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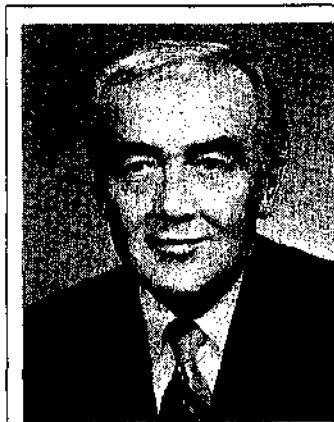
On May 1, 1981, the Veterans Administration awarded the contract for the design of an epidemiological study of Vietnam veterans exposed to phenoxy herbicides to a team of scientists at the University of California at Los Angeles.

Drs. Gary Spivey and Roger Detels will direct the design effort. Dr. Spivey is associate professor of epidemiology at the UCLA School of Public Health. Dr. Detels is dean of that school.

The VA should be provided with the design in August. The results will then be evaluated by the National Academy of Sciences-National Research Council, Congressional Office of Technological Assessment, the Interagency Work Group to Study the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants, and the Veterans Administration Advisory Committee on Health-Related Effects of Herbicides.

The epidemiological study was mandated by the Veterans Health Programs Extension and Improvement Act of 1979, Public Law 96-151, enacted in December 1979. The Veterans Administration issued a request for proposals to design the study in March 1980, but complex legal challenges significantly delayed the awarding of the design contract.

The study is being designed at the cost of \$114,288.



Donald L. Custis, M.D., Chief
Medical Director of Veterans
Affairs

The Chief Medical Director on Agent Orange examinations:

"The entire examination process, from the time the veteran first enters the outpatient clinic to the conclusion of the physical examination, should be an experience which affirms our commitment to allaying unfounded fears and responding to medical needs in a warm, friendly, and compassionate manner."

- DONALD L. CUSTIS, M.D.

Follow Up Improved:

Every veteran to be advised personally

In response to problems noted by an internal survey, Agent Orange examinations and follow-up procedures have been revised and improved.

A sample survey of veterans' satisfaction with Agent Orange examinations was conducted in October/November 1980 by the Office of Environmental Medicine (102) at the request of the Administrator and the Chief Medical Director. Responses

See Follow Up page 2

International Dioxin Symposium Planned in Washington, D.C.

An international symposium on chlorinated dioxins and related compounds will meet in Washington, D.C. this fall, under the sponsorship of health agencies and independent professional societies.

Barclay M. Shepard, M.D., Special Assistant to the Chief Medical Director for Environmental Medicine (102), said current plans are to convene the meeting in the final week of October 1981.

The purpose of the symposium will be to address the risk of chlorinated dioxins and related compounds to human health

and the environment. Principal objectives are to present new information, summarize existing and contradictory data, and through panel discussion, establish scientifically valid conclusions and future research needs.

The symposium is an outgrowth of the international workshop addressing similar matters held in Rome, Italy, October 22-24, 1980.

Although plans have not yet been finalized, an outline for the meeting has emerged. The four-day symposium,

See Symposium page 2

Follow Up contd.

were received by approximately 55 percent of the 643 veterans to whom the questionnaire was distributed.

The veterans participating were examined at one of the following seven medical centers: Allen Park, Columbia, Madison, Minneapolis, San Francisco, St. Louis, and Washington.

An analysis of the survey suggested that in many cases VA physicians did not discuss the results of the physical examination with the veteran nor was the veteran apprised of the finding of laboratory tests.

Although the survey represented a very small sample of the more than 45,000 veteran examinations, it was deemed a useful indicator of some of the strengths and weaknesses of the examination. It suggested that some improvements in the examination procedures were necessary.

On January 15, 1981, revised directions for Agent Orange examination procedures (DM&S Circular 10-81-12) were distributed to all VA health care facilities to accomplish the needed improvements.

The circular directs that each veteran examined be advised personally of the results of the physical examination (including both positive and negative findings) by the environmental physician (or other designated physician familiar with the Agent Orange program).

In addition to this personal interview, a follow-up letter must be sent to each veteran explaining the results of the examination and associated laboratory tests, including those within the normal range. The circular also directed that each veteran be given the pamphlet "Worried About Agent Orange?" at the time of the initial examination.

Symposium contd.

scheduled for October 26-29 (with registration on October 25), will be held at the Sheraton National in Arlington, Virginia.

