Uploaded to VFC Website

November 2012

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

Veterans-For-Change is a 501(c)(3) Non-Profit Corporation
Tax ID #27-3820181

If Veteran's don't help Veteran's, who will?

We appreciate all donations to continue to provide information and services to Veterans and their families.

https://www.paypal.com/cgi-bin/webscr?cmd=_s-xclick&hosted_button_id=WGT2M5UTB9A78

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members.

Item ID Number	05740 ☐ **Not Scanned**
Author	
Corporate Author	
Report/Article Title	Compilation of Information on the Federal Government and Agent Orange
Journal/Book Title	
Year	0000
Month/Day	
Color	☐
Number of Images	0
Description Notes	13 sections, including a history of the AOWG, studies of note, and Congressional committees.

I N D E X

Index (cont'd)

EXECUTIVE SUMMARY

The Agent Orange Issue

A legacy of the Vietnam conflict is the concern of many Vietnam veterans that they may be at risk of a spectrum of adverse health effects as a result of their service in Vietnam. These concerns focus largely on Agent Orange, a herbicide used for defoliating areas of enemy troop concentration and staging.

History

In late 1979, the White House established an Interagency Work Group to bring together knowledgeable government scientists to oversee the research, develop areas where scientific study is needed, and report the results as soon as they become available to the Congress and the public. On August 21, 1981, President Reagan established an Agent Orange Working Group (AOWG) as part of the Cabinet Council on Human Resources, elevating and enlarging the scope of the prior group. Secretary Margaret Heckler, as Chair pro tempore of this Cabinet Council, named John (Jack) Svahn, at that time Under Secretary, to chair the AOWG and in a Press Release dated June 6, 1983 stated her well known concern for veterans and her particular concern in the Agent Orange question "By designating the second highest official of my department as Chairman, I am reaffirming this administration's commitment to the prompt and scientifically responsible resolution of the health concerns of Vietnam veterans who were exposed to Agent Orange and other environmental factors during their service to their country in that conflict. His leadership of this vital working group will help us get the answers we need " the Secretary said.

Subsequent chairpersons have been Assistant Secretary for Health, Dr. Edward Brandt September 1983 - December 1984, Under Secretary Charles N. Baker, December 1984 - August 1985.

On April 11, 1985 the eight Cabinet Councils, including Human Resources were combined into two, the Council on Economic Policy Council and the Council on Domestic Policy to which the AOWG now reports.

Organization

The Agent Orange Working Group is under the leadership of the Department of Health and Human Services and includes scientific, legal and policy representatives from that Department, the Departments of Defense and State, the Veterans Administration, the Environmental Protection Agency, the Department of Agriculture, the Occupational Safety and Health Administration of the Labor Department, the White House Offices of Policy Development and of

the Science and Technology Policy, Office of Management and Budget, Council of Economic Advisors, ACTION, and Congress' Office of Technology Assessment (observor status).

The Science

The issue of possible adverse health effects in humans as a consequence of exposure to Agent Orange in Vietnam has attracted and maintained the attention of the nation for nearly a decade.

For the past four years, the AOWG has been evaluating the direction and extent of the government's scientific research in Agent Orange and related issues. When the AOWG was formed in 1981, it was clear from animal studies and the limited human studies that the toxic contaminant of Agent Orange (TCDD) has the potential to cause a broad range of deleterious effects. The extent to which these effects were likely to appear in humans exposed to Agent Orange in Vietnam, however, was unknown.

Between 1981 and 1987, AOWG member agencies will have expended $150 million in Agent Orange-related research with over one hundred and fifty (150) studies. The majority of these funds has been directed at closing the largest gap in our knowledge on Agent Orange: the effects of Agent Orange on humans. Ten major epidemiological studies scheduled for completion by 1990, and five ongoing health surveillance projects should provide information on whether exposure to Agent Orange has affected the health of Vietnam veterans and for framing hypotheses which can be tested in follow-up studies if necessary. Additional resources have been expended to better characterize known toxic properties of 2,3,7,8-TCDD and Agent Orange.

The Public

The Agent Orange Working Group has received support from veterans organizations and members of Congress and its recommendations have been accorded significant weight.

The President

In a July 17, 1981 meeting with veterans leaders, President Reagan indicated that the Administration took seriously the concerns of Vietnam veterans and their families about their health status as a result of their actual or presumed exposure to Agent Orange in Vietnam and was firmly committed to con- tinuing and according the highest priority to the current scientific research studies now being conducted and planned by Federal agencies.

The President cautioned that the scientific research may never yield definitive answers to the question of whether Agent Orange -- or any other single factor -- has adversely affected the health of an individual veteran but that we can learn whether Vietnam veterans as a group are suffering any chronic health effects not present in a comparable population that did not serve in Vietnam.

The Results

The results of the scientific research will prove useful in helping to formulate sound public policy regarding health care and compensation for Vietnam veterans. Some studies are completed and are inconclusive; the major Epidemiologic studies underway by the Centers for Disease Control, mandated by Congress is the most comprehensive but will not be completed until late 1989.

Based on the growing body of information in hand, the worst case scenarios envisioned by some as a consequence of exposure to Agent Orange are not being realized. Populations known or possibly exposed to Agent Orange which are being studied have not so far exhibited increased incidences of cancer, or death from other causes, or abnormally high rates of birth defects in their offspring. This optimism is tempered by the knowledge that other, less-well characterized effects of concern may by associated with 2,3,7.8-TCDD (e.g., immunotoxicity). Some effects (e.g., cancer) may not become manifest for several more years, due to a longer latency period.

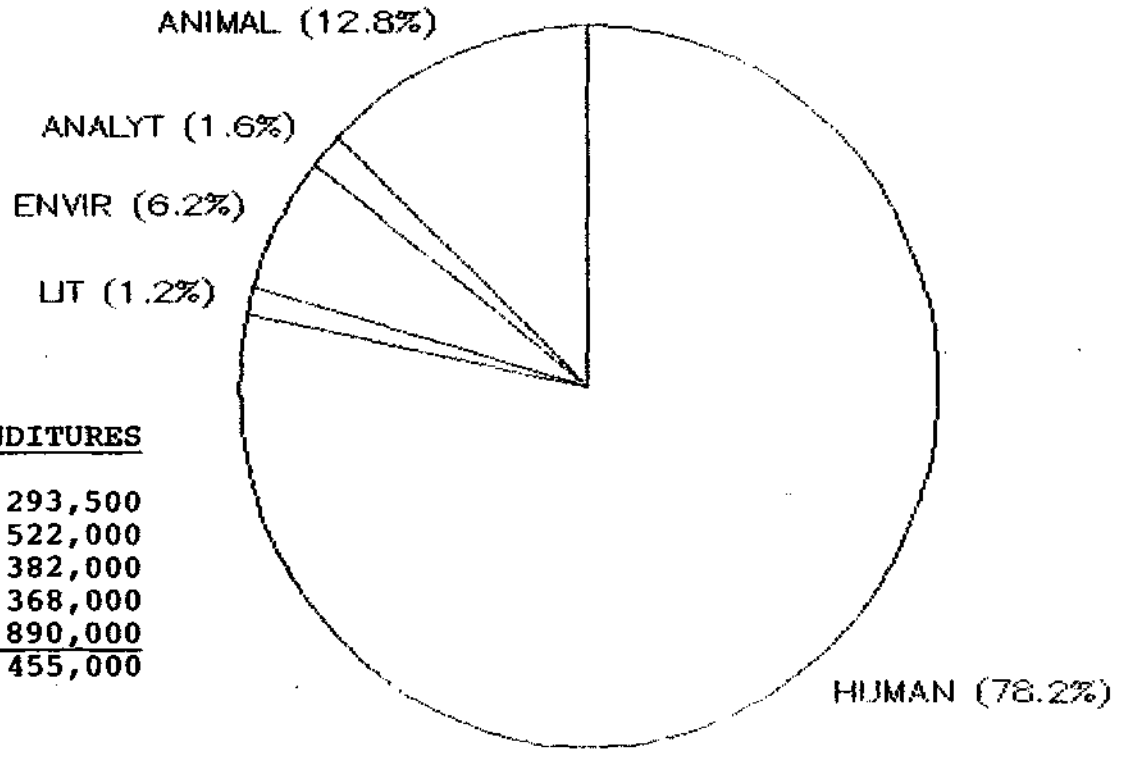
The consensus of the Science Panel is that initiation of any new, major epidemiological study should await and be built upon the results of studies already underway.

A large number of ongoing research projects designed to characterize the toxicity and mechanisms of action of 2,3,7,8-TCDD in laboratory animals will also help to identify possible adverse human health effects and will assist in the interpretation of epidemiologic study results.

AGENT ORANGE/DIOXIN EXPENDITURES

AGENCY EXPENDITURES BY STUDY TYPE

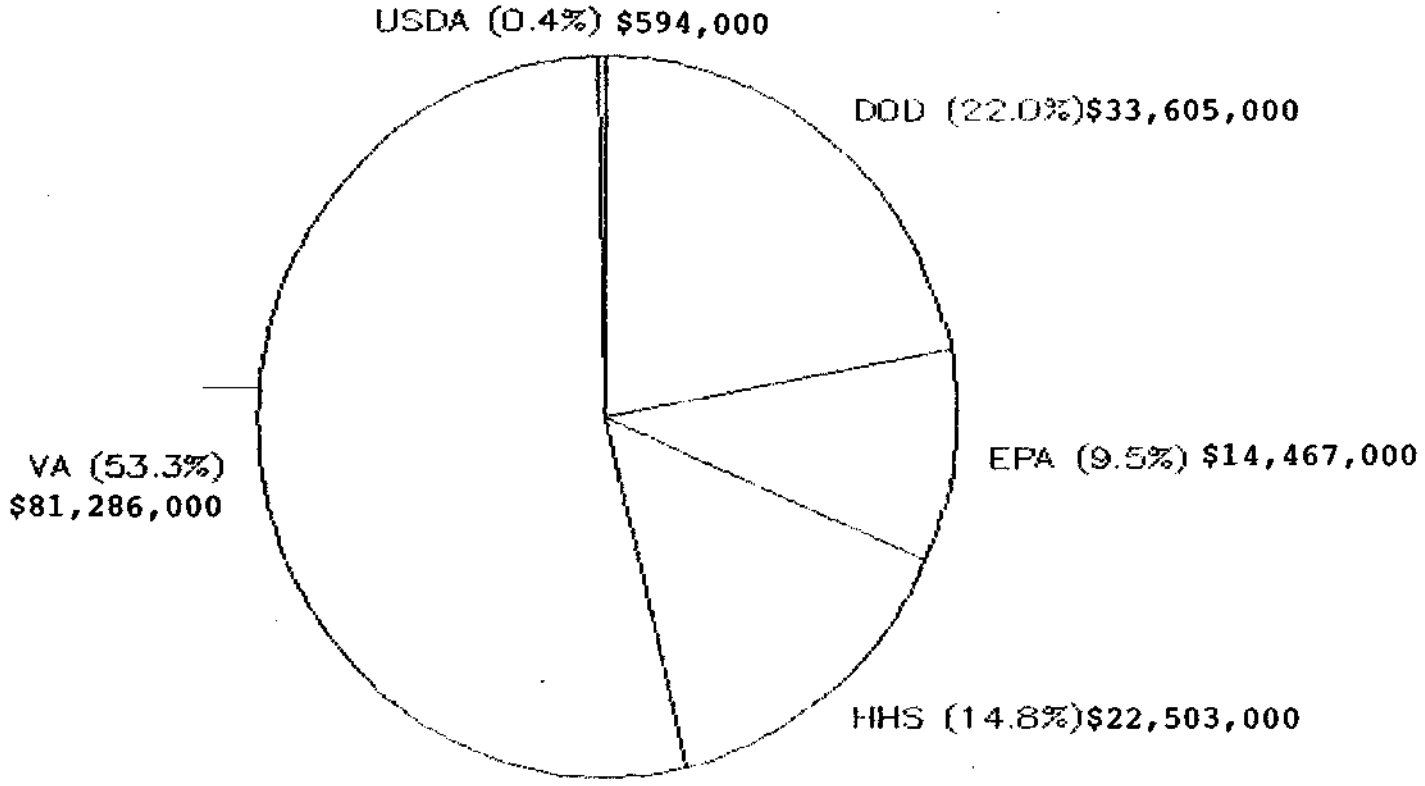
$152,455,000 TOTAL EXPENDITURES



STUDY TYPE	EXPENDITURES
HUMAN	$119,293,500
ANIMAL	19,522,000
ENVIRONMENT	9,382,000
ANALYTICAL	2,368,000
LITERATURE	1,890,000
TOTAL	$152,455,000

