being associated with exposure to an herbicide, the NAS will review and summarize the relevant scientific evidence and determine (1) whether there is a statistical association with exposure to the herbicide; (2) the increased risk of disease among those exposed to the herbicides during service in Vietnam; and (3) whether there is a plausible biological mechanism or other evidence of a causal relationship between herbicide exposure and the disease.

The Secretary of Veterans Affairs will establish in regulations a presumption of service connection for diseases that the Secretary determines to have a positive association with exposure to Agent Orange or other herbicides used in Vietnam. These determinations will be based on sound medical and scientific evidence, taking into account reports from the NAS under Section 3 and all other scientific information available.

The NAS also may make recommendations for further studies to resolve areas of continuing scientific uncertainty about the health effects of exposure to herbicide agents.

Under the term of the contract with VA, the first report by the NAS is due not later than July 31, 1993.

The initial NAS report is to include recommendations as to whether programs described in sections 6-9 of Public Law 102-4 should be implemented. Any VA action on these sections will be based, to a large extent, on the recommendations in the NAS report.

The effective date of sections 6-9 is 90 days after receipt of the report unless VA determines that it is not feasible or cost-effective to carry out any or all of these programs or that implementation would not make a material contribution to the body of scientific knowledge concerning the health effects in humans of herbicide exposure. If such a determination is made, VA must notify the Senate and House Committees on Veterans’ Affairs. Implementation of each of these programs can begin only if Congress specifically makes funds available.

Section 6 requires the compilation and analysis of data from VA examinations and treatment.

Section 7 requires the establishment of an archiving system for blood and tissue samples contributed voluntarily by Vietnam veterans to facilitate scientific research on the effects of veterans’ exposure to dioxin and other agents in herbicides.

Section 8 requires VA to establish, in consultation with the NAS, a program of pilot studies of the feasibility of conducting additional scientific research on health hazards resulting from exposure to herbicide agents or service in Vietnam.

Section 9 requires VA to test for dioxin (TCDD) in any blood sample voluntarily provided by Vietnam veterans who seek VA health care under priority eligibility based on exposure to Agent Orange.

The law also authorizes follow-up reviews by the NAS, to the extent that appropriations are available, at least once every two years for ten years after the initial report.

(For additional information regarding the contract between VA and the NAS, see the April 1992 issue of the "Agent Orange Review").

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 initial newsletter was released in November 1982. Twenty issues have been published to date.

The "Review" is prepared approximately one to two months prior to the publication date. This issue was written in early July and does not include developments that occurred during much of July or August 1992.

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 requested. A limited supply of the last eight issues (October 1989, May 1990, August 1990, February 1991, April 1991, August 1991, December 1991, and April 1992) is also available. VA facilities should order additional copies from the VA Supply Depot.

VA updates the "Review" mailing address listing annually based on IRS records. "Review" recipients who have not been filing Federal income tax returns annually and have moved to another residence are encouraged to send their old and new addresses and Social Security number to the Department of Veterans Affairs, Automation Center (200/397), 1615 Woodward Street, Austin, Texas 78772-0001.

Questions about the Agent Orange Registry examination program should be directed to the Environmental Physician or Agent Orange Coordinator at the nearest VA medical center. Questions regarding VA benefit programs, including disability compensation, should be referred to a veterans benefits counselor at the nearest VA facility. The telephone numbers can be found in the telephone directory under the "U.S. Government" listings.

Vietnam Veteran Designated Acting Director of VA Agent Orange Program

On July 6, 1992, Susan H. Mather, M.D., Assistant Chief Medical Director for Environmental Medicine and Public Health, designated Layne A. Drash as Acting Director, Environmental Agents Service. That office is responsible for the development and implementation of national VA medical policies and procedures for regarding exposure by military veterans to possible environmental hazards, including Agent Orange.

Drash is a veteran of the Navy and Marine Corps. He served a 13-month tour in Vietnam in 1965-66. Since 1980, Drash has been a manager in the Agent Orange program at VA headquarters in Washington, DC. He has been the Deputy Director of the program since 1989. Drash succeeds Lawrence B. Hobson, M.D., Ph.D., who has been the Director since 1987.
Dr. Hobson retired on July 4, 1992, after an extensive and distinguished career with VA and in the private sector.

