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MEMORANDUM FOR DR. BEVERLY J. BERGER

FROM: DR. ALVIN L. YOUNG

SUBJECT: Talking Paper on Agent Orange

BACKGROUND: In 1981, President Reagan established the White House Agent Orange Working Group (AOWG) of the Cabinet Council on Human Resources (now Domestic Policy Council). Lead Agency responsibility for the Working Group was given to the Department of Health and Human Services (generally, the Under Secretary or Assistant Secretary for Health has chaired). Twelve Federal Agencies, including the Office of Science and Technology Policy, were initial members of the AOWG. For the past year, membership in the "policy" body of the AOWG (a Science Panel reports to the Chair) has consisted of Departments of Defense, Health and Human Services, and Justice, Veterans Administration, OMB and OSTP. Current research is conducted by the Air Force (The Air Force Health Study), the Department of Health and Human Services and the Veterans Administration. In the last five years the Administration has spent \$155 million on the conduct of health-related studies.

CURRENT RESEARCH: The AOWG Research Agenda has primarily focused on the issues of birth defects in children of the Vietnam veterans, early death of Vietnam veterans, rare cancers, and dioxin in human tissues. A large case-control epidemiologic study by the Centers for Disease Control, and a large cohort epidemiologic study by the Australian Government of their Vietnam veterans, have addressed the issue of birth defects. Both studies concluded that Vietnam veterans are not at increased risk of fathering children with birth defects.

The following pages highlight the results of the mortality, cancer, and dioxin studies.

POSTSERVICE MORTALITY AMONG VIETNAM VETERANS

- o December 1986 Mortality Update of The Air Force Health Study. (1)
 - The Air Force Health Study is a cohort epidemiologic study to determine whether those individuals involved in the aerial spraying of herbicides in Vietnam during the RANCH HAND Operation have experienced any adverse health effects as a result of their participation in that program.
 - The study is designed to evaluate both mortality and morbidity over a 20-year period beginning in 1982.
 - As of December 1985, 4.7% of the Ranch Hand cohort (59 of 1257) had died compared to 5.1% of the control cohort (312 of 6171). The difference in percentage is not statistically significant.
 - The study has so far failed to demonstrate health effects which can be attributed to herbicide or dioxin exposure.

- o February 1987 Mortality Results of the CDC Vietnam Experience Study. (2)
 - Postservice mortality (through December 1983) of a cohort of 9324 U.S. Army veterans who had served in Vietnam was compared with that of a cohort of 8989 Vietnam-era Army veterans who did not serve in Southeast Asia.
 - Total mortality was 17% higher in Vietnam Veterans. (246 of 9324 vs. 200 of 8989).
 - Excess mortality occurred mainly in the first five years after discharge from active duty and involved motor vehicle accidents, suicide, homicide, and accidental poisonings.
 - Drug-related deaths for Vietnam veterans continued to be elevated beyond the first five years.
 - A deficit in deaths from diseases of the circulatory system was found among Vietnam veterans.
 - Although this mortality study failed to demonstrate that any cause of death was associated with Agent Orange exposure, the morbidity report of these cohorts has not been released. That report is due in early fall 1987.

RARE CANCERS IN VIETNAM VETERANS OR IN POPULATIONS EXPOSED TO PHENOXY HERBICIDES

- 1986 NCI Study of Lymphoma and Soft-Tissue Sarcoma in Kansas. (3)
 - In a case-control study of 443 rare cancers identified from the State of Kansas Cancer Registry (diagnosed 1976-1982) and compared to 948 controls, men exposed to phenoxy herbicides more than 20 days per year had a sixfold increased risk of Non-Hodgkin's Lymphoma (NHL).
 - Neither Soft-Tissue Sarcoma nor Hodgkin's Disease was associated with pesticide exposure.
- 1986 Study by the Veterans Administration of Soft-Tissue Sarcoma and Military Service. (4)
 - A hospital-based case comparison group study was undertaken to examine, through a comprehensive review of medical records and military personnel records, the association between previous military service in Vietnam and Soft-Tissue Sarcoma.
 - The case group comprised 234 Vietnam-era veteran patients who served in U.S. military between 1964 and 1975 and were treated in one of the 172 VA hospitals between 1969 and 1983 with a diagnosis of Soft-Tissue Sarcoma.
 - The comparison group consisted of 13,496 patients who ^{were} systematically sampled from the same Vietnam-era veteran patient population from which the cases were drawn.
 - The study found no association of Soft-Tissue Sarcomas and previous military service in Vietnam.
- 1987 Western Washington Study of Soft-Tissue Sarcoma and Non-Hodgkins Lymphoma in Forestry and Farm Workers. (5)
 - *Study consisted of 694 cases of cancer and 704 controls.*
 - Estimated risks of Non-Hodgkins Lymphoma were elevated among men who had been farmers (1.33), forestry applicators (4.80). and for those exposed to phenoxy herbicides in any occupation for at least 15 years (1.71).
 - No increased risk for Soft-Tissue Sarcoma.
 - Scandinavian heritage may increase risk to NHL.