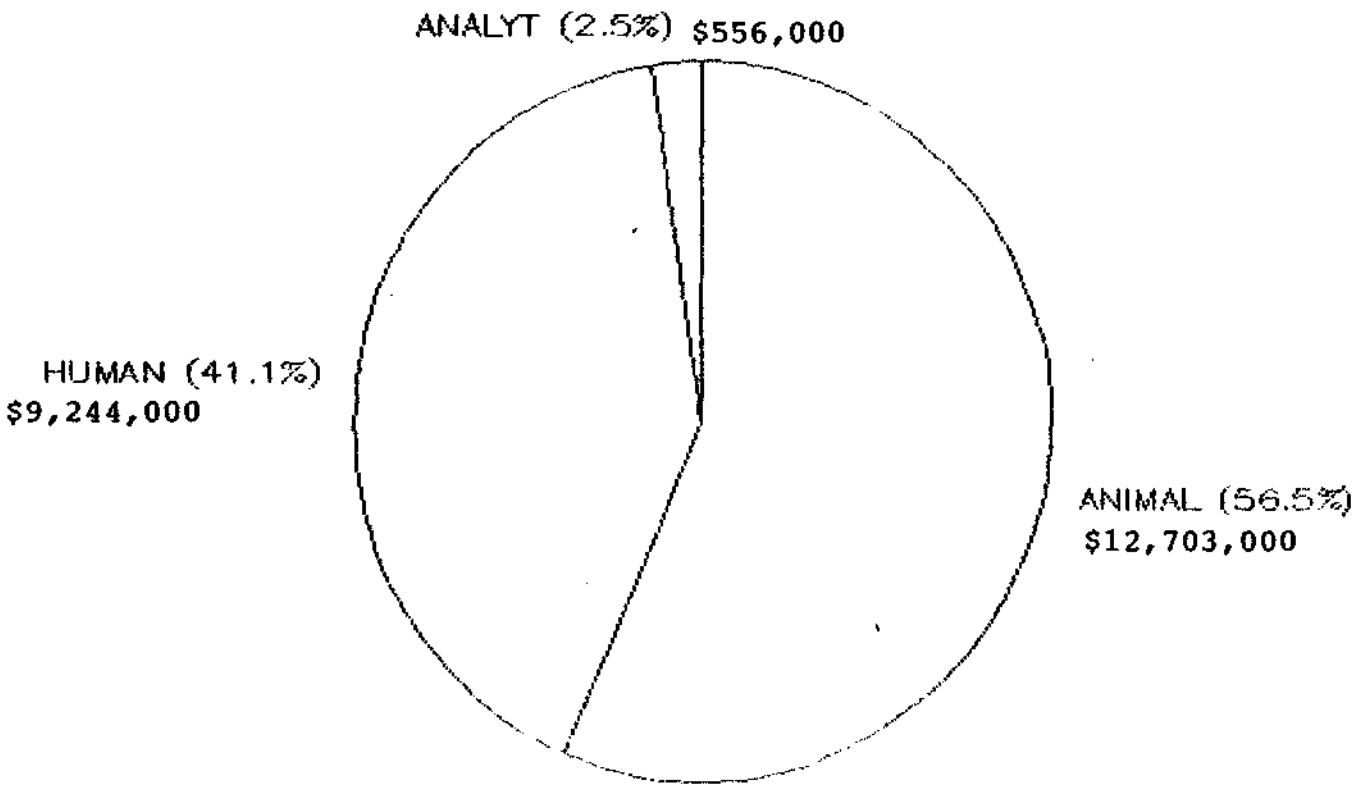
AGENT ORANGE/DIOXIN EXPENDITURES

$152,455,000 TOTAL COST



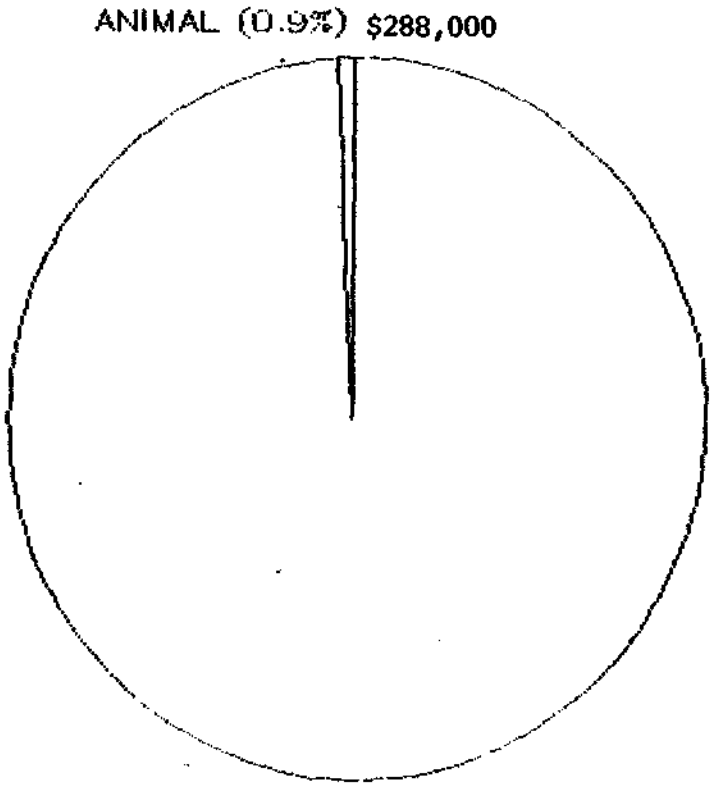
HHS A.O./DIOXIN EXPENDITURES

$22,503,000 TOTAL EXPENDITURES



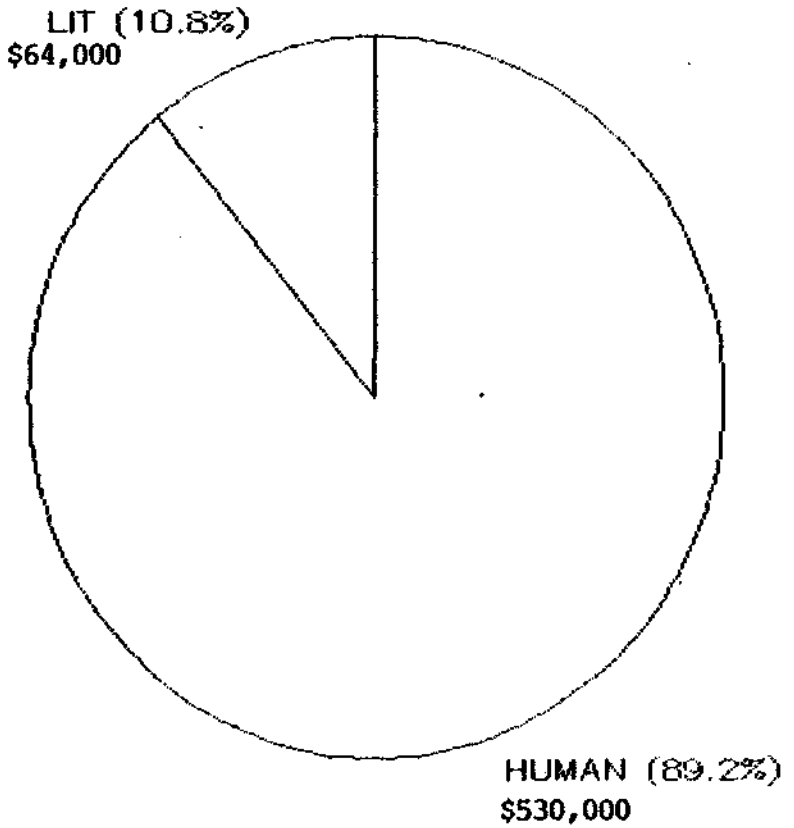
DOD A.O./DIOXIN EXPENDITURES

$33,605,500 TOTAL EXPENDITURES



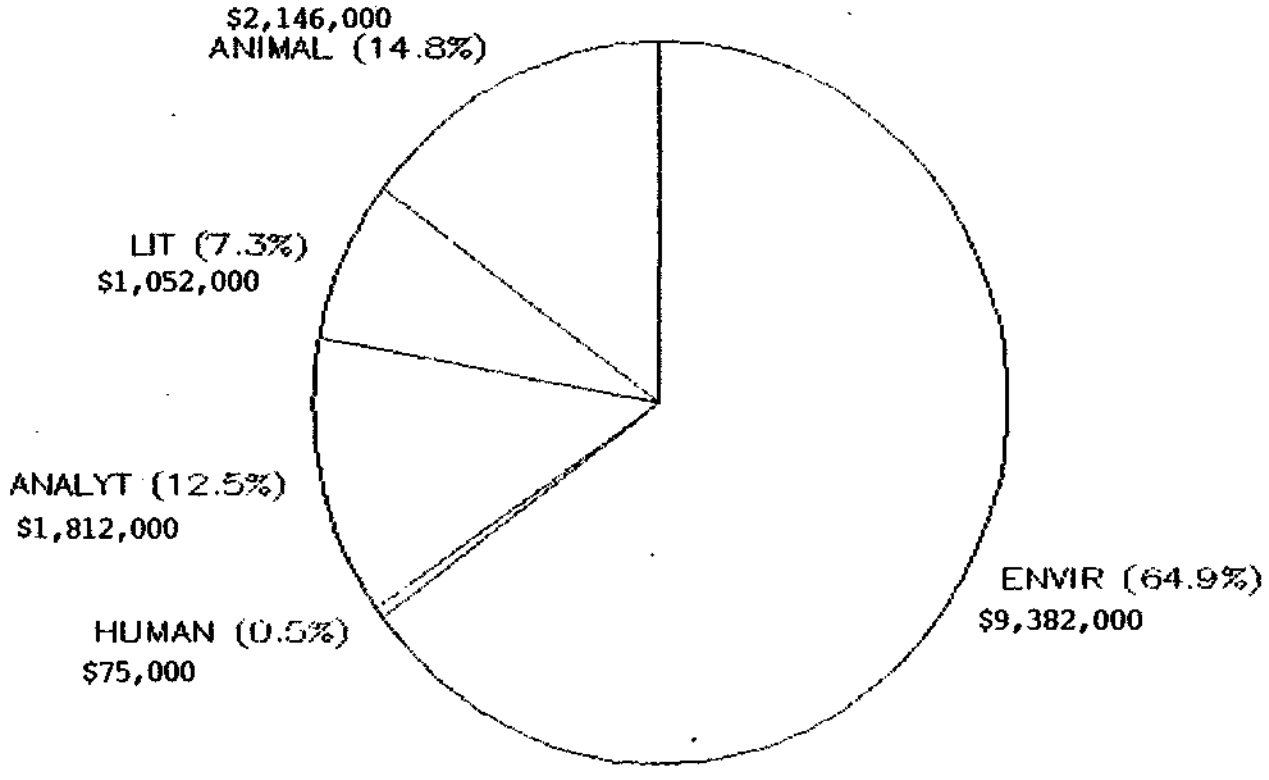
USDA A.O./DIOXIN EXPENDITURES

$594,000 TOTAL EXPENDITURES



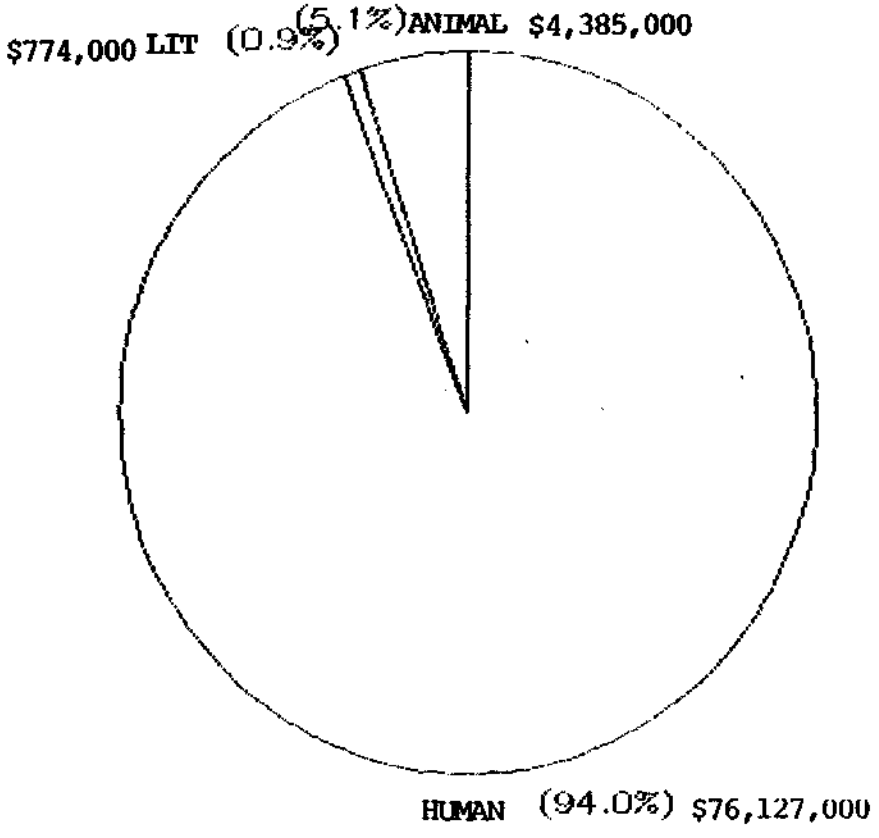
EPA A.O./DIOXIN EXPENDITURES

$14,467,000 TOTAL EXPENDITURES



V.A. A.O./DIOXIN EXPENDITURES

$81,286,000 TOTAL EXPENDITURES



HHS NEWS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOR IMMEDIATE RELEASE
DRAFT

Contact:
Telephone

HHS Secretary Margaret M. Heckler today forwarded to the Cabinet Council on Domestic Policy an updated report from the Agent Orange Working Group suggesting no new major studies are needed on the subject until evaluations have been done on those already completed or continuing through 1987 at a cost of more than $150 million.

Terming results of the studies thus far as "reassuring," Secretary Heckler said, "Completed studies show no increase in birth defects among children of Vietnam veterans or higher mortality due to Agent Orange exposure.

"However, careful and intensive epidemiological studies in other areas are going on and we must await their findings."

The advisory science panel formed by the AOWG says in the report that the numerous research projects completed or already underway are the ones it considers both essential and feasible.

It recommends "that any additional major research efforts involving Vietnam veterans' exposure to Agent Orange should await evaluation of the results of studies which are currently in progress."

Created in 1979 as a small interagency work group, the AOWG was enlarged and elevated to cabinet council status in July 1981 by President Reagan to show his concern over the fears of Vietnam veterans that they may suffer ill effects from exposure to phenoxy acid herbicides, principally Agent Orange. The herbicides were sprayed to defoliate dense jungle areas from which enemy troops operated.

- MORE -

Veterans groups have maintained they were endangered by an increase in cancers and liver disorders, and expressed fears that their children might be born with defects. They called for scientific research, compensation and treatment.

In forwarding the new AOWG report to the Cabinet Council on Domestic Policy, Secretary Heckler, a long-time advocate of veterans' rights, said, "The president's promise to support any research necessary to learn whether Vietnam veterans as a group are suffering any chronic health effects not present in a comparable population that did not serve in Vietnam, will be kept."

Twelve federal departments or independent agencies are represented on the Agent Orange Working Group. It sets priorities, coordinates and overses federal research into the possibility of long-term adverse health effects resulting from exposure to the herbicides used in Vietnam.

The science panel's report says HHS, the departments of Defense and Agriculture; the Environmental Protection Agency; and the Veterans Administration are conducting ongoing studies with the other AOWG members providing advice and guidance.

The others are the Department of State; Department of Labor; ACTION; the White House Offices of Policy Development, Science and Technology Policy; Office of Management and Budget; Council of Economic Advisors; and the Congressional Office of Technology Assessment, the latter as an observer.

####

STATEMENT OF PRESIDENT REAGAN
JULY 17, 1981

"One of the most unfortunate legacies of the Vietnam conflict is the continuing concern of many Vietnam veterans that they are, or may be, at increased risk of a broad spectrum of adverse health effects as a result of their service in Vietnam. These concerns have largely focused on Agent Orange, a herbicide used for defoliating areas of enemy ground troop concentrations and staging. Agent Orange was made by combining two herbicides that were in widespread use in forestry and agriculture.

Unfortunately, despite much discussion in the media and among scientists, there are still few definitive answers to the difficult scientific issues involved. Indeed, we may never be able to determine with certainty whether Agent Orange -- or any other single factor -- has adversely affected the health of an individual veteran. The scientists working on this problem are hopeful, however, that we can learn whether Vietnam veterans as a group are suffering any chronic health effects not present in a comparable population that did not serve in Vietnam. In addition, several studies -- including an epidemiological study of the Air Force Personnel who sprayed Agent Orange -- are directly examining the Agent Orange issue. The results of these and other studies, including a congressionally mandated VA epidemiological study of the health status of Vietnam veterans, should be extremely useful in helping to formulate sound public policy regarding health care and compensation for Vietnam veterans.

I believe that the Federal Government has made significant progress in the past year in organizing and beginning a serious scientific inquiry into the Agent Orange issue. Much, however, remains to be done and I share the deep and abiding concern of Vietnam veterans about their health and that of their children. I am committed to assuring that the important scientific research now under way and being planned under the overall guidance and coordination of the White House Interagency Work Group continue to completion in an efficient, expeditious manner, consistent with sound scientific principles. Accordingly, I am hereby reaffirming the mandate of the Work Group and making its work a major priority of my Administration."