The symposium will include platform sessions and "blue-ribbon" panel meetings. As presently conceived, the first day's activities will consist of two sessions. The morning session will be an overview of the problem from various perspectives. In the afternoon, the technical session chairpersons will present overviews of the technical areas that are to be addressed during the remainder of the symposium.

The second and third days will contain concurrent sessions on analytical and environmental chemistry, toxicology, human observation, laboratory safety and waste management.

The final day will be devoted to sessions on risk assessment and panel reports. The reports will be developed by the various panels and will contain conclusions on existing information and recommendations for further research and analysis.

Each panel will be chaired by the corresponding technical session chairperson and will consist of the leading experts in industry, government, and academia.

When additional information and details are available, they will be disseminated through the *Bulletin* and/or by other means.

Recent Conferences /Hearings/Meetings

April 18-19 Second Annual Western Regional Conference of Vietnam Veterans in Eugene, Oregon. **Dr. Donald Belcher** of VAMC Seattle and **Dr. Keith Marton** of VAMC Palo Alto, advised the conferees of the agency's activities relative to the Agent Orange problem. Drs. Belcher and Marton are environmental physicians at the above mentioned VA facilities.

April 28 Congressional Hearing—Subcommittee on Hospitals and Health Care, Committee on Veterans' Affairs, U.S. House of Representatives. **Dr. Donald L. Custis**, Chief Medical Director, testified on legislation that would expand the scope of the Agent Orange epidemiological study mandated by Public Law 96-151. He also explained the VA position on legislation that would authorize hospital or outpatient care for a Vietnam veteran if a VA or fee basis physician determine that such care is necessary for the treatment of a condition that may be associated with exposure to Agent Orange.

April 30 Congressional Hearing—Committee on Veterans' Affairs, U.S. Senate. **Dr. Turner Camp**, Associate Deputy Chief Medical Director, expressed the VA views on a number of proposals. Legislation discussed included bills to provide for compensation and treatment for conditions deemed to have resulted from exposure to toxic substances or radiation, to authorize expansion of the epidemiological study, and to require the VA to develop regulations for resolving claims for benefits based on Agent Orange exposure.

May 5 Public Meeting - VA Advisory Committee on Health-Related Effects of Herbicides, VA Central Office. The eighth meeting of the Advisory Committee featured the announcement of the awarding of the epidemiological study design contract, a progress report on the literature analysis, reports from veterans' service organizations and state governmental units, a presentation concerning the research efforts of the Environmental Epidemiology Branch of the National Cancer Institute, and an open discussion of future educational needs. As in earlier meetings, a period was reserved for questions from the audience. Approximately 60-75 people attend the quarterly meetings. The next meeting is planned for August 19. **Dr. Barclay M. Shepard**, Special Assistant to the Chief Medical Director for Environmental Medicine, chairs the Advisory Committee. In April 1981, the Committee was renewed for a two year period. It was established in April 1979.

May 6 Congressional Hearing—Subcommittee on Oversight and Investigations, Committee on Veterans' Affairs, U.S. House of Representatives. **Dr. William J. Jacoby, Jr.**, Deputy Chief Medical Director, provided an update of the VA Agent Orange-related activities. He elaborated on the status of the epidemiological study and literature analysis. **Dr. Barclay M. Shepard** accompanied Dr. Jacoby and those who testified at the earlier Congressional hearings.

Advisory Committee Briefed on Monsanto Studies

The latest in a series of three extensive studies of the workers in a Nitro, West Virginia, herbicide production plant indicates deaths among the group were unrelated to dioxin exposure.

William R. Gaffey, Ph.D., presented these and other findings to the VA Advisory Committee on Health-Related Effects of Herbicides on November 6, 1980. The study focused on possible relationship between TCDD and the cause of death of 58 employees potentially exposed to the contaminant during 2, 4, 5-T herbicide production at the Monsanto plant in Nitro.

Dr. Gaffey is the Manager of Epidemiology in the Department of Medicine and Environmental Health for the Monsanto Company at St. Louis. He co-authored the study with another Monsanto epidemiologist, Judith A. Zack.

Their investigation examined the cause of death of workers who had been active employees of the plant for one or more years between 1955 and 1977 and have since died. The entire group was successfully traced and all deaths verified by death certificates.