A population-based case-control study was conducted to evaluate relationship between occupational exposure of men aged 20 to 79 to phenoxy herbicides and chlorophenols and the risk of developing Soft-tissue

Sarcoma & Non-Hodgkins Lymphoma.

RESULTS OF VA MORTALITY STUDY TO BE PUBLISHED IN JAMA, LATE
SUMMER 1987

- o Mortality patterns were compared between 24,235 Vietnam veterans (Army and Marine) and 26,685 Vietnam-Era Veterans who served in the Army, Marine Corp other than in Southeast Asia.
or
- o Analyses were done for 12 major disease groups, 23 selective cancers, 18 categories of diseases of the circulatory, respiratory and digestive systems, and deaths from accidents, suicides, homicides and other trauma.
- o With the exception of deaths by accidents, violence and trauma, there appears to be little difference in mortality patterns between men who served in Vietnam and the men who did not serve in Southeast Asia.
- o There is no evidence that suicides were in excess among Vietnam Veterans.
- o Among approximately 4,000 Marine veterans with service in Vietnam, a significant excess was observed for lung cancer (observed 130; expected 83; $P < 0.02$) and non-Hodgkin's lymphoma (observed, 35; expected, 17; $P < 0.02$)

DIOXIN IN HUMAN TISSUE

Three Agencies currently have studies underway on levels of TCDD in human tissues.

- o VA Retrospective Study of Dioxin in Adipose Tissue.
 - VA/EPA are analyzing adipose tissue from 200 males of the Vietnam-era age group. Approximately 40 specimens represent tissue from men who had served in Vietnam. All tissues were collected through the EPA Adipose Tissue program and span the years from 1972 through 1982. The study results are expected in December 1987.
- o CDC Agent Orange Validation Study
 - The Army Environmental Support Group, through examination of Vietnam Combat Records and record data on the location of herbicide applications, have identified 200 veterans likely exposed repeatedly to Agent Orange in Vietnam
 - 100 veterans identified as moderately likely to have been exposed and 100 veterans identified as Vietnam-era but no Vietnam service and hence unlikely to have been exposed.

- All 400 veterans have contributed blood serum.
- Analyses for TCDD to be completed in July 1987 and a report prepared for release in the fall of 1987.
- o Air Force/CDC Dioxin Half-Life Study
 - Blood Serum from 150 Ranch Hand and 55 matched controls were obtained in April 1987.
 - The Ranch Hand samples were collected from individuals at high risk to Agent Orange exposure.
 - All participants had previously participated in the Air Force Health Study and blood serum collected and frozen in 1982 is available for analysis.
 - CDC is doing the analysis and should complete the study in July 1987. A report for publication will be prepared immediately following the completion of ~~the~~ analyses

LYMPHOMA
NON-HODGKIN'S LYMPHOMA - A BRIEF OVERVIEW

The term non-Hodgkin's Lymphoma refers to a group of malignant neoplasms within the larger category of malignant lymphomas. These tumors arise from the lymphoreticular system which consists primarily of lymph nodes and collections of specialized cells in many organs including the spleen, liver, bone marrow, and portions of the gastrointestinal system. the annual incidence of malignant lymphomas in the United States is Non-Hodgkin's Lymphoma (NHL) is relatively uncommon in the United States with about 25,000 new cases estimated each year (2 per cent of all cancers). NCI reported the average annual age-adjusted incidence rates for the period 1973-1984 were 12.0 per 100,000 for white males, 9.0 for white females, 7.9 for black males, and 5.9 for black females. Overall, the male to female rates is 1.4:1. Age - specific incidence rates for U.S. white males reveal a pre-adolescent peak (~14 year olds - 0.8 per 100,000) followed by a decrease in late teenage (19 year olds-0.5 per 100,000); rates then rise logarithmically with increasing age:

<u>Age</u>	<u>Incidence Rate/100,000</u>
30	2.0
40	4.0
50	8.0
60	20.0
70	30.0

NCI reported the average annual age-adjusted mortality rates for the period 1973-1984 were 6.2 per 100,000 for white males, 4.3 for white females, 4.2 for black males and 2.5 for black females. The five-year relative survival rate for white cancer patients having Non-Hodgkin's Lymphoma is 49 percent. Survival rate has increased significantly over the past decade due to the success of new chemotherapeutic regimens.

PUBLICATIONS

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2. Center For Disease Control. 1987. Postservice Mortality Amog Vietnam Veterans. JAMA 257(6): 790-795.
3. Hoar, S. K. et al. 1986. Agricultural Herbicide Use and Risk of Lymphoma and Soft-Tissue Sarcoma. JAMA 256(9): 1141-1147.
4. Kang, H. K. et al. 1986. Soft-Tissue Sarcomas and Military Service in Vietnam: A Case Comparison Group Analyses of Hospital Patients. JOM 28(12): 1215-1218.
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