Agent Orange

The term "Agent Orange" is derived from the orange color code painted on the barrels of herbicide shipped to Vietnam. Other herbicides used in Vietnam carried various other color codes depending on the nature of the herbicide.

Agent Orange was a 50/50 mixture of the herbicide 2,4,-D and 2,4,5-T. The product was provided on contract with the Department of Defense by a number of chemical companies.

A by-product created in extremely small amounts during the manufacture of 2,4,5-T was the chemical, dioxin. The average contamination amount of dioxin was, according to the Veterans Administration, two parts per million.

Dioxin has caused lethal and toxicological effects in some laboratory animals at lower levels than any other man-made chemical. However, both the lethal dose levels and the toxicological effects vary considerably among different animal species. The toxicological effect upon humans remains under study and additional work must be done before an authorized view of the risks can be made.

THE HUMAN STUDY

CABINET COUNCIL ON DOMESTIC POLICY
AGENT ORANGE WORKING GROUP

FEDERALLY SPONSORED HUMAN STUDIES RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY					STATUS		
STUDY TITLE	Mortality	Morbidity	Cancer	Repro-duction	Analytical	Completed	Ongoing	Estimated Completion Date
DEPARTMENT OF HEALTH AND HUMAN SERVICES								
NIOSH Investigation of Leukemia Cluster in Madison County, Kentucky Allegedly Associated with Pentachlorophenol Treated Ammunition Boxes			X			X		Published NTIS 1984
NIOSH Dioxin Registry	X		X				X	Late 1985
NIOSH Soft Tissue Sarcome Investigation			X					Published Scan. J. Work Environ Health 1984
NIOSH NJ/Missouri plant worker and worker's spouse reproductive outcome study	X	X	X	X			X (begins 1985)	
Reproductive outcomes in persons possibly exposed to 2,3,7,8 RDP				X			X	
Measurement of TCDD levels in adipose tissue from potentially exposed persons in Missouri.			X	X	X	X	X	

FEDERALLY SPONSORED HUMAN STUDIES RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY					STATUS		
STUDY TITLE	Mortality	Morbidity	Cancer	Repro-duction	Analytical	Completed	Ongoing	Estimated Completion Date
DEPARTMENT OF HEALTH AND HUMAN SERVICES cont'd								
NIEHS Establishment and Maintenance of an International Register of Persons Exposed to Phenoxy Acid Herbicides and Contaminants	X		X				X	Indefinite
NIEHS Effects on Intestinal Cells UNC-CU Grad student	X					X 1984		
Lipid Assimilation NRSA						X 1984		
Membrane/LP Receptor NRSA	X						X	1986
NIEHS Pesticides and transport across bilayer Lipid membranes (toxicology)	X						X	1987
NIEHS Occupational and Environmental Health Center Grant (toxicology)	X						X	1987
NIEHS - Dioxin Environmental Health Sciences Center Grant Clinical Studies	X						X	1987
NIEHS Dioxin Mechanism(s) for toxicity of chlorinated dibenzodioxins (toxicology)	X						X	1987

FEDERALLY SPONSORED HUMAN STUDIES RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY					STATUS		
STUDY TITLE	Mortality	Morbidity	Cancer	Reproduction	Analytical	Completed	Ongoing	Estimated Completion Date
NIEHS Dioxin Environmental pollutants and toxicology of the liver	X						X	1986
NIEHS Dioxin Xenobiotic induction of pleiotropic responses in liver	X						X	1986
NIEHS Dioxin molecular toxicology of TCDD	X						X	1986
NIEHS Dioxin chlorinated dibenzo-p-dioxins; mechanisms of toxicity	X						X	1987
NIEHS Dioxin - Toxic halogenated wastes: In vitro bioassay development	X						X	1986
NIEHS Dioxin - Atomic emission spectrometry for dioxin trace anlaysis (detection)	X						X	1986
NCI Study of Mortality Among Pesticide Applicators from Florida						X		Publications in Press
NCI Case Control Study of Lymphoma and Soft Tissue Sarcoma			X				X	Indefinite

FEDERALLY SPONSORED HUMAN STUDIES RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY					STATUS		
STUDY TITLE	Mortality	Morbidity	Cancer	Repro-duction	Analytical	Completed	Ongoing	Estimated Completion Date
CDC Birth Defects and Military Service in Vietnam Study				X			X	Published Aug. 1984
*CDC Epidemiologic Study of Ground Troops Exposed to Agent Orange during the Vietnam Conflict	X	X	X	X	X		X	Sept 1989
CDC Study for Body Burden for Dioxin in the General Population					X		X	Late 1988
VETERANS ADMINISTRATION								
Vietnam Veteran Mortality Studies	X						X	December 1985
Vietnam Veteran Identical Twin Studies		X		X				Under Review by OTA and AOWG
VA/AFIP Case Control Study of Soft Tissue Sarcoma			X				X	July 1986

*Mandated to the VA by P.L. 96-151 Sec. 307. Transferred from VA to CDC under Interagency Agreement January 14, 1983.

FEDERALLY SPONSORED HUMAN STUDIES RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY					STATUS		
STUDY TITLE	Mortality	Morbidity	Cancer	Repro-duction	Analytical	Completed	Ongoing	Estimated Completion Date
VETERANS ADMINISTRATION cont'd								
Survey of Patient Treatment File for Vietnam Veteran In-Patient Care		X	X				X	Initial 1983 Survey
Review of Soft Tissue			X				X	December 1985
Sarcoma Study in Patient Treatment File Agent Orange Registry Examinations		X	X				X	Indefinite
TCDD in Body Fat of Vietnam Veterans and Other Men		X		X	X			Published
Retrospective Study of Dioxins and Furans in Adipose Tissue of Vietnam-Era Veterans					X		X	1986
DEPARTMENT OF DEFENSE								
Epidemiologic Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicide Orange (Air Force Health Study)	X	X	X	X			X	Baseline 1983 Complete 1999
Armed Forces Institute of Pathology Agent Orange Registry of Vietnam Veteran Biopsy Tissues			X				X	Indefinite

FEDERALLY SPONSORED HUMAN STUDIES RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY					STATUS		
STUDY TITLE	Mortality	Morbidity	Cancer	Reproduction	Analytical	Completed	Ongoing	Estimated Completion Date
ENVIRONMENTAL PROTECTION AGENCY								
Report of Assessment of a Field Investigation of Six-Year Spontaneous Abortion Rates in Three Oregon Areas of Relation to Forest 2,4,5-T Spray Practices				X		X (Published)		
National Pesticide Monitoring Project of Human Adipose Tissue					X		X	Indefinite (Annual Reports)
DEPARTMENT OF AGRICULTURE								
A Case Control Study of the Relationship Between Exposure to 2,4-D and Spontaneous Abortions in Humans				X		X		
Exposure Measurements of Mixers, Loaders and Applicators of 2,4-D on Wheat					X	1982		
Exposure of Forest Workers to Ground Applications of 2,4-D					X	1983		

THE ANIMAL STUDY

FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
DEPARTMENT OF HEALTH AND HUMAN SERVICES							
NIEHS							
Bioassay of Octachlorodibenzo-p-dioxin	X					X	Indefinite
Carcinogenesis Bioassay of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in Swiss Webster Mice	X					X	Indefinite
Carcinogenesis Bioassay of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in Osborne-Mendel Rats and B6C3F1 Mice	X				X		
Bioassay of a Mixture of 1,2,3,6,7,8- and a Mixture of 1,2,3,6,7,8-Hexachlorodibenzo-p-dioxins for Possible Carcinogenicity	X					X	Indefinite
Comparative species Evaluation of Chemical Disposition and Metabolism of 2,3,7,8-Tetrachlorodibenzofuran (TCDF) in Rat, Monkey, Guinea Pig and Two Strains of Mice	X				X		
Neurotoxicity of 2,4,-D in Rodents	X				X		

FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
DEPARTMENT OF HEALTH AND HUMAN SERVICES cont'd							
Studies of the Chemical Disposition and Metabolism of Octachlorodibenzodioxin (OCDD)	X					X	Indefinite
Effects of Agent Orange Components on Male Fertility and Reproduction		X			X		
Mutagenicity Studies of TCDD, 2,4-D; 2,4,5-T and Esters of 2,4-D and 2,4,5-T		X				X	Indefinite
Implications of Low Level Exposure of Dioxins		X				X	Indefinite
Mechanisms of Toxicity of the Chlorinated-p-dioxins		X				X	Indefinite
Research Toward Understanding the Molecular Level Mechanisms of Toxicity of TCDD and Related Compounds	X					X	Indefinite
Synthesis of Selected Chlorinated dibenzo-p-dioxins and Related compounds as Analytical Standards			X			X	Indefinite

FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
DEPARTMENT OF HEALTH AND HUMAN SERVICES cont'd							
Methods for the measurement of dioxins and furans in human adipose tissue			X			X	Indefinite
Matrix Effect and Sub Parts-per-billion Quantitative Analysis of TCDD by Mass Spectrometry - With Special Reference to Milk	X		X			X	Indefinite
Toxic Actions of Tetrachloroazobenzene Dioxins	X					X	Indefinite
Xenobiotic Induction of Pleiotropic Responses in Liver	X					X	Indefinite
Molecular, Biochemical Actions of Chlorinated-p-dioxins	X					X	Indefinite
Mechanism(s) for Toxicity of Chlorinated Dibenzo-dioxins	X					X	Indefinite

FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
NIEHS							
Teratogenicity of TCDD - Cleft palata Induction (mice)	X					X	1986
Disposition of TCDD Fetal Distribution in mice	X					X	1986
2,3,7,8-Tetrachlorodibenzofuran-Disposition in Rats, Mice, Guinea Pigs	X				disposition 1983	metabolism	1986
1,2,4,6,8,9 Hexachlorodibenzofuran-Disposition	X				disposition	X	1986
DIOXIN							
Structure-Toxicity Relationships	X				1984		
Theoretical Modeling of Dioxin Receptor					1984		
Molecular Modeling of Dioxin Binding Proteins						X	1986
Molecular Basis of Dioxin Toxicity	X Theoretical Biochemical					X	July 1986
Lipid Assimilation NRSA	X				X		
Membrane /LP Receptor NRSA	X					X	Nov. 1986

FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
ENVIRONMENTAL PROTECTION AGENCY							
Evaluation of Large Scale Combustion Sources		X	X			X	
Evaluation of Municipal Waste Combustors		X				X	
Bacterial Decomposition of TCDD		X				X	
Investigation of Bioavailability to Fresh Water Fish of TCDDs in Fly Ash	X	X				X	
Analysis of Environmental Samples for PCDDs and PCDFs		X	X			X	
DEPARTMENT OF AGRICULTURE							
Survey of Phenoxy Herbicide Use by Agricultural Commodity				X		X	
Survey of Phenoxy Herbicide Literature				X		X	Annaul Bibliographies Published

FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
DEPARTMENT OF AGRICULTURE cont'd							
Photolysis of 2,4,5-T			X			X	
Biological and Economic Assessment of 2,4,5-T and Silvex				X		X	
TCDD Residue Monitoring in Deer	X	X			X		Report in Preparation
DEPARTMENT OF DEFENSE							
Environmental Chemistry of Herbicide orange and TCDD		X	X			X	Indefinite
VETERANS ADMINISTRATION							
Review of Literature on Herbicides, Including Phenoxy Herbicides and Associated Dioxins				X	Published 1981		Annual Update Approved
Urinary 6-Hydroxy Cortisol: Physiological and Pharmacologic Studies (Including Agent Orange)	X					1982	
Effect of TCDD on Lipid Metabolism	X					1983	

FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
VETERANS ADMINISTRATION cont'd							
Mechanisms of Dioxin Induced Toxicity Using the Chloracne Model - Phase I	X				X		Publication in Press
Behavioral Toxicity of An Agent Orange Component 2,4-D	X					1984	
Effects of 2,3,7,8-Tetra-chlorodibenzodioxin on Hepato-biliary Function in Animals	X					X	1986
Mechanism of TCDD Absorption and Toxicity on Lipid and Lipoprotein Metabolism	X					X	1986
Metabolism of the Herbi-cides Present in Agent Orange and Agent White	X					X	1986
TCDD Exposed Rhesus Monkeys: Effects on Behavior and Stress Hormones	X					X	1986

FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
VETERANS ADMINISTRATION cont'd							
Neuromuscular Toxicity of Agent Orange	X					X	1986
Mechanisms of Dioxin Induced Toxicity Using the Chloracne Model - Phase II	X					X	1986
Effects of Low Dose TCDD on Mammalian Chromosomes and Liver Cells	X					X	1986
Mechanism of Porphyria Caused by TCDD and Related Chemicals	X					X	1986
Effects of Agent Orange on Sleep	X					X	1986

FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
ENVIRONMENTAL PROTECTION AGENCY							
Evaluation of TCDD destruction technologies		X				X	December 1985
Assessment of exposure to TDCC from contaminated media			X(Thought-wise)			X	December 1985
Assessment of methods used for analysis of human adipose tissue			X(Lab-wise)		Oct. 1984		
Behavior of TCDD in blood	X		X			X	December 1985
Clearance of TCDD from dose organisms	X	X	X				December 1985
Analytical methods development of monoclonal antibodies			X				December 1985
Workshop report on bioavailability				X		X	December 1985
Movement of TCDD in the environment		X				X	December 1985
Evaluation of combustion sources		X	X	X		X	December 1985

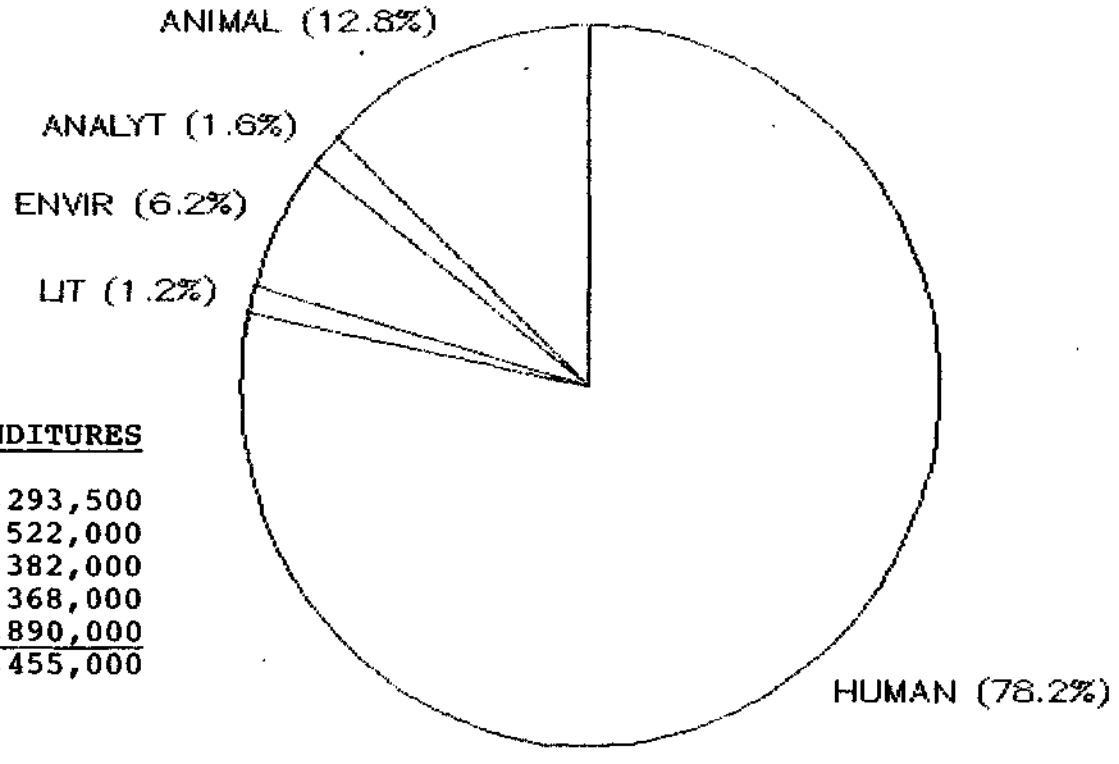
FEDERALLY SPONSORED LABORATORY STUDIES AND LITERATURE SURVEYS RELATED TO AGENT ORANGE