"It's been a very long and often frustrating search for answers to the many questions raised about the delayed health consequences of Agent Orange exposure," noted Drash. "I am pleased that progress is being made. With the completion of each study, we are hopefully a little closer to an ultimate resolution of this matter. As a Vietnam veteran and as the manager of the office responsible for Agent Orange-related issues, I follow both the conduct and findings of research with special interest."

Donald J. Rosenblum, Writer/Editor, has assumed the duties and responsibilities of Deputy Director on a temporary basis.

Malaskiewicz Named to Manage Registries

Helen A. Malaskiewicz, formerly of VA's Nuclear Medicine Service, recently joined the Environmental Agents Service. Her primary responsibilities include management of several registry programs (Agent Orange Registry, Ionizing Radiation Registry, and soon to be activated Persian Gulf Registry). She filled the vacancy created when Eunice Sokol transferred to a VA health care facility. Malaskiewicz works closely with Michelle B. Williams who serves as national coordinator for the registries.

The other Environmental Agents Service staff members are Laverne L. Cooper, Program Analyst, and Theresa F. Howerton, Secretary.

The mailing address for the office is Environmental Agents Service (116A), VA Central Office, 810 Vermont Avenue, NW, Washington, DC 20420. The telephone number is (202) 535-7183. The Environmental Agents Service is part of the Office of Environmental Medicine and Public Health, which also includes VA's AIDS Service, the Women Veterans Program, and the Smoke-Free Program. As Assistant Chief Medical Director for Environmental Medicine and Public Health, Dr. Mather is responsible for all of these programs.

Q's and A's

The Q's and A's (Questions and Answers) feature of the "Review" responds to questions that have been received from various sources. 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 guarantee that all questions received will be used in this column.

An individual from Parma, Ohio, recently wrote to ask about studies of Vietnam civilians. She also asked about what is included in the VA Agent Orange Registry examination. A reader in Hartford, Connecticut asked about the relationship between exposure to Agent Orange and subsequent development of testicular cancer and sterility. A man in Philadelphia asked what diseases the NAS have included in its review. Also, several inquiries have been received about skin conditions, including chloracne, basal cell carcinoma, and malignant melanoma, reported by Vietnam veterans.

Why hasn't there been more scientific research regarding the long-term health consequences of Agent Orange in the Vietnamese? It seems that this information would be helpful to Americans who served in Vietnam.

Unfortunately, medical records maintained by the Vietnamese and by many other third world countries are rather primitive. Documentation is well below standards maintained by U.S. health care professionals and by others in developed societies. This deficiency significantly hinders use of such records for scientific research.

Studies using data from Vietnam also have limited acceptance in the scientific community because of suspected political intervention into scientific matters and manipulation of medical information for political purposes. Results of research on Vietnamese were reported in the May 1990 issue of the "Review."

What is included in the Agent Orange Registry examination? How does a veteran benefit from taking the examination?

The Registry examination includes a medical history, a physical examination and special tests and consultations if the examining physician thinks one or more is needed. Each Vietnam veteran participating in this voluntary program, offered at all VA medical centers, is given the following baseline laboratory studies: chest x-ray (if one has not been done within the past 6 months); complete blood count; blood chemistries and enzyme studies; and urinalysis.

Evidence is also sought concerning the following potentially relevant symptoms or conditions: altered sex drive; congenital deformities (birth defects) among children; neoplasms or cancers, including soft tissue sarcomas and lymphomas (including non-Hodgkin's lymphomas); repeated infections; sterility; and difficulties in carrying pregnancies to term.

The examination provides participating veterans with an opportunity to receive a complete health evaluation and answers to questions concerning the current state of knowledge regarding the possible relationship between herbicide exposure and subsequent health problems.