Earlier Study

This study represents the second major effort undertaken to examine the mortality of Nitro plant workers, exposed or potentially exposed to TCDD. Mrs. Zack and VA Advisory Committee member Raymond R. Suskind, M.D., of the University of Cincinnati Medical Center co-authored a related study of employees who experienced high peak exposure to TCDD during a plant accident in 1949. The results of that investigation, published in *The Journal of Occupational Medicine* in January 1980, indicated no excess in total deaths or in deaths from cancer or cardiovascular disease.

In this larger follow-up effort, the mortality experience of the total Nitro plant workforce was analyzed by the modified life-table method using the U.S. population as the standard. Of the 884 men identified for study, 721 (82%) were verified as still alive and 163 (18%) were confirmed dead by death certificates. The study found no statistically significant excess in total deaths or deaths due to cancer or disease of the nervous system, circulatory system, respiratory system or digestive system.

The study did confirm and quantify an apparent excess in bladder cancer among Nitro plant workers (nine observed vs. 0.91 expected), a finding known for many years. This result reflects the established and previously documented association between exposure to Para-aminobiphenyl (PAB) and cancer in man. PAB was used at Nitro from 1941 through 1952, as a rubber antioxidant and dye intermediate. Its use was discontinued when its cancer-causing potential was confirmed.

The author pointed out that an intensive screening program was instituted by the company about 1955 to examine, on a continuing basis, all workers exposed to this chemical. Seven PAB-related deaths from bladder cancer have occurred among Nitro plant employees enrolled in this program over these 25 years. These seven deaths are included in this study.

A review of the work history records of the 163 decedents further revealed that 58 (35.6%) had been exposed to 2, 4, 5-T and potentially to TCDD. One hundred four (63.8%) were considered non-exposed and the exposure of one dece-

dent was not determined. The mortality experiences of these two subgroups were then compared using the proportional mortality method. This was done to test whether any relationship existed between potential TCDD exposure and proportional mortality. No such relationship was observed nor were any unusual patterns of mortality found in this exercise other than the PAB-related deaths described earlier.

The expected number of deaths in the 2, 4, 5-T subgroup was calculated on the basis of the percentage of deaths from various causes in the U.S. general population. Specifically, cancer deaths among 2, 4, 5-T workers (nine observed versus 10.94 expected) were found to be lower than in the non-exposed group (25 observed versus 20.43 expected).

Deaths due to disease of the nervous system, respiratory system and digestive system were also found to be lower than one would expect to find in a group of this size.

While not statistically significant, deaths due to disease of the circulatory system (largely arteriosclerotic heart disease) were elevated at 31 versus 26.48 expected. The analysis of the total Nitro plant population found a similar excess in deaths from arteriosclerosis. In the discussion section, the author pointed out that these excesses most likely reflect the higher mortality from heart disease which has been observed for the general population of Charleston and Kanawha County, W. Va.

Third Study

A third study, based on health information gathered from extensive physical examinations of over 400 present and former Nitro plant employees is currently being conducted solely by Dr. Suskind and his medical team from the University of Cincinnati's Institute of Environmental Health.

Included in this ongoing study are both those workers exposed during the 1949 accident as well as those exposed during normal 2, 4, 5-T operations between 1948 and 1969 when the unit was shut down. A control group of employees who worked in other areas of the plant during that time frame is also being studied for comparative purposes.



William R. Gaffey, Ph.D.

Literature Review Progresses

On December 15, 1980, the Veterans Administration awarded a nine-month contract to JRB Associates, Inc., of McLean, Virginia, to conduct a review and analysis of the world-wide literature on herbicides used in Vietnam, including the phenoxy herbicides and their associated dioxins.

The primary aim of this effort is a critical appraisal of the world literature on phenoxy herbicides and their contaminants. The review includes both automated and manual searches of literature sources, analysis of relevant documents by JRB scientists and a panel of expert consultants, and the preparation of a comprehensive annotated bibliography.

JRB Project Manager James F. Striegel, Ph.D., anticipates that "1,500 articles relevant to the research criteria will be identified, acquired, annotated, and reviewed for scientific merit and pertinent findings."

The investigation concentrates on the two phenoxy herbicides in Agent Orange, 2, 4-D and 2, 4, 5-T and the contaminant 2, 3, 7, 8-tetrachlorodibenzo-*p*-dioxin. Areas of concern include environmental transport and fate, and potentials for prolonged chronic toxicity, delayed toxicity, carcinogenicity, and birth defects that may result from applications similar to those used in Vietnam.