AGENCY	TYPE OF STUDY				STATUS		
STUDY EFFORT	Animal	Environmental	Analytical	Literature	Completed	Ongoing	Estimated Completion Date
Analysis of background levels of TCDD in the US environment		X	X	X		X	December 1985
Health assessment of PCDDs		X	X			X	December 1985
Health assessment of PCDFs				X		X	December 1985

AGENT ORANGE/DIOXIN EXPENDITURES

AGENCY EXPENDITURES BY STUDY TYPE

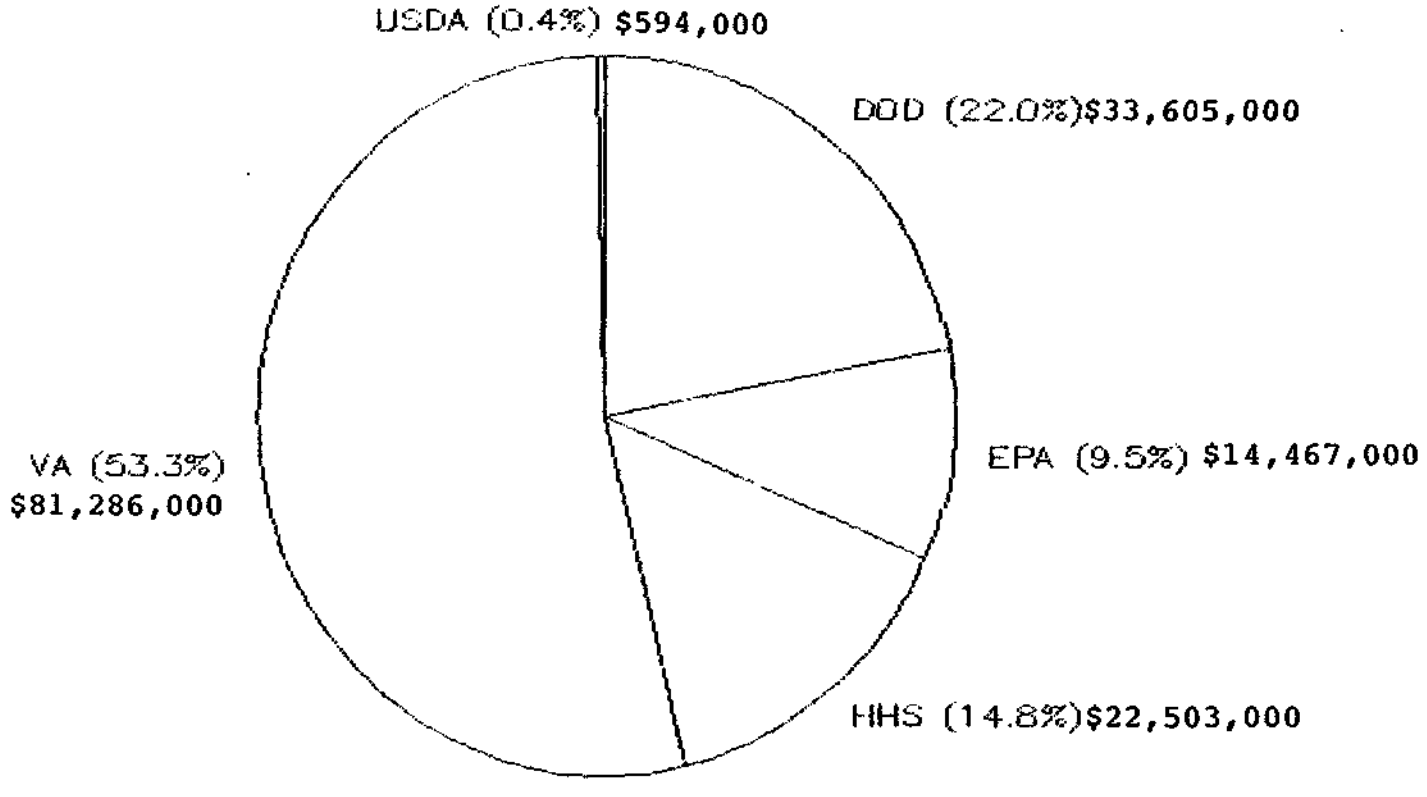
$152,455,000 TOTAL EXPENDITURES



STUDY TYPE	EXPENDITURES
HUMAN	$119,293,500
ANIMAL	19,522,000
ENVIRONMENT	9,382,000
ANALYTICAL	2,368,000
LITERATURE	1,890,000
TOTAL	$152,455,000