Following completion of the examination, the veteran is given the results of the physical exam and laboratory studies. This information is provided to the veteran by both a face-to-face discussion with a physician familiar with the health aspects of the Agent Orange issue and a follow-up letter summarizing results of the examination.

Occasionally, previously undetected medical problems are found. With prompt attention, many times these illnesses can be successfully treated. Registry participants are automatically added to the mailing list for the "Review." The Registry permits VA to contact veterans for further testing if continuing research efforts should make this action advisable.

What is the relationship between exposure to Agent Orange and the development of testicular cancer and sterility?

We have long been aware of concerns expressed by Vietnam veterans about testicular cancer, sterility, and their possible relationship with exposure to Agent Orange.

A considerable amount of scientific and medical research has been initiated to assess the possible long-term health...
consequences of Agent Orange and other aspects of military service in Vietnam. While some research efforts are still ongoing, many studies have been completed. At present, there is no conclusive evidence that exposure to Agent Orange or Vietnam service is associated with either testicular cancer or sterility.

**Does VA have a list of diseases that the NAS will consider?**

Public Law 102–4, the "Agent Orange Act of 1991," directed the Department of Veterans Affairs (VA) to seek to enter into an agreement with the National Academy of Sciences (NAS) under which the NAS would review and evaluate "available scientific evidence regarding associations between diseases and exposure to dioxin and other chemical compounds in herbicides." The agreement was signed in January 1992.

The NAS review will be very broad in scope. It will undoubtedly include a wide range of illnesses that have been alleged to be related to Agent Orange and other herbicides used in Vietnam. The NAS committee conducting the review is responsible for determining what disorders will be included. VA has no definitive list of diseases to be considered and will not attempt to influence the conduct of this independent project.

We understand that the NAS review will consider the following diseases and adverse effects: (1) cancers of the stomach, colon, hepatobiliary tract, testis, prostate, kidney, and brain; Hodgkin’s disease, non-Hodgkin’s lymphoma, leukemia, and soft tissue sarcoma, and other cancers; (2) metabolic disorders, including altered lipid metabolism, porphyria cutanea tarda, and diabetes; (3) autoimmune and other immunological disorders; (4) neurologic and psychosocial disorders; (5) disorders of the digestive system, including gastrointestinal ulcers and hepatotoxic effects; (6) reproductive disorders, birth defects, miscarriages, and abnormal sperm morphology; (7) chloracne and other skin disorders; (8) circulatory disorders; and (9) respiratory disorders. Other conditions also may be considered.

**What is chloracne?**

Chloracne is a skin condition that looks like common forms of acne that affect teenagers. At present, chloracne is the only well established long-term effect of exposure to TCDD or dioxin, the contaminant found in one of the ingredients of Agent Orange.

The first sign of chloracne may be excessive oiliness of the skin. This is accompanied or followed by the appearance of numerous blackheads. In mild cases the blackheads may be limited to the area around the eyes extending along the temples to the ears.

In more severe cases blackheads may appear in many places on the body, especially over the malar (or cheek bone) area, other facial areas, behind the ears, and along the arms. The blackheads are usually accompanied by fluid-filled cysts and by an increased or darker growth of body hair. The skin may become thicker and flake or peel. In severe cases, the acne may result in open sores and permanent scars. The condition fades slowly after exposure. Most cases disappear within months, but more severe cases may persist for years after the exposure.

Physicians, even dermatologists, sometimes have difficulty in distinguishing chloracne from other more common skin disorders. While chloracne may be a sensitive indicator of exposure to dioxins in some people, it may not be in other individuals who had equal or greater exposure to dioxins. The absence of chloracne is not necessarily a reliable basis for concluding that a person has not been exposed to a chemical which is known to cause chloracne.

While a large number of veterans have complained of skin problems, chloracne has not been diagnosed in many of these veterans. Skin ailments are the most common medical problem in veteran and non-veteran populations.

Vietnam veterans who think they may have chloracne are encouraged to contact the nearest VA medical center for an examination. These veterans may be eligible for medical treatment. They may also wish to file a claim for disability compensation at the nearest VA medical center or regional office. For many years, VA has recognized chloracne as a service-connected disability based on the results of scientific research that links this condition with exposure to dioxin.