JRB Associates

JRB is a part of Science Applications, Inc. Together, JRB and SAI have a professional staff of over 4,000 scientists and researchers, with offices in 70 cities across the country. JRB has major contractual commitments with the Environmental Protection Agency, the National Institutes of Health, the Occupational Safety and Health Administration, the National Institute of Occupational Safety and Health, the Department of Defense, and other Federal, State, and private agencies. Its staff includes one of the largest environmental and occupational health and safety consulting groups in the country.

JRB is conducting an independent literature search and analysis, and will not be directed to findings or conclusions by the Veterans Administration.

The review was mandated by the Veterans Health Programs Extension and Improvement Act of 1979, Public Law 96-151. The review is being performed at a cost of \$109,402.

Library Notes

(Library Notes is a regular feature of the *Bulletin*. It is intended to advise physicians of publications concerning Agent Orange and related subjects).

DiGiovanni, J.; Berry, D.L.; Gleason, G.L.; Kishore, G.S.; and Slaga, T.J. "Time-dependent Inhibition by 2, 3, 7, 8-tetrachlorodibenzo-*p*-dioxin of Skin Tumorigenesis with Polycyclic Hydrocarbons," *Cancer Res.* 40(5):1580-87. May 1980.

Homberger, E.; Regianni, G.; Sambeth, J.; and Wipf, H.K. "The Seveso Accident: Its Nature, Extent and Consequence," *Ann. Occup. Hyg.* 22(4):327-67. 1979.

Kimble, B.J.; and Gross, M.L. "Tetrachlorodibenzo-*p*-Dioxin Quantitation in Stack-Collected Coal Fly Ash," *Science* 207(4426):59-61. Jan. 4, 1980.

Correspondence Symbol Change

Additional mailing symbols for the Office of the Special Assistant to the Chief Medical Director for Environmental Medicine (often shortened to the Office of Environmental Medicine) have been established. Dr. Barclay M. Shepard, the Special Assistant, and secretary Elaine M. Beauparlant will continue to be assigned the symbol 102. Dr. Lawrence B. Hobson, Clinical Assistant, and Layne A. Drash, Staff Assistant, will be designated 102A and 102B, respectively. Correspondence to all other office staff should be addressed with the symbol 102C. Examination code sheets should be sent to 102D.

AO Conference Calls

On March 16, 1981, the Office of Environmental Medicine (102) conducted the first of a series of ongoing nationwide conference calls on the subject of Agent Orange. A second conference call was held on May 18.

The one-hour sessions provide Central Office staff an opportunity to inform key health care personnel at VA medical facilities of new developments. These calls serve as a training mechanism and provide for a dialogue on significant Agent Orange issues or problems.

Field participants include Chiefs of Staff, Associate Chiefs of Staff for Ambulatory Care, Environmental Physicians, Chiefs of Medical Administration Service, Agent Orange Coordinators and other staff who may be designated by the health care facilities to participate in these conferences.

The next conference call is scheduled for July 20, 11:30 a.m. EST. It is anticipated that these conferences will continue to be held approximately nine weeks apart.

GAO Reviews AO Program

At the request of Senator John Heinz (Pennsylvania) and Congressman Thomas Downey (New York), the General Accounting Office is conducting a review of the efforts of the Veterans Administration to assist veterans exposed to Agent Orange.

The review includes evaluations of the implementation of the agency's Agent Orange examination program at VA medical centers, policies for adjudicating Agent Orange-related disability compensation claims, and the need for an Agent Orange outreach program.

Much of the review is being conducted at VA Central Office. However, a number of medical centers were scheduled for on-site visits. These included Atlanta, Augusta, Birmingham, Chicago (Westside), East Orange, Hines, Long Beach, Minneapolis, New York, Northport, Pittsburgh (University Drive), Wadsworth, and Wilkes-Barre.

John C. Hansen, Senior GAO Evaluator is directing the review.

Pamphlets at Depot

The VA pamphlet "Worried about Agent Orange?" has been reprinted and substantial supplies are available at the VA Forms and Publication Depot (036B), from which they can be ordered directly when the supply at a field station nears depletion. A total of 700,000 copies of the pamphlet were printed since the summer of 1980.