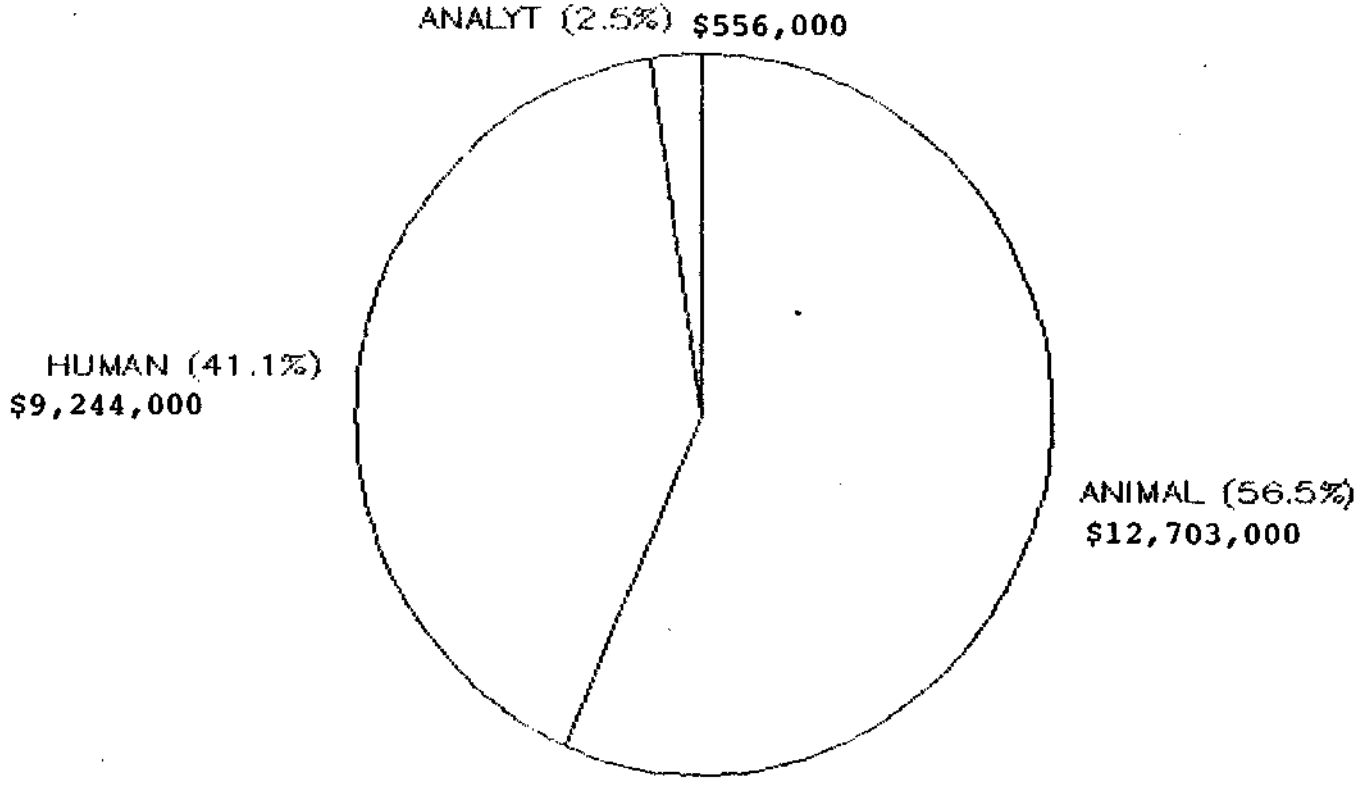
AGENT ORANGE/DIOXIN EXPENDITURES

$152,455,000 TOTAL COST



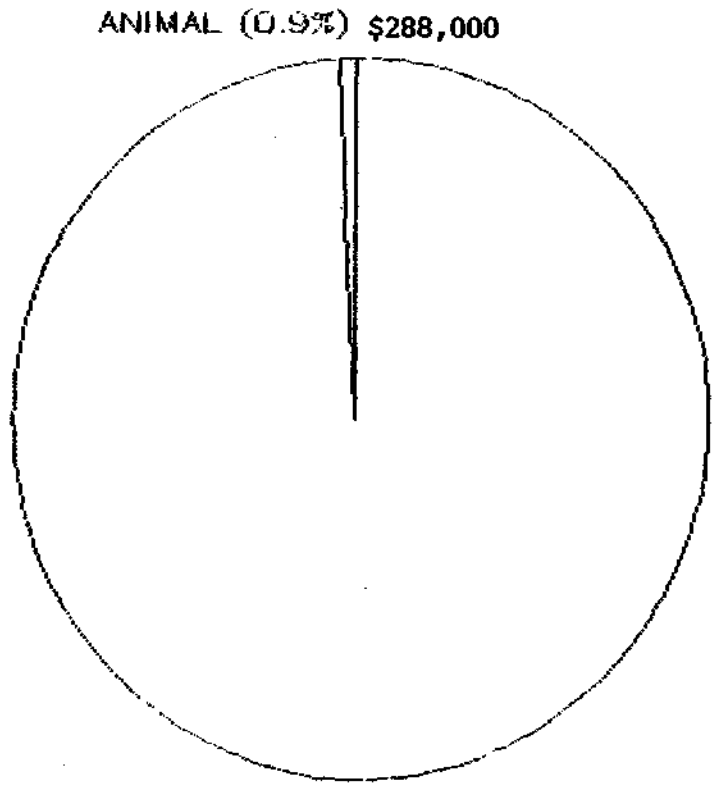
HHS A.O./DIOXIN EXPENDITURES

$22,503,000 TOTAL EXPENDITURES



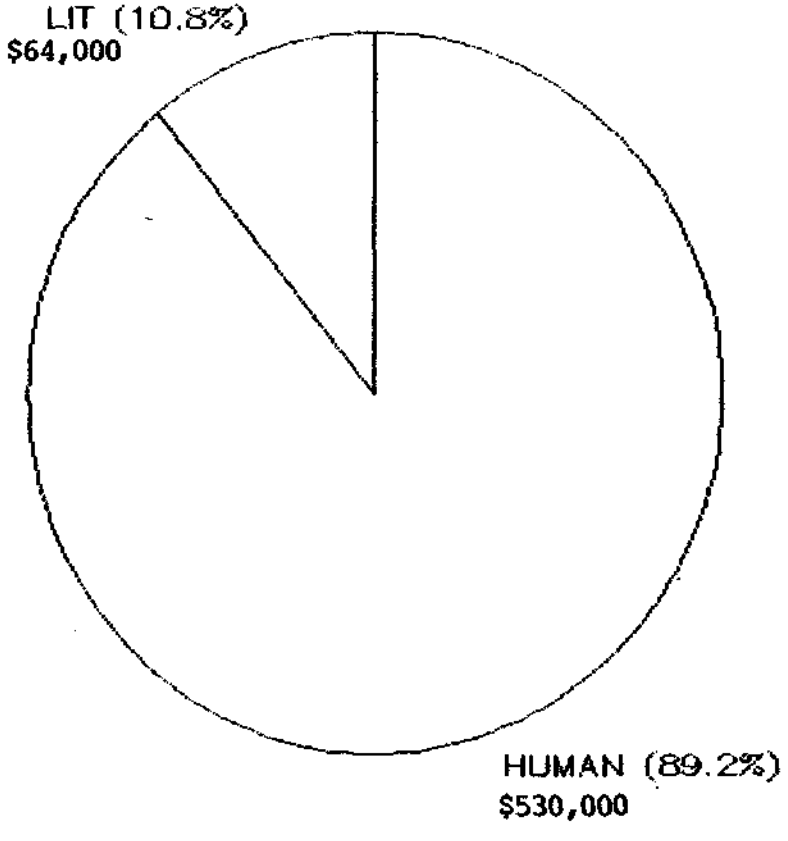
DOD A.O./DIOXIN EXPENDITURES

$33,605,500 TOTAL EXPENDITURES



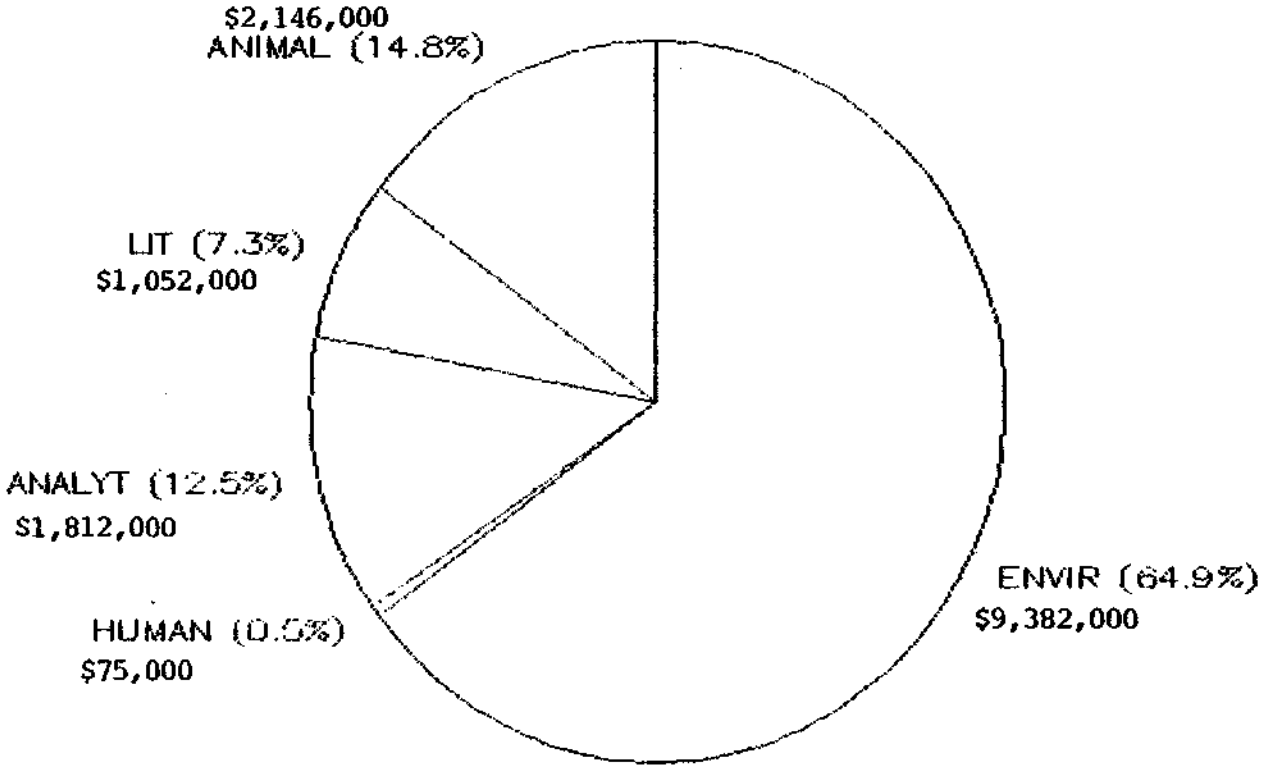
USDA A.O./DIOXIN EXPENDITURES

$594,000 TOTAL EXPENDITURES



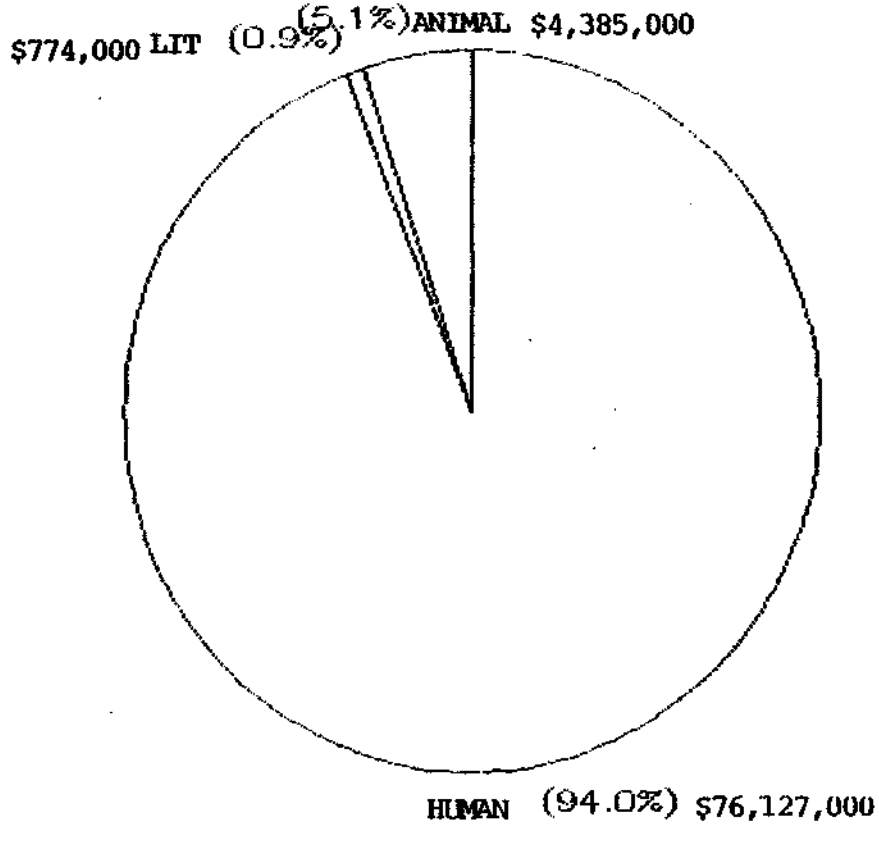
EPA A.O./DIOXIN EXPENDITURES

$14,467,000 TOTAL EXPENDITURES



V.A. A.O./DIOXIN EXPENDITURES

$81,286,000 TOTAL EXPENDITURES



Agent Orange Use In Vietnam

Agent Orange was the most widely used of the various herbicides. During the period 1964-1970, approximately 12 million gallons were sprayed in Vietnam. In addition, approximately five million gallons of Agent White, composed of the chemical Picloram and 2, 4-D, and approximately three million gallons of Agent Blue composed of cacodylic acid were sprayed. Neither Agent White nor Agent Blue contained the contaminant dioxin.

The herbicides were used to defoliate jungle areas to expose enemy troop movements and staging areas and to eliminate ambush opportunities. Base perimeters, river banks and enemy crop resources were also defoliated. The principal means of distribution was by C-123 fixed wing aircraft (Operation Ranch Hand). Helicopters, back-packs, truck-equipped equipment and Navy river boats were also used. In all, it is estimated that 10% of the land area of South Vietnam was sprayed at least once.

Its use was discontinued in late 1970 because of allegations of a link between 2, 4, 5-T and birth defects of children born in South Vietnam. These allegations have never been substantiated.

All remaining stocks of Agent Orange were incinerated at sea near Johnston Island (a remote island in the South Pacific) in 1977.

T-3

THE WHITE HOUSE

WASHINGTON

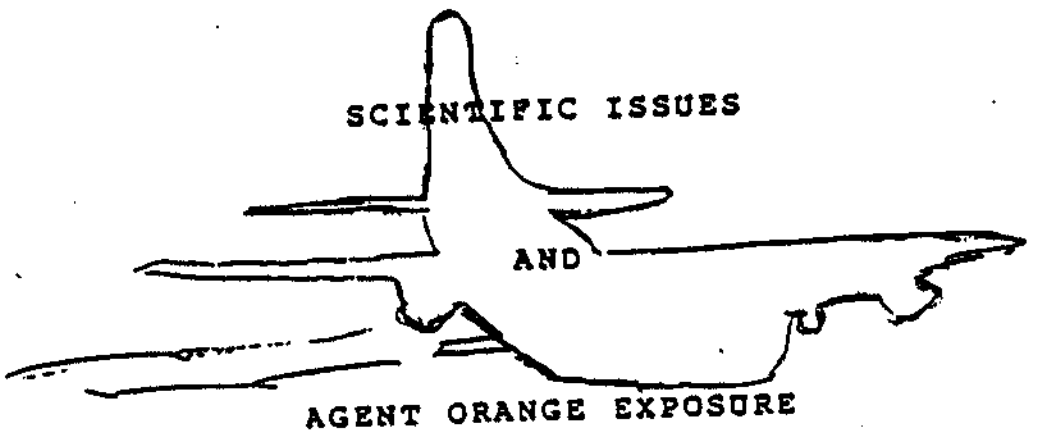
SCIENTIFIC ISSUES AND AGENT ORANGE EXPOSURE

October 27, 1983

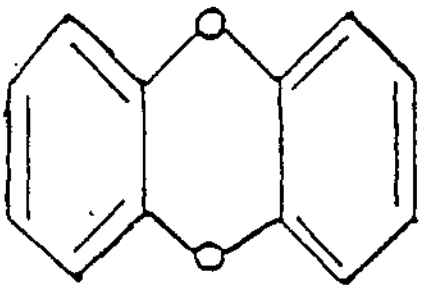
Introduction: Dr. G. A. Keyworth
Science Advisor to the President

Briefing: Dr. Alvin Young
Scientific Advisor, Veterans Administration

Discussion

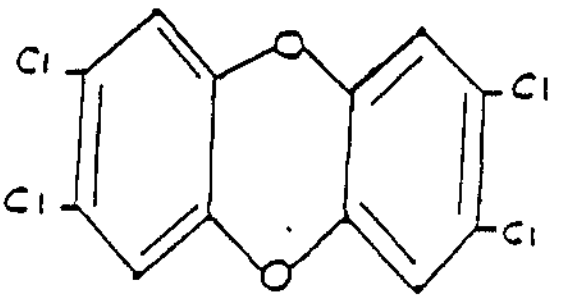

SCIENTIFIC ISSUES
AND
AGENT ORANGE EXPOSURE

"DIOXIN" IS A FAMILY OF 75 COMPOUNDS



DIBENZO-PARA-DIOXINS

DIOXIN OF CONCERN



2,3,7,8-TCDD

TOXICITY OF 2,3,7,8-TCDD

Acute Toxicity:	Single Dose LD_{50} (µg/kg)
Guinea Pig	0.6
Rat	40
Monkey	70
Rabbit	115
Dog	150
Mouse	200
Hamster	3,500
Bullfrog	Over 1,000
Man	No deaths reported

IN LABORATORY ANIMALS, DIOXIN CAUSES

- BIRTH DEFECTS
- FETAL DEATH
- CANCER
- MUTATION?

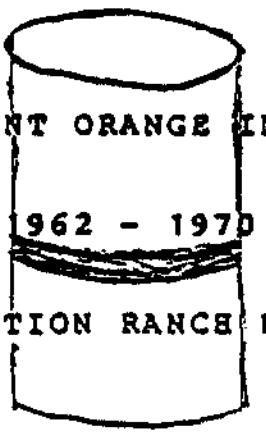
SOURCES OF HUMAN EXPOSURE

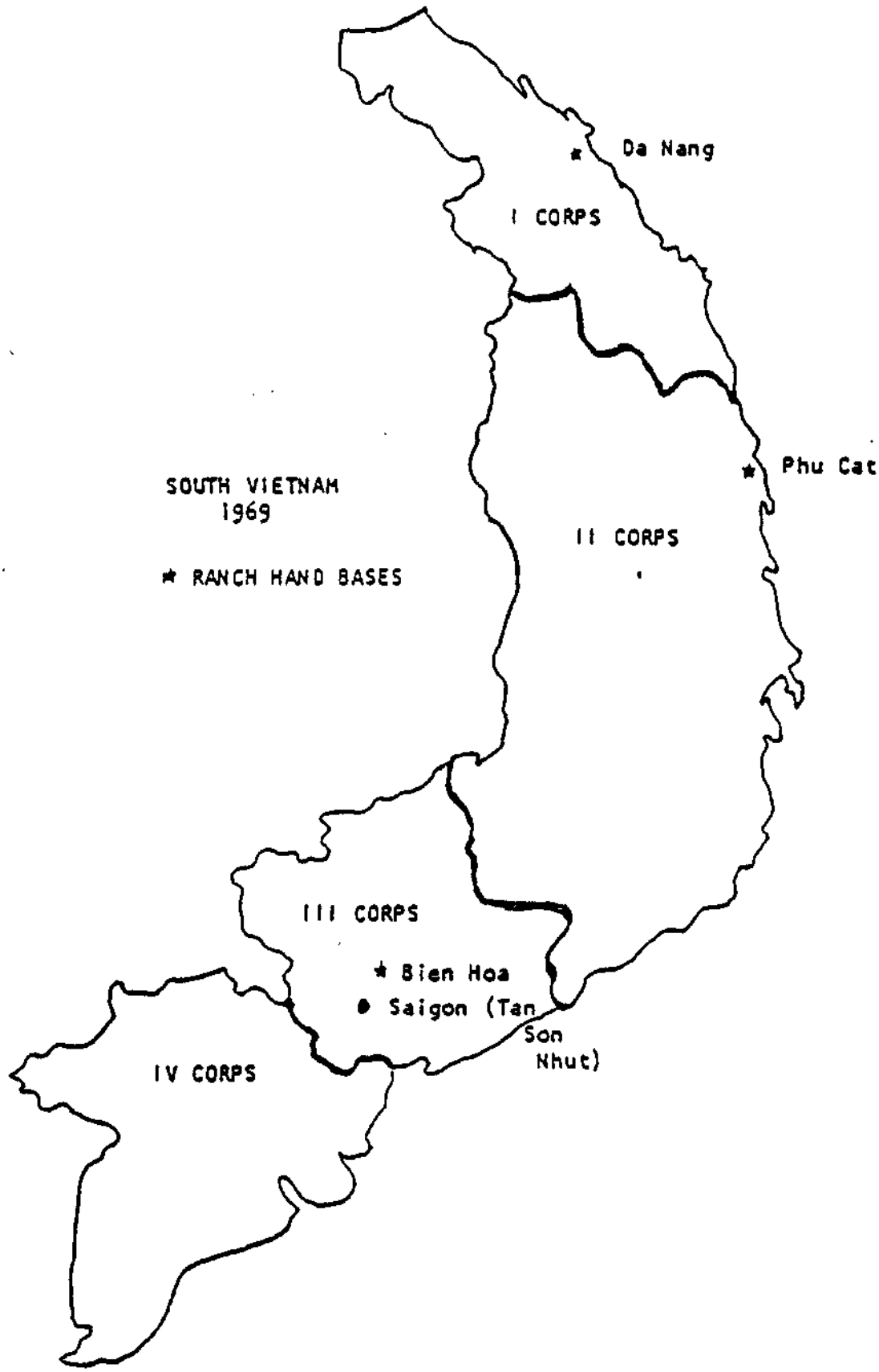
- Industrial Accidents
- Occupational Exposure
- Contaminated Industrial Wastes
- Herbicide Applications
- Contaminated Food
- Low Temperature Combustion

USE OF AGENT ORANGE IN VIETNAM -

1962 - 1970

"OPERATION RANCH HAND"




SOUTH VIETNAM
1969
★ RANCH HAND BASES
Da Nang
I CORPS
Phu Cat
II CORPS
III CORPS
★ Bien Hoa
● Saigon (Tan Son Nhut)
IV CORPS

ESTIMATED QUANTITES OF HERBICIDES AND
TCDD SPRAYED IN VIETNAM,
JANUARY 1962 - FEBRUARY 1971

Chemical	Pounds
2,4-D	55,940,150
2,4,5-T	44,232,600
TCDD	368

ESTIMATED QUANTITES OF HERBICIDES AND
TCDD SPRAYED IN UNITED STATES,
JANUARY 1962 - JANUARY 1971

Chemical	Pounds
2,4-D	327,627,000
2,4,5-T	78,100,000
TCDD	650

VIETNAM VETERANS ARE WORRIED ABOUT

- Birth Defects and Miscarriages
- Cancers
  - Soft Tissue Sarcoma
  - Other
- Early Death
- Skin Disorders
  - Chloracne
  - PCT
- Disease Due to Dioxin in Tissue

HOW DO SCIENTISTS ADDRESS THESE CONCERNS?

EPIDEMIOLOGY: STUDY OF FREQUENCY AND CAUSE OF DISEASE IN HUMAN POPULATIONS

CASE-CONTROL STUDY -

- Experiences compared between subjects selected for Disease and Subjects without the disease.

COHORT STUDY -

- Exposed and non-exposed populations examined for disease.

SCIENTIFIC CONSENSUS ACHIEVED WHEN:

- Statistically significant data
- Withstand peer review, and
- Results duplicated by others

MEDICAL CONSENSUS NOW RELATES DIOXIN EXPOSURE TO:

- Chloracne
- Porphyria Cutanea Tarda (PCT)
- Temporary Health Effects

DIOXIN EXPOSURE - TEMPORARY EFFECTS

- Headache
- Fatigue
- Muscle and Joint Pain
- Tingling in extremities
- Sexual dysfunction
- Loss of appetite and weight
- Sleep disturbances
- Impaired memory and learning ability
- Abnormal liver function

FEDERAL GOVERNMENT ADDRESSES VETERAN CONCERNS:

WHITE HOUSE

CAPITOL

CONCERN - BIRTH DEFECTS AND MISCARRIAGES

COMPLETED: EPA ARKANSAS STUDY-1979

NIOSH NEW YORK STATE STUDY 1979

NEW ZEALAND APPLICATOR STUDY-1982

AUSTRALIAN BIRTH DEFECTS STUDY-1983

CONCLUSION: MEN AND WOMEN ARE AT NO INCREASED RISK

ON-GOING: CDC/DOD/VA BIRTH DEFECTS STUDY- 1984

AIR FORCE HEALTH STUDY- 1984

CONCERN - MORTALITY: NUMBER/AGE/CAUSE

COMPLETED: FOUR INDUSTRIAL HEALTH STUDIES-1980-1983

FINLAND MORTALITY STUDY OF HERBICIDE APPLICATORS-1982

AIR FORCE HEALTH STUDY-BASELINE MORTALITY-1983

CONCLUSION: NO EVIDENCE OF INCREASED DEATH RATE

ON-GOING: NEW YORK STATE MORTALITY STUDY - 1984

VA MORTALITY STUDY - 1984

CONCERN - CONNECTIVE TISSUE CANCER
(SOFT TISSUE SARCOMA, STS)

COMPLETED: SWEDISH STS STUDIES - 1978-1983
NEW ZEALAND STS STUDY-1982
FINLAND CANCER STUDY-1982
INDUSTRIAL STUDIES-1980-1983

CONCLUSION: NO CONSENSUS

ON-GOING: NEW YORK STATE STUDY - 1984
NCI STUDIES - 1984-85
VA/AFIP STUDY - 1985
NIOSH REGISTRY STUDY - 1985
CDC STUDY - 1986

CONCERN - OTHER FORMS OF CANCER

COMPLETED: FINLAND CANCER STUDY-1982

SWEDISH RISK EVALUATION OF PESTICIDES-1982

NCI FLORIDA PESTICIDE APPLICATOR STUDY-1983

INDUSTRIAL STUDIES-1980-1983

CONCLUSION: NO CONSENSUS

ON-GOING: AIR FORCE HEALTH STUDY-1984

NIOSH DIOXIN REGISTRY-1985

CDC AGENT ORANGE STUDY-1987

CONCERN - CHLORACNE

CURRENT EVIDENCE: RARE

ON-GOING STUDIES: AIR FORCE HEALTH STUDY

CONCERN - OTHER HEALTH PROBLEMS

ON-GOING STUDIES: AIR FORCE HEALTH STUDY-1984
VA TWIN STUDY-1986
CDC STUDIES-1987

OTHER EFFORTS: VA AGENT ORANGE REGISTRY
VA PATIENT TREATMENT FILE

CONCERN - DIOXIN IN BODY TISSUE

COMPLETED: VA FEASIBILITY STUDY-1982
CANADIAN STUDY-1983

CONCLUSIONS: SMALL AMOUNTS DETECTED
NO CORRELATION WITH EXPOSURE
OR HEALTH

ON-GOING: VA/EPA DIOXIN STUDY

SUMMARY

- Short-term health effects do occur
- Long-term health effects may occur
  - No conclusive evidence to date
- Massive research program underway on long-term effects

SCIENTIFIC CONSENSUS EXPECTED

- Birth Defects 1984
- Mortality 1984
- Soft Tissue Sarcoma 1985
- Other Health Problems 1986-87

ON-GOING VA PROGRAMS WHILE RESEARCH IN PROGRESS

- Health Surveillance
  - Agent Orange Registry
  - Patient Treatment File
- Health Care
  - Public Law 97-72

CONCERN - OTHER FORMS OF CANCER

COMPLETED: FINLAND CANCER STUDY-1982

SWEDISH RISK EVALUATION OF PESTICIDES-1982

NCI FLORIDA PESTICIDE APPLICATOR STUDY-1983

INDUSTRIAL STUDIES-1980-1983

CONCLUSION: NO CONSENSUS

ON-GOING: AIR FORCE HEALTH STUDY-1984

NIOSH DIOXIN REGISTRY-1985

CDC AGENT ORANGE STUDY-1987

CONCERN - CHLORACNE

CURRENT EVIDENCE: RARE

ON-GOING STUDIES: AIR FORCE HEALTH STUDY

CONCERN - OTHER HEALTH PROBLEMS

ON-GOING STUDIES: AIR FORCE HEALTH STUDY-1984
VA TWIN STUDY-1986
CDC STUDIES-1987

OTHER EFFORTS: VA AGENT ORANGE REGISTRY
VA PATIENT TREATMENT FILE

CONCERN - DIOXIN IN BODY TISSUE

COMPLETED: VA FEASIBILITY STUDY-1982
CANADIAN STUDY-1983

CONCLUSIONS: SMALL AMOUNTS DETECTED
NO CORRELATION WITH EXPOSURE OR HEALTH

ON-GOING: VA/EPA DIOXIN STUDY

SUMMARY

- Short-term health effects do occur
- Long-term health effects may occur
  - No conclusive evidence to date
- Massive research program underway on long-term effects

SCIENTIFIC CONSENSUS EXPECTED

- Birth Defects 1984
- Mortality 1984
- Soft Tissue Sarcoma 1985
- Other Health Problems 1986-87

ON-GOING VA PROGRAMS WHILE RESEARCH IN PROGRESS

- Health Surveillance
  - Agent Orange Registry
  - Patient Treatment File
- Health Care
  - Public Law 97-72

Background of Agent Orange Working Group

On December 11, 1979, Stuart Eizenstat, Assistant to President Carter, requested HHS to take the lead in convening an Interagency Work Group (IWG) to study possible long-term health effects of phenoxy herbicides and contaminants (Tab A). The IWG was to oversee, coordinate and set priorities among Federal government research activities in this area. In designing a research agenda, the IWG was to take into consideration the possible health effects of exposure to Agent Orange by Vietnam veterans.

President Reagan announced on July 17, 1981, that he was reaffirming the mandate of the Interagency Work Group and his intention to "make its work a major priority of my Administration". The Interagency Working Group was renamed the Agent Orange Working Group (AOWG) and raised in status to Cabinet Council level (Tab B). In his implementing memorandum of August 21, 1981, Secretary Schweiker stated that the President had been motivated because he shared the widespread public and Congressional concern over possible adverse health effects among Vietnam veterans exposed to Agent Orange and other substances (Tab C). In the same memorandum the Secretary reaffirmed the charter language of December 11, 1979, and added the responsibility for guiding the epidemiologic study of the health of Vietnam veterans authorized by P.L. 96-151 as amended by P.L. 97-72.

In appointing her Under Secretary as chair of the AOWG in a Press Release dated June 6, 1983, Secretary Heckler added her personal long time interest and concern for Vietnam veterans. "I am reaffirming this administration's commitment to the prompt and scientifically responsible resolution of the health concerns of Vietnam veterans who were exposed to Agent Orange and other environmental factors during their service to their country in that conflict" she said. (Tab D)

The charter of IWG, and now of AOWG, is a broad mandate which provides in explicit terms the authority to design and direct all research activities on the health effects of exposure to phenoxy herbicides and contaminants, with exposure to Agent Orange by Vietnam veterans as one part of the total research design (Tab E). The contaminants mentioned include that class of chemicals known as the dioxins produced during the manufacture of these herbicides The renaming of the IWG by President Reagan focused the Work Group's primary responsibility on Agent Orange, but without a change in the language of the charter, a lack of clarity regarding the AOWG's purpose and scope resulted.

Telecopy: Sandy Lange 629-3360
7 of 4 pages

12/11 This is Original Copy to Secretary & Randy Linder
Will be controlled first thing in A.M.

RECEIVED IMMEDIATE OFFICE OF THE SECRETARY-HEW
DEC 11 12 13 PM '79

THE WHITE HOUSE

WASHINGTON

December 11, 1979

MEMORANDUM FOR SECRETARY OF DEFENSE
SECRETARY OF HEALTH, EDUCATION, AND WELFARE
ADMINISTRATOR OF VETERANS AFFAIRS

SUBJECT: Interagency Work Group to Study the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants

In recent months the public and the Congress have become concerned about adverse health effects to veterans following their possible exposure to herbicides, particularly Agent Orange, while serving in Vietnam. Although there are suggestions of adverse health effects of human exposure to such herbicides and contaminants, there is currently an inadequate scientific basis for concluding that health problems experienced by Vietnam veterans were caused by previous exposure to herbicides. Moreover, there is inadequate information on the long-term health effects of phenoxy herbicides in general.

Individually, each of your agencies has a strong interest in resolving this issue. Several studies have been initiated to answer questions about the possible health effects of exposure to herbicides and more generally to the class of substances called the dioxins. Collectively, the Federal government needs to have reliable data and criteria on which to base decisions and policies which affect the entire country. Although I am aware that there has already been extensive interagency cooperation on these issues, I believe there is a need for formal interagency coordination.

Therefore, I request that you establish an interagency work group to coordinate agency efforts to determine if there are long-term health effects following exposure to phenoxy herbicides and contaminants, with special immediate focus on exposure of Vietnam veterans to Agent Orange. This interagency group should:

1. Oversee, coordinate, and set priorities among Federal government research activities designed

to relate exposure to phenoxy herbicides to long-term health effects.

2. Develop a research agenda to assure that the Federal government conducts comprehensive research on the long-term health effects of these compounds, in response to both scientific and policy needs. The type and duration of exposure to Agent Orange by Vietnam veterans must be considered in the research agenda design so that the Veterans Administration will be able to establish sound policies for determining compensation for veterans exposed to Agent Orange in Vietnam, should a relationship between herbicide exposure and long-term adverse health effects be established. The research agenda should build on current agency activities, including the Department of Defense's Ranch Hand study. The interagency work group should identify the appropriate agencies to conduct the recommended research, either individually or through joint efforts.

3. Provide technical support to individual agencies and independent researchers in the formulation, development, and implementation of research on the biomedical effects of phenoxy herbicides and contaminants.

4. Assure that the protocols and methodology of ongoing and proposed Federally funded research studies will produce valid, reliable, timely, and relevant data, and periodically review the status of such research.

5. Assure that all relevant research findings, whether publicly or privately financed, are promptly made available to the public and the Congress, in a comprehensible and comprehensive fashion. The work group should establish a working relationship with the Veterans Administration's Advisory Committee on Health-Related Effects of Herbicides and should promptly provide the Committee all relevant information as it becomes available.

I am asking Secretary Harris to take the lead in convening the interagency group and would like to have an initial report on the progress of the group submitted to me by

February 15. The initial report should indicate the status of current agency activities, a proposed schedule for public progress reports, and any recommendations for inclusion of other agencies on the work group.

I have asked the Office of Science and Technology Policy to be an ex-officio participant on the work group. In addition, the Department of Agriculture, the Environmental Protection Agency, and the Occupational Safety and Health Administration will initially participate on the work group in an observer status.

Stuart E. Eizenstat
Assistant to the President
for Domestic Affairs and Policy

cc: Secretary of Agriculture
Administrator, Environmental Protection Agency
Assistant Secretary of Labor for Occupational Safety and Health
Director, Office of Science and Technology Policy

I-3

THE WHITE HOUSE

WASHINGTON

July 17, 1981

MEMORANDUM FOR: SECRETARY RICHARD SCHWEIKER
CHAIRMAN PRO-TEM, CABINET COUNCIL
ON HUMAN RESOURCES

FROM: ROBERT CARLESON
EXECUTIVE SECRETARY OF HUMAN RESOURCES
CABINET COUNCIL

SUBJECT: Agent Orange Working Group

The Secretariat of the Human Resources Cabinet Council has established an Agent Orange Working Group. The lead agency will be HHS, and participating members drawn from:

Department of Defense
Department of Agriculture
Department of Health and Human Services
Department of Labor
Environmental Protection Agency
Veterans Administration
Action
Office of Management and Budget
Council of Economic Advisers
Office of Science and Technology
Office of Policy Development

cc: Martin Anderson
Edwin Gray

THE WHITE HOUSE

WASHINGTON

AUG 21 1981

MEMORANDUM FOR: SECRETARY OF DEFENSE
SECRETARY OF AGRICULTURE
SECRETARY OF LABOR
DIRECTOR, OFFICE OF MANAGEMENT AND BUDGET
ASSISTANT TO THE PRESIDENT FOR POLICY DEVELOPMENT
CHAIRMAN, COUNCIL OF ECONOMIC ADVISERS
DIRECTOR OF ACTION
ADMINISTRATOR, ENVIRONMENTAL PROTECTION AGENCY
ADMINISTRATOR OF VETERANS AFFAIRS
DIRECTOR, OFFICE OF SCIENCE AND TECHNOLOGY POLICY

FROM : SECRETARY RICHARD SCHWEIKER
CHAIRMAN PRO-TEM, CABINET COUNCIL ON HUMAN RESOURCES

SUBJECT : Agent Orange Working Group

The Administration has reviewed the excellent work of the Interagency Work Group to Study the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants and believes that it has made significant progress toward fulfilling its important mandate. By bringing together knowledgeable scientists from the various Federal departments and agencies the Work Group has identified ongoing research activities on phenoxy herbicides and contaminants and begun to develop and organize the means to carry out additional needed scientific research.

President Reagan shares the widespread public and congressional concern over possible adverse health effects among Vietnam veterans exposed to Agent Orange and other substances. The President stated, during his meeting with national veterans organization leaders at the White House on July 17, 1981, that the Administration is giving special consideration to those concerns of Vietnam veterans.

At the White House meeting, the President announced that the administration had re-established an expanded Working Group as the Agent Orange Working Group and raised its status to Cabinet Council level. The President is personally determined to assure that the full resources of the Federal government are

available to support the Working Group's continuing efforts. The decision to re-establish and expand the membership of the Working Group and to make it an integral part of the Cabinet Council on Human Resources reflects the President's commitment and accords the highest priority to its mission.

As Chairman Pro-Tem of the Cabinet Council on Human Resources, I am, accordingly, reaffirming by this memorandum the Agent Orange Working Group's mandate of December 11, 1979 and providing specific guidance as to how that mandate is to be carried out in accordance with the Cabinet Council's decisions.

The Department of Health and Human Services shall continue to have lead responsibility for overall direction and management of the Agent Orange Working Group. The Secretary of Defense and the Administrator of Veterans Affairs shall continue to assure that their respective agencies participate fully in all Working Group activities. The Departments of Agriculture and Labor and the Environmental Protection Agency, each of which have until now been observers, shall assume full membership and their respective agency heads shall assure that those agencies participate fully in all Work Group activities.

In addition, ACTION, the Office of Management and Budget, and the Council of Economic Advisers, as well as the White House Office of Science and Technology Policy and the Office of Policy Development, shall assume membership on the Working Group and the heads of those agencies and offices shall assure that the resources of their respective agency or office are fully available to support it.

Also, the congressional Office of Technology Assessment, which has been actively involved in all Working Group activities as an observer, will be invited to continue to participate in that capacity, and the General Accounting Office, which has been extremely helpful to the Working Group in the past, will continue to be kept abreast of developments and invited to advise and assist as appropriate.

The Working Group has initiated research efforts designed to find answers to many of the questions surrounding Agent Orange that have been raised. These efforts include the birth defects study being conducted by HHS' Centers for Disease Control, the Ranch Hand Study being conducted by the Air Force, the epidemiological study being planned by the Veterans Administration pursuant to P.L. 96-151, and the compilation by HHS' National Institute of Occupational Safety and Health of a national registry of workers exposed to dioxins. Each of these research activities, as well as the other important research

activities being conducted under the overall guidance of the Working Group, are to be continued without interruption or delay.

The Working Group has developed an impressive record of scientific objectivity, impartiality and integrity and it is imperative to the success of the Working Group effort that this record and the Group's credibility be maintained. In this regard, regular progress reports to the Cabinet Council, the Congress and the public will continue to be made by the Agent Orange Working Group.

To assure effective leadership of the Working Group, I am hereby appointing James Stockdale, HHS Deputy Under Secretary for Intergovernmental Affairs, as Chair. Also, I am appointing Dr. Vernon N. Houk of the Center for Environmental Health of the Centers for Disease Control as Chair of the Working Group's Science Panel. In addition, I am appointing HHS Legal Counsel Leslie A. Platt, who has served as legal adviser to and staff director of the Working Group since its inception, to continue in those capacities. I know and believe you will find that these individuals share my commitment to carrying out this important mission.

Please review your representation on the Working Group to assure that your agency or office is adequately represented by appropriate technical experts, scientists and policy-level officials. In order to facilitate the Group's effectiveness, it is of course important that each agency's total membership be limited.

The first meeting of the full Working Group has been scheduled for Friday, August 28, 1981 and a meeting of the Science Panel will be scheduled for shortly thereafter. Accordingly, please let Mr. Bart Kull, Special Assistant to the Deputy Under Secretary for Intergovernmental Affairs (245-6156), or Dr. Peter Beach, HHS Director of Veterans Affairs (245-2210), know as soon as possible the name(s) of your designated representative(s) so that briefing materials may be forwarded to them.

Attached for your information is a copy of the memorandum of the Executive Secretary to the Cabinet Council on Human Resources establishing the Working Group.

Attachment

cc: Comptroller General of the United States
Director, Congressional Office of Technology Assessment
Mr. Robert Carleson
Mr. Edwin Gray

HHS NEWS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOR IMMEDIATE RELEASE
Monday, June 6, 1983

Russell Mack--(202) 245-6343

Health and Human Services Secretary Margaret M. Heckler today named her department's under secretary, John A. Svahn, as chairman of the Agent Orange Working Group of the Cabinet Council on Human Resources.

The working group coordinates and oversees federal research into the possibility of long term adverse health effects resulting from exposure to phenoxy acid herbicides used during the Vietnam War. The herbicides, principally Agent Orange, were used primarily to defoliate dense jungle cover to reveal enemy troop movements and staging areas.

"By designating the second highest official of my department as chairman, I am reaffirming this administration's commitment to the prompt and scientifically responsible resolution of the health concerns of Vietnam veterans who were exposed to Agent Orange and other environmental factors during their service to their country in that conflict. Jack Svahn's leadership of this vital working group will help us get the answers we need," Secretary Heckler said.

In response to veterans' concerns about the possibility of illness as a result of their exposure, the working group was created in late 1979. It was reestablished and upgraded to Cabinet Council reporting level by President Reagan in July 1981.

Under the aegis of the working group, various federal agencies, including HHS' Public Health Service, the Veterans Administration and Department of Defense, are conducting 64 separate research studies relating to Agent Orange and other health effects of service in Vietnam, at a cost estimated in excess of $100 million.

As chairman of the working group, Svahn will report to the president through Secretary Heckler in her capacity as chairperson pro-tem of the Cabinet Council on Human Resources.

Svahn was appointed under secretary of the Department of Health and Human Services March 8. Prior to that appointment he served as commissioner of Social Security since May 6, 1981.

Following service in the U.S. Air Force in 1968, Svahn held administrative positions with the state of California, the federal government and the private sector.

# # #

CHARTER
Cabinet Council Agent Orange Working Group
December 11, 1979, as Reaffirmed
on August 21, 1981

The Agent Orange Working Group shall:

1. Oversee, coordinate, and set priorities among Federal government research activities designed to relate exposure to phenoxy herbicides to long-term health effects.

2. Design a research agenda to assure that the Federal government conducts comprehensive research on the long-term health effects of the compounds, in response to both scientific and policy needs. The type and duration of exposure to Agent Orange by Vietnam veterans must be considered in the research agenda design so that the Veterans Administration will be able to establish sound policies for determining compensation for veterans exposed to Agent Orange in Vietnam, should a relationship between herbicide exposure and long-term adverse health effects be established. The research agenda should build on current agency activities, including the Department of Defense's Ranch Hand study. The Working Group should identify the appropriate agencies to conduct the recommended research, either individually or through joint efforts.

3. Provide technical support to individual agencies and independent researchers in the formulation, development, and implementation of research on the biomedical effects of phenoxy herbicides and contaminants.

4. Assure that the protocols and methodology of ongoing and proposed federally funded research studies will produce valid, reliable, timely, and relevant data, and periodically review the status of such research.

5. Assure that all relevant research findings, whether publicly or privately financed, are promptly made available to the public and the Congress, in a comprehensible and comprehensive fashion. The work group should establish a working relationship with the Veterans Administration's Advisory Committee on Health-Related Effects of Herbicides and should promply provide the Committee all relevant information as it becomes available.

6. Provide guidance to the epidemologic study of the health of Vietnam Veterans authorized by P.L. 96-151 as amended by P.L. 97-72.

Agent Orange Working Group Organization

Following a review of the work of the Interagency Working Group, President Reagan in July 1981 re-established and expanded the Interagency Work Group, raised its status to Cabinet Council level and renamed it the Agent Orange Working Group (AOWG). The purpose was to reflect his commitment to the work of the group and to place high priority on its mission. The President asked the Secretary of HHS, as Chair Pro-Tem of the Cabinet Council on Human Resources, to oversee its work. The AOWG now reports to the Cabinet Domestic Council.

The AOWG membership includes representatives from the Veterans Administration (VA), Departments of State, Defense and Labor, the Office of Management and Budget, the Environmental Protection Agency, the ACTION Agency, the Council of Economic Advisors, the White House Office of Science and Technology Policy and the Assistant to the President for Policy Development. The Congressional Office of Technology Policy participates as an observer.

The AOWG organization is headed by a Chair appointed by the Secretary as a member of the Cabinet. The Chair, AOWG, in turn appoints:

1. Chair, Science Panel
2. Legal Counsel
3. Executive Secretary
4. Chair, Resources Panel
5. Chair, Public and Congressional Affairs Panel

The Science Panel, composed of expert medical and scientific personnel drawn from various government agencies concerned with issues of public health, advises the AOWG on the conduct of research related to Agent Orange. The Science Panel includes two subpanels: a Research Agenda Subpanel to recommend needed research and a Research Review Subpanel to review all planned research for adequacy of design and conformance with the AOWG mission.

The Resources Panel is concerned with the proper allocation of available resources among planned and on-going research and the avoidance of duplication of effort.

The Public and Congressional Affairs Panel defines policies to be used in information dissemination to insure that such dissemination is timely, accurate and complete.

In addition to these structures, the AOWG is advised by the Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants. This Advisory Committee is composed of pre-eminent scientists from outside the Government.

The agency membership with the current designated represenatives from each and the staff of the AOWG are listed at Tab A.

AGENT ORANGE WORKING GROUP
MEMBERSHIP

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Lead Representatives:

Mr. Dixon Arnett
Acting Chair Pro Tempore, AOWG
Deputy Under Secretary
for Intergovernmental Affairs
Department of Health and Human Services
200 Independence Avenue, S.W.
Room 606-E, HHH Building
Washington, D.C. 20201
(202) 245-0409

Dr. James O. Mason
Vice-Chair, AOWG
Acting Assistant Secretary for Health
Department of Health and Human Services
200 Independence Avenue, S.W.
Room 716-H, HHH Building
Washington, D.C. 20201
(202) 245-7694

Dr. Carl Keller*, Chair
Science Panel
Epidemiologist
National Institute of Environmental
Health Sciences
Room 2B55, Building 31
National Institute of Health
Bethesda, Maryland 20205
(301) 496-3511

Mr. Edwin Weiss (AOWG Legal Counsel)
Office of the General Counsel
330 Independence Avenue, S.W.
North Building, Room 4460
Washington, D.C. 20201
(202) 475-0155

Dr. Peter Beach
AOWG Executive Secretary
Director of Veterans Affairs
Office of the Under Secretary
Room 632-F, HHH Building
200 Independence Avenue, S.W.
Washington, D.C. 20201
(202) 245-2210 or 245-6156

*Denotes Science Panel Member

Revised: September 1985

DEPARTMENT OF HEALTH AND HUMAN SERVICES cont'd (Members)

Dixon Arnett
Deputy Under Secretary
for Intergovernmental Affairs
Department of Health and Human Services
200 Independence Avenue, S.W.
Room 606-E, HHH Building
Washington, D.C. 20201
(202) 245-0409

Shirley Barth
AOWG Public/Congressional
Affairs Panel, Chair
US/PHS
200 Independence Avenue, S.W.
Room 716-G, HHH
Washington, D.C. 20201
(202) 472-5663

Lee Mosedale
Policy Coordinator
OS/ES
HHH Building, Room 635-G
200 Independence Avenue, S.W.
Washington, D.C. 20201
(202) 245-7462

Dr. Vernon Houk*
Director
Center for Environmental Health
Centers for Disease Control
1600 Clifton Road, N.E.
Atlanta, Georgia 30333
FTS 236-4111 Commercial (404) 452-4111

Dr. David Rall*
Director, National Institute of
Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, N.C. 27709
FTS 629-3201 Commercial (919) 541-3201

Dr. James S. Dickson, III
Senior Advisor for Environmental Affairs
Office of the Assistant Secretary
for Health
Department of Health and Human Services
200 Independence Avenue, S.W.
Room 701-H, HHH Building
Washington, D.C. 20201
(202) 245-6811

DEPARTMENT OF HEALTH AND HUMAN SERVICES cont'd

Dr. Renata Kimbrough*
Research Medical Officer
Centers for Disease Control
1600 Clifton Road, N.E.
Atlanta, Georgia 30333
FTS 236-4324 Commercial (404) 454-4324

Dr. Philip Landrigan, Director*
Division of Surveillance, Hazard
Evaluations and Field Studies
4673 Columbia Parkway
Cincinnati, Ohio 45226
FTS 684-4428 Commercial (513) 684-4428

Miriam Davis, Ph.D.*
Staff Assistant/PHS
AOWG Science Panel
200 Independence Avenue, S.W.
Room 716-G, HHH
Washington, D.C. 20201
(202) 245-6301

Dr. Robert W. Miller*
Chair, Advisory Committee
Clinical Epidemiology Branch
National Cancer Institute - NIH
Room 5A21, Landow Building
Bethesda, Maryland 20205
(301) 496-5785

Dr. Marilyn Fingerhut*
Section Chief
NIOSH - EPI I
4676 Columbia Parkway
Mail Stop R-15
Cincinnati, Ohio 45226
(FTS) 684-4411 Commercial (513) 684-4411

WHITE HOUSE OFFICE OF POLICY DEVELOPMENT

Lead Representative: Dr. William Roper*
Special Assistant to the
President for Health Policy
Old Executive Office Building
Room 235
Washington, D. C. 20500
(202) 456-6722

WHITE HOUSE OFFICE OF SCIENCE AND TECHNOLOGY POLICY

Lead Representative:

Dr. George Keyworth*
Science Adviser to the President
& Director, Office of Science
Technology Policy
Old Executive Office Building
Room 358
Washington, D.C. 20500
(202) 456-7116

Dr. Alvin Young*
Senior Policy Anaylst
Office of Science Technology Policy
New Executive Office Building
Room 5005
Washington, D.C. 20500
(202) 395-3125

VETERANS ADMINISTRATION

Lead Representative:

Mr. Everett Alvarez
Deputy Administrator
Veterans Administration
810 Vermont Avenue, N.W., Rm. 1000N
Washington, D.C. 20420
(202) 389-5428

Dr. Barclay Shepard (102)*
Director, Agent Orange Projects Office
Veterans Administration
810 Vermont Avenue, N.W., Room 308
Washington, D.C. 20420
(202) 376-7528

Dr. Lawrence B. Hobson (102)*
Deputy Director
Agent Orange Projects Office
Veterans Administration
810 Vermont Avenue, N.W., Rm. 116
Washington, D.C. 20420
(202) 389-5534

DEPARTMENT OF DEFENSE

Lead Representative:

Captain Peter A. Flynn, MC, USN*
Director, Professional Services
ODASD(Health Promotion),
OASH (Health Affairs)
The Pentagon, Room 3E337
Washington, D.C. 20301
(202) 697-8973

DEPARTMENT OF DEFENSE cont'd

Richard S. Christian, C.R.M.*
Director, Environmental Support Group
Army Agent Orange Task Force
1730 K Street, N.W., Room 210
Washington, D.C. 20006
(202) 653-1832

Lt. Col. Robert Capell*
Asst. for Bioenvironmental Engineering
Office of Surgeon General
USAF/SGES
Bolling Air Force Base
Washington, D.C. 20332
(202) 767-5078

DEPARTMENT OF AGRICULTURE

Lead Representative:

Dr. Philip Kearney*
Chief, Pesticide Degradation Lab
U.S. Department of Agriculture
BARC-West
Building 050 - Room 100
Beltsville, Maryland 20705
(301) 344-3533

ENVIRONMENTAL PROTECTION AGENCY

Lead Representative:

Dr. Jack Moore*
Assistant Administrator
for Pesticides & Toxic Substances
U.S. Environmental Protection Agency
401 M Street, S.W., (TD788)
Washington, D. C. 20460
(202) 382-2902

Dr. Donald Barnes*
Senior Science Adviser to the
Assistant Administrator
for Pesticides and Toxic Substances
U.S. Environmental Protection Agency
401 M Street, S.W., (TS788)
Washington, D.C. 20460
(202) 382-2897

DEPARTMENT OF LABOR

Lead Representative: Mr. Donald Shasteen
Assistant Secretary for
Veterans Employment and Training
Department of Labor
Francis Perkins Building, Rm. S-1315
200 Constitution Avenue, N.W.
Washington, D.C. 20210
(202) 523-9116

Mr. Stephen Mallinger*
Deputy Director for the Director
of Technical Support
U.S. Department of Labor
OSHA
200 Constitution Avenue, N.W.
Room N-3651, FPB
Washington, D.C. 20210
(202) 523-7047

ACTION

Lead Representative: Vacant

James Hearn
Deputy Director
The President's Vietnam Veterans
Leadership Program
ACTION
806 Connecticut Ave., N.W. Room 1006
Washington, D.C. 20525
(202) 634-9339

COUNCIL OF ECONOMIC ADVISERS

Lead Representative: Vacant

OFFICE OF MANAGEMENT AND BUDGET

Lead Representative:

Mr. John Cogan
Associate Director for Human
Resources, Veterans & Labor
Office of Management and Budget
Old Executive Office Building
Room 246
Washington, D.C. 20503
(202) 395-3120

Mr. Bernard H. Martin
Deputy Associate Director for
Labor, Veterans & Education Division
Office of Management and Budget
New Executive Office Building
Room 7025
Washington, D.C. 20503
(202) 395-3971

Susan Jacobs
Chief of Veterans Affairs Branch
Veterans Affairs Branch
Office of Management and Budget
New Executive Office Building
726 Jackson Place, N.W., Rm. 7007
Washington, D.C. 20503
(202) 395-4500

Ms. Annette Rooney
Budget Examiner
Veterans Affairs Branch
Office of Management and Budget
New Executive Office Building
726 Jackson Place, N.W., Rm. 7013
Washington, D.C. 20503
(202) 395-4500

CONGRESSIONAL OFFICE OF TECHNOLOGY ASSESSMENT (OBSERVER)

Lead Representative:

Dr. Michael Gough*
Senior Analyst
United States Congress
Office of Technology Assessment
Washington, D.C. 20510
(202) 226-2070

CONGRESSIONAL OFFICE OF TECHNOLOGY ASSESSMENT (OBSERVER) (cont'd)

Ms. Hellen Gelband*
Analyst
Office of Technology Assessment
United States Congress
Washington, D.C. 20510
(202) 226-2070

DEPARTMENT OF STATE

Lead Representative:

Mr. William J. Walsh, III
Biomedical Research Officer
Office of Environment and Health
Department of State
Room 7820
Washington, D.C. 20520
(202) 632-4824

Dr. Charles E. Brodine, M.D.*
Assistant Medical Director for
Environmental Health and
Preventive Medicine
Office of Medical Services, M/MED
Department of State, Rm. 4253
Washington, D. C. 20520
(202) 632-5337

Mr. Steve Johnson
Vietnam Desk Officer
Bureau of East Asia and Pacific Affairs
Department of State, Room 5210
Washington, D.C. 20520
(202) 632-3132

Agent Orange Working Group
Public Affairs Panel

Ms. Shirley Barth
Chair USPHS/Public Affairs
Room 716G Hubert H. Humphrey Bldg.
200 Independence Avenue, S. W.
Washington, D.C. 20201

Mr. William J. Walsh, III
Biomedical Research Officer
Office of Environment and Health
Department of State
Room 7820
Washington, D.C. 20520

Lt. Colonel Edwina Palmer
Department of Defense
Public Affairs
Room 1E794
The Pentagon
Washington, D.C. 20301

Mr. Robert Putnam 106
Veterans Administration
Public Affairs
810 Vermont Avenue, N.W.
Washington, D.C. 20420

Ms. Inez Artico A-107
Public Affairs
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 2046

Mr. Donald Berreth
Centers for Disease Control
Room 2067, Building 1
Atlanta, Georgia 30333

Advisory Committee on Special Studies

The Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants had its genesis in the directives of the White House for an independent review from scientists outside the Government of the Air Force Ranch Hand Study (Tab A). This study compared mortality and morbidity of the Air Force personnel involved in the spraying of Agent Orange in Vietnam with a group of Air Force personnel who were not exposed to the herbicide.

Because of the value of this kind of independent review, the Advisory Committee on Special Studies was chartered to permit it, at the discretion of the Chair, Agent Orange Working Group (AOWG), to undertake a review of any study, proposed or on-going, which falls within the purview of the AOWG.

The Advisory Committee on Special Studies is established under the provisions of the Advisory Committee Act and is governed by the regulations of 45 CFR Part 11. The Charter of the Committee is at Tab B, and its membership is listed at Tab C.

THE WHITE HOUSE

WASHINGTON

September 16, 1980

MEMORANDUM FOR THE SECRETARY OF DEFENSE
THE SECRETARY OF HEALTH AND HUMAN SERVICES
THE SECRETARY OF AGRICULTURE
THE ADMINISTRATOR OF VETERANS AFFAIRS
THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY
THE ASSISTANT SECRETARY OF THE OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION

SUBJECT: Epidemiological Study of Ranch Hand Personnel

Last December, I asked you to participate in an interagency work group to coordinate federal agency efforts to determine if there are long-term health effects following exposure to phenoxy herbicides and contaminants, with special immediate focus on exposure of veterans to Agent Orange in Vietnam.

I am gratified by the progress that the Work Group has made in a short period and by the respect that the Work Group has earned with the Congress and the public. The members of your agencies who have participated on the Work Group should be commended for their diligence and spirit of cooperation.

Today, I am informing Secretary Brown that I have concurred with the Interagency Work Group's recommendation that the Air Force proceed to conduct the Epidemiological Study of Ranch Hand Personnel. I strongly believe that an essential component of this effort must be independent review and monitoring over the next few years by the Interagency Work Group's Scientific Panel.

In addition, I look to the Work Group to provide substantial assistance to the Veterans Administration, who also will conduct a major epidemiological study of the possible long-term health effects in veterans of service in Vietnam. The Work Group's expertise and credibility will provide valuable assistance to the VA.

Because of the ability that the Work Group has clearly demonstrated as well as the continuing requirements for governmental studies on phenoxy herbicides, Frank Press and I wish now to reaffirm the mandate of the Interagency Work Group. I hope that your agencies continue to give participation on the Work Group as much importance in the future as they have in the past.

Stuart E. Eizenstat
Assistant to the President
for Domestic Affairs and Policy

THE WHITE HOUSE

WASHINGTON

September 16, 1980

MEMORANDUM FOR THE SECRETARY OF DEFENSE

The Air Force has sought guidance from the Interagency Work Group on the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants on whether it should proceed with the Epidemiological Study of Ranch Hand Personnel because the National Academy of Sciences review of the Air Force protocol had expressed concern about the credibility of the Air Force to conduct the study.

Ranch Hand personnel, who applied Agent Orange between 1962 and 1971 in Vietnam, are the only population whose frequency and duration of exposure to Agent Orange are known with any accuracy. The Interagency Work Group agrees with the Air Force that the results of the Ranch Hand study should provide valuable information about the long-term health effects of exposure by veterans to Agent Orange in Vietnam.

Over the past 20 months, the Air Force has made a conscientious effort to design a scientifically valid study responsive to the recommendations of five separate peer reviews, including that of the National Academy of Sciences. After a thorough review of the proposed final study protocol, which includes certain changes based on the separate peer reviews, and after consultation with the Air Force scientists responsible for the study, the Work Group recommended to me that the Air Force be instructed to carry out the Ranch Hand study. In light of the progress already made by the Air Force and the need to proceed expeditiously with this important study, Frank Press and I concur with the Work Group's recommendation.

There remains deeply felt concern among some Vietnam veterans and others about the objectivity of the Air Force to study the possible health effects of Agent Orange. While affirming the capability of the Air Force to assure the proper conduct of the study, the Interagency Work Group has suggested that this concern can be reasonably addressed by independent review and monitoring of the study. I believe that the Scientific Panel of the Interagency Work Group, which is already familiar

with the Ranch Hand protocol, is the appropriate body to oversee the study and to provide technical assistance, as needed, to the Air Force scientists responsible for the study. For the purpose of assuring the public that the study results are reliable and valid, the Work Group plans to augment the Scientific Panel with reputable scientists from outside the government, including those suggested by veterans organizations.

The Interagency Work Group noted that the evaluation of Ranch Hand personnel may have to continue for a lengthy period of time in order to have a better chance of detecting latent or subtle health effects, particularly related to cancer. The Air Force, in consultation with the Scientific Panel, has already designed the protocol to reflect this recommendation.

I am advised that the Ranch Hand study presents a number of difficult technical problems. While recognizing the need to obtain study results promptly, the Air Force's primary responsibility must be to assure that the results will be reliable and valid. I urge the Air Force to utilize fully the expertise of the Scientific Panel of the Interagency Work Group to advise them on the difficult decisions that will surely arise during the course of the study.

In closing, I would like to reaffirm the importance of the Ranch Hand study to Vietnam veterans and their families. The Interagency Work Group and the White House are prepared to offer any assistance that the Air Force may require in discharging its responsibility to conduct a high quality scientific investigation.

Stu Eizenstat

Stuart E. Eizenstat
Assistant to the President
for Domestic Affairs and Policy

CHARTER
(As Amended May 1984)

Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants

Purpose

By memorandum of December 11, 1979, the Assistant to the President for Domestic Affairs and Policy directed the establishment of an Interagency Work Group to Study the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants (Work Group) under the leadership of the Secretary of Health and Human Services. The Work Group was specifically directed to assure that the protocols and methodology of proposed federal research studies will provide reliable data, as well as to provide technical support to individual agencies in the implementation of research.

On August 1, 1980, the Work Group recommended that the United States Air Force conduct its proposed Epidemiologic Studies of Ranch Hand Personnel (Rand Hand Study) and that the conduct of the study be overseen by an independent monitoring committee. By memorandum of September 16, 1980, the Assistant to the President for Domestic Affairs and Policy directed the Air Force to conduct the Ranch Hand Study. In addition, the memorandum directed the Scientific Panel of the Work Group, augmented by scientists from outside the government and including those suggested by veterans organizations, to oversee the study and to provide technical assistance, as needed, to the Air Force.

On July 17, 1981, the President re-established the Interagency Work Group as the Agent Orange Working Group (AOWG) and elevated it to Cabinet Council status. On August 21, 1981, the Secretary, DHHS, Acting as Chairman Pro-Tem, Cabinet Counsel on Human Resources, reaffirmed the Work Group's mandate of December 11, 1979 and appointed the Deputy Undersecretary for Intergovernmental Affairs as Chair of the AOWG.

Authority

The Committee on Special Studies was established under the provisions of section 222 of the Public Health Service Act, as amended, 42 U.S.C. 217a. The Committee is governed by the provisions of 45 CFR Part 11 which sets forth standards for the creation and use of advisory committees.

Function

The Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants shall advise the Secretary and the Chair, Cabinet Council Agent Orange Working Group (AOWG), concerning:

1. Its oversight of the conduct of the Ranch Hand Study by the Air Force;

2. Its oversight and evaluation of the Agent Orange/Vietnam Experience Study mandated by Section 307 of P.L. 96-151 as amended by P.L. 97-72; and

3. Other studies in which the Secretary or the Chair, AOWG, believes involvement by the Advisory Committee is desirable.

The Advisory Committee may provide technical assistance to the study under its consideration.

On the basis of its oversight and evaluation, the Advisory Committee may, inter alia, recommend to the Secretary and the Chair, AOWG, (a) approval, (b) deferral because of a need for further evaluation, (c) disapproval in whole or in part, or (d) imposition of additional conditions which in its judgemnt are necessary to assure or protect advancement of the study under consideration.

Structure

The Committee shall consist of the Secretary, or designee, as Chair, and eight members selected by the Secretary from authorities knowledgeable in fields related to the studies under its oversight and evaluation. The Executive Secretary shall be selected by the Chair.

Management and support services shall be provided by the National Cancer Institute.

Meetings

Meetings shall usually be held quarterly at the call of the Chair, who shall also approve the agenda. A government official shall be present at all meetings.

Meetings shall be open to the public except as determined otherwise by the Secretary; notice of all meetings shall be given to the public.

Meetings shall be conducted, and records of the proceedings kept, as required by applicable laws and Departmental regulations.

Compensation

Members who are not full-time federal employees shall be paid at the rate of $100 per day, plus per diem and travel expenses in accordance with Standard Governmental Travel Regulations.

Annual Cost Estimate

Estimated annual cost for operating the Committee, including compensation and travel expenses for members but excluding staff support, is $19,736. Estimate of annual man years of staff support required is one-quarter, at an estimated annual cost of $8,380.

Reports

An annual report shall be submitted to the Secretary through the Chair, AOWG, not later than November 1 of each year, which shall contain as a minimum a list of members and their business addresses, the Committee's functions, dates and places of meetings, and a summary of Committee activities and recommendations made during the fiscal year. A copy of the report shall be provided to the Department Committee Management Office.

Termination Date

The duration of the Advisory Committee on Special Studies Relating to the Possible Long-Term Effects of Phenoxy Herbicides and Contaminants is five years. Unless renewed by appropriate action prior to its expiration, the Committee will terminate on January 19, 1985.

PROFESSIONAL AREA BREAKDOWN - ADVISORY COMMITTEE ON SPECIAL STUDIES RELATING TO THE POSSIBLE LONG-TERM HEALTH EFFECTS OF PHENOXY HERBICIDES AND CONTAMINANTS

Authorized Positions: 8

Name	Term Ending	Expertise	Prof./Lay/Res.	Geog. Dist.	Minority/Female
Comstock	Duration of Committee	Epidemiology	X	MA	
Friedman	Duration of Committee	Pediatrics, human genetics	X	TX	
Kreiss	Duration of Committee	Occupational Health, epidemiology	X X	CO	X
Kurland	Duration of Committee	Epidemiology, neurology	X	MN	
Monson	Duration of Committee	Epidemiology	X	MD	
Nelson	Duration of Committee	Toxicology	X	NY	
Ramey	Duration of Committee	Statistics, psychology	X	NC	

PROPOSED CANDIDATE FOR VACANCY

Pardes	Duration of Committee	Psychiatry	X	NY	

CONGRESSIONALLY AUTHORIZED EPIDEMIOLOGICAL STUDY

In January 1979, the Congress enacted P.L. 96-151 which directed the Veterans Administration (VA) to investigate health effects of Agent Orange. The authorization was expanded in November 1981 by P.L. 97-72 to include "other factors."

In January 1983, responsibility for design and execution of the study was formally transferred from VA to the Centers for Disease Control (CDC), with resources, both FTE's and funding, to be provided by VA.

The CDC protocol for conducting the study was completed and distributed for scientific review in May 1983. Principal review was conducted by the Office of Technology Assessment. Reviews were also conducted by the Agent Orange Working Group Science Panel, by the Advisory Committee on Special Studies Relating to the Possible Long Term Health Effects of Phenoxy Herbicides and Contaminants (which oversees the Air Force Ranch Hand Study), and by the CDC Ad Hoc Review Panel. National veterans' organizations were invited to comment. All reviews were completed by September 1983.

The CDC protocol contains three study components: (1) Vietnam Experience; (2) Agent Orange; and (3) Selected Cancers Study.

1. The Vietnam Experience Study is to determine whether veterans who served in Vietnam are at greater risk for poor health than are similar veterans who did not serve in Vietnam. The study will identify, from personnel records, 6,000 one-term Army veterans who have served in Vietnam and 6,000 similar veterans who have never been in Vietnam. All of these will be followed for mortality or given a telephone interview covering general health information and demographic data. 2,000 from each group will be given comprehensive physical and psychological examination and health outcomes for the two groups will be compared.

   The questionnaire for this study has been reviewed by the Science Panel and cleared by OMB. A pilot test to determine locatability and participation rates of prospective subjects has been completed and reviewed by the Science Panel. Participation rates