**What is basal cell carcinoma?**

Basal cell carcinoma has a number of other names, including basal cell epithelioma and rodent ulcer. It is said to be the most common malignant tumor of the white population being especially common among fair-skinned people. It usually occurs in skin areas exposed to sunlight and most frequently in men over 40 years old whose occupations regularly expose them to the sun. Sunlight-induced skin changes called actinic keratoses often preceed or accompany basal cell carcinoma.

These associations suggest that the tumors are caused by the actinic or UV rays of sunlight but this is less certain than is the association of UV exposure with some other skin diseases. Basal cell carcinoma has followed exposure to large doses of other radiation such as x-ray and it occurs in burn or vaccination scars. It has not been linked to chemical contact or poisoning.

Basal cell carcinoma spreads, usually slowly, into adjacent skin areas. The center of the area may slough, the rim may thicken, and the edge may be undermined. While unsightly and occasionally extensive, the spread involves only the skin. The outcome is rarely if ever fatal even though a person may have several areas affected. Basal cell carcinoma has been called the most benign of cancers, and some scientists doubt that it is a true cancer.

Treatment, especially if early, is comparatively simple and almost always successful. The carcinoma usually is removed surgically although small ones may be managed with drugs. The cure rates generally are 90-95 percent, with local recurrences accounting for most failures.

**What is malignant melanoma?**

Malignant melanoma is a skin cancer arising from pigment cells and is black or dark brown. It may arise in a mole, a dark freckle, or in an unpigmented area, such as the palm or sole. White persons, especially those with very light skin, are most susceptible. They may experience a malignant melanoma on most parts of the body. Dark-skinned persons who develop a malignant melanoma usually have the cancer on the palm or sole. There is evidence of a clear association between malignant melanoma and exposure to sunlight, but the cancer may appear on a part of the body not ordinarily exposed to the sun.
Dermatologists recognize several types of malignant melanoma. All are potentially serious and may be fatal if not treated early and well. The recommended treatment is surgical and involves wide removal, usually including taking out all of the regional lymph nodes. Drug treatment has met with little success to date although some newer agents offer promise.

There are few clues, other than those suggesting sunlight, as to the cause of malignant melanoma and the recent observation of an increasing occurrence among young women in northern countries and Australia. There is no accepted evidence of a link between malignant melanoma and any substance whether through skin contact or general poisoning.

Note: There are other pigmented skin diseases called melanomas that are not cancerous. Properly speaking, moles, freckles, "age spots," Mongolian spots (in the congenital condition of trisomy 21), and some birthmarks are melanomas. Although not cancers, some have been misdiagnosed at times as "malignant melanoma."

**Research Office Wins Group Award**

*Environmental Epidemiology Service Award-Winning Research Organization*

On June 12, 1992, Robert H. Roswell, M.D., Associate Deputy Chief Medical Director (Clinical Programs), presented a group citation to the Environmental Epidemiology Service (EES), the VA office responsible for the conduct of Agent Orange research and scientific investigations on related matters.

The award acknowledges the "outstanding support" of the EES staff in conducting "significant scientific research designed to assist in the resolution of health care issues of concern to our Nation's veterans."

Han K. Kang, Dr. P.H., has been the Director of the EES since 1983. The other current staff members are Larry Stockmoe, Administrative Officer; Nancy Dalager, Health Statistician; Hazel M. Hawkins, Computer Systems Analyst; Tim A. Bullman, Statistician; Claire M. Mahan, Ph.D., Statistician; Kevin K. Watanabe, Statistician; Lillian B. Gore, Research Assistant; Shirley Conover, Secretary; and Antoinette Workman, Secretary.

EES personnel have authored or co-authored the articles about completed scientific studies as described below:

**Terminology**

Some people have experienced difficulty understanding medical or technical language often used in discussions of Agent Orange-related matters. The August 1991 issue of the "Agent Orange Review" included a glossary designed to assist readers having this problem.