Displaying the pamphlet in prominent locations ensures that veterans are aware of VA programs and activities.

It is anticipated that the pamphlet will be updated and revised later this year. Suggestions and recommendations may be directed to Layne Drash (102B), VA Central Office, Washington, D.C. 20420. He can be contacted by telephone at FTS 389-5411.

European Studies Reviewed

In recent months considerable attention has been given the so-called "European Studies," i.e., four from Sweden and one from West Germany. There are a number of publications on the carcinogenic potential of herbicides and dioxins, but these five have been given prominence during the current EPA hearings on 2, 4, 5-T and recent congressional hearings on Agent Orange.

The Swedish studies comprise three case-control investigations of forestry and other rural workers, by Hardell and his co-workers* and a cohort study of railroad workers by Axelson and his collaborators.** The German paper by Thiess and Frentzel-Beyme dealt with workers who were exposed to TCDD during an industrial accident in 1953.***

Hardell's group matched 52 patients who had soft-tissue sarcoma with 208 controls without the tumors and found that 19 sarcoma patients were reported to have been exposed to chemicals as were 19 of the controls. They concluded that there was a 6-fold increase in the risk of sarcoma in those exposed to phenoxyacetic acid defoliants (of the 2, 4, 5-T type) or to chlorophenol. Exposure to only phenoxyacetic acids apparently increased the risk by 5-fold but it was not possible to determine what specific compounds were responsible.

The second study by the group used the same technique as the first with 110 men who had soft-tissue sarcoma and 219 controls. Workers in forestry and agriculture had a risk for soft-tissue sarcoma 5-fold greater than that of other workers. It was calculated that exposure to phenoxyacetic acid herbicides carried a risk of slightly less than 6-fold that of unexposed workers.

Hardell's group in their third study concentrated on malignant lymphoma, including 60 patients with Hodgkin's disease, 53 with follicular center cell and 52 with other types of non-Hodgkin's lymphoma. There were 335 controls. Exposure to phenoxyacetic acids or chlorophenols increased the risk by 5.6 fold; the phenoxy acids by almost 5-fold.

Axelson's group studies 348 Swedish railroad workers and concluded that those exposed to phenoxyacetic acid herbicides had a 1.9 risk ratio of cancer deaths when compared to workers without known exposure. The difference was most marked for stomach cancer although the numbers were very small - two cases observed versus 0.33 expected.

The Bulletin

The *Bulletin* is prepared by the Office of the Special Assistant of the Chief Medical Director for Environmental Medicine (102). This newsletter is published on an irregular basis, approximately 3-4 times annually. It is not directive in nature and does not have the force of law or regulation. It is intended, rather, as an unofficial means of providing physicians and other medical staff charged with the responsibility of coordinating Agent Orange activities at VA facilities with information regarding recent developments.

Comments, criticisms, and articles from physicians and other interested staff members are encouraged. Material should be sent to Donald Rosenblum (102C), VA Central Office, Washington, D.C. 20420. Environmental physicians are urged to submit articles or notes of significant activities and events at or near their facilities.

Beginning with the next issue, the *Bulletin* will include articles on a variety of environmental concerns. Possible subjects include Dapsone, sulfa drugs, arsenic, and radiation exposure.

Frentzel-Beyme followed 75 persons exposed to TCDD and compared them to the local population, to that of the government district and to that of West Germany. Six fatal malignancies among the workers were almost double the expected rates; gastrointestinal cancers occurred in four of the six.

Criticisms have been leveled at some or all of these studies by various reviewers. The authors themselves caution that the design of the case-control studies and the small numbers in the others limits the significance of the results to something less than proof of a causal relationship between exposure to phenoxyacetic acids or TCDD and the subsequent development of cancer. They must, however, be carefully considered as guides to future investigations.

*Hardell, L. and A. Sandstrom. 1979. *Brit. J. Cancer*, 39:711-717. Eriksson, M., L. Hardell, N. O. Berg, T. Moller, and O. Axelson. 1979. *Lakartidningen*, 76:3872-3875. Hardell, L., M. Eriksson, and Per Lenner. 1980. *Lakartidningen*, 77:208-210.

**Axelson, O., L. Sundell, K. Anderssen, C. Eding, C. Hogstedt, and H. Kling. 1980. *Scand. J. Work Environ. Health*, 6:73-79.

***Thiess, A. M. and R. Frentzel-Beyme. 1977. V International Conference of MEDICHEM, San Francisco.



Clinical Assistant Lawrence B. Hobson, M.D., Ph.D. briefs several members of Environmental Medicine Staff on European studies, from left, Secretary Elaine Beauparlant, Staff Assistant Layne Drash, Dr. Hobson, Program Analyst Don Rosenblum, and Technical Assistant Fran Reed.

Videotape Distributed

In January 1981, a copy of the recently completed videotape, "Agent Orange: A Search for Answers" was distributed to all VA medical centers, independent outpatient clinics, regional offices, operation outreach vet centers, and Information Service Area Directors.

The videotape has three primary objectives: (1) to relieve unwarranted anxiety about possible health effects resulting from exposure to Agent Orange, (2) to reassure concerned veterans and the public that everything possible is being done to resolve the remaining issues about the use of herbicides in Vietnam, and (3) to inform veterans on the most effective ways to utilize VA health care resources.

Essentially, the videotape explains what Agent Orange is, where and how it was used in Vietnam, why concerns have arisen among those exposed to it, and what the VA is doing in response to these concerns.

The videotape, produced under the guidance of the Department of Medicine and Surgery by the Learning Resources Medical Media Production Service in St. Louis, Missouri, is currently being shown to veterans and the general public at VA facilities on a regular basis. Medical centers are encouraged to provide frequent showings in outpatient waiting areas where possible.

Requests from television stations for showing the videotape should be directed to the appropriate Information Service Area Director.

The 16mm film reproduction of the videotape was delayed by the recently imposed government-wide moratorium on reproduction of audiovisuals, but reproduction is now proceeding.

Questions regarding the videotape may be referred to Layne Drash, Office of Environmental Medicine, (FTS) 389-5412 or Stratton Appelman, Information Service (FTS) 389-2741.

AFIP Registry Seeks Tissue from Hospitals Across Nation

The Agent Orange Registry of the Armed Forces Institute of Pathology (AFIP) was established to find out what the current medical problems of Vietnam veterans are, as reflected in biopsy and autopsy material, and to assist in determining whether any of the illnesses seen are related to exposure to Agent Orange in Vietnam.



Dr. Nelson Irey Directs AFIP Agent Orange Registry

(For directions concerning the AFIP Registry, please refer to Circular 10-80-229, dated October 15, 1980).

This Registry was designated as a center for the collection and study of biopsied and autopsied tissue by the VA and the Surgeons General of the Army, Navy, and Air Force. It has been operational for more than two years and is receiving

Agent Orange Registry Statistics

Agent Orange Examinations Reported (as of April 30, 1981) Cumulative number of initial examinations - 46,745

Top Ten Stations -

Minneapolis	5152	Buffalo	1072
Allen Park	1400	Martinez	1061
East Orange	1294	Wilkes-Barre	1052
Wood	1203	Nashville	1013
Fargo	1169	Baltimore	942

A.O. Film Becomes Award Winner

The videotape "Agent Orange: A Search for Answers" described to the left received recognition from two sources during the month of May.

On May 10, the Health Education Communication Association and the Network for Continuing Medical Education presented an award of merit for "outstanding achievement in the use of television for education in the health sciences."

The International Television Association (ITVA) awarded its Golden Reel of Excellence, May 30, for the program's "highly effective form of communication, which helped the user organization better achieve its stated goals." The program was also cited by ITVA for creativity, innovative techniques, and high production values.

pathological material from various hospitals, including VA medical centers throughout the country. Specimens from more than 200 Vietnam veterans have been received.

The Registry is particularly focusing on tumors and on changes in the various organs that might be a consequence of previous toxicity. No conclusions can be drawn yet as to a possible relationship between its findings and causation by Agent Orange exposure in Vietnam.

Because of the nature of the materials received, the Registry will not take part in the study of deformities of veteran's children nor will it address problems of a neurobehavioral nature.

Findings that would be of particular significance are the appearance of unusual tumors or increased frequency of any particular category of tumors. Such findings would prompt appropriate epidemiological studies with matched controls of persons that have not served in Vietnam.

Dr. Nelson Irey chairs the Department of Environmental and Drug Induced Pathology which maintains the AFIP Agent Orange Registry.