The following items were described in the August 1991 listing: Agent Orange, Agent Orange Brief, Agent Orange Coordinator, Agent Orange Registry, Agent Orange Review, Agent Orange Veteran Payment Program, chloracne, Compensation and Pension Service, diabetes, dioxin, disability compensation, Environmental Agents Service, Environmental Physician, non-Hodgkin’s lymphomas, peripheral neuropathy, porphyria cutanea tarda (PCT), Ranch Hand, and Soft tissue sarcomas.

Additional terms are defined below. Other words may be explained in future issues of the "Agent Orange Review."

**Agents Blue and White**: two of fifteen herbicides used in Vietnam. The names are derived from the color of the stripe on the storage drums. (Over eighty percent of the herbicides sprayed in Vietnam was Agent Orange). The active components of Agent Blue were primarily cacodylic acid and the sodium salt of cacodylic acid. Agent White was a formulation of picloram and 2,4-D. Agent Orange was a reddish-brown or tan liquid; Blue, a clear yellow-tan liquid; and White, a dark brown liquid.

**Bias**: systematic error which leads to a distortion of the relationship between two variables in an epidemiologic study, for example, between exposure to a chemical and the appearance of a specific disease.

**Cacodylic acid**: an arsenic-containing herbicide. The cacodylic acid and the sodium salt of cacodylic acid were used to make Agent Blue.
**Case:** a subject in a case-control study who is selected on the basis of having some particular disease.

**Case-control study:** a scientific investigation in which case subjects are chosen on the basis of having a particular disease and control subjects are selected on the basis of absence of the disease. Controls are usually selected to be as similar as feasible in such ways as age, sex, race, and experiences.

**Cohort:** a group of individuals who share certain characteristics (examples, military service in Vietnam, military service in I Corps in Vietnam).

**Cohort study:** a scientific investigation in which the study cohorts selected differ in certain characteristics (a cohort of Vietnam veterans might be compared to a cohort of veterans who served elsewhere). The cohorts are followed into the future and the occurrence of disease is observed.

**Confounding factors:** in epidemiology, characteristics which may distort the apparent relationship between two variables under study, for example, a marked age difference between members of two cohorts.

**Congenital:** medical condition present at birth.

**Control group:** a comparison group. In a case-control study, the control group consists of those without the disease of interest; in a cohort study, the control group consists of those without the characteristic of interest.

**Defoliant:** an agent capable of causing leaf shedding by plants.

**Epidemiologic study:** research into the distribution and determinants of stages of health in human populations.

**Half life:** the time required for one-half of the amount of a chemical present to be removed, destroyed, or changed to another form.

**Herbicide:** a chemical that injures or kills plants.

**Malathion:** a compound used in Vietnam as an insecticide to control mosquito populations.

**Morbidity:** refers to disease. A morbidity study examines the types and occurrence of diseases in a population.

**Mortality:** refers to death. A mortality study examines causes and frequencies of death in a population.

**Neuropathy:** a disease or disorder of the nervous system.

**Pathology:** the study of the structural and functional changes that cause or are caused by disease.

**Pesticide:** a chemical used to kill plant or animal pests.

**Picloram:** an herbicide used in combination with 2,4-D to form Agent White.

**Proportionate Mortality Study:** an analysis which compares the relative importance of a specific cause of death to the total number of deaths.

**Samoma:** a malignant tumor (cancer) derived from the connective tissue.

**Spina bifida:** a class of birth defects characterized by an abnormal opening in the bony casing of the spinal cord.

**Subcutaneous:** beneath the skin.

**Syndrome:** a set of signs and symptoms that occur together.

**Teratogenic:** capable of causing birth defects, either anatomic or functional.

**Toxicologic:** pertaining to the study of poisonous (toxic) substances.

**Trisomy:** three chromosomes of one type in a person (example: three number 21 chromosomes in Down syndrome due to trisomy 21).

**UV:** ultraviolet.

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**Class Action Lawsuit Referral Information**

The Department of Veterans Affairs (VA) has received many inquiries regarding the status of claims for 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 t 10, Hartford, Connecticut 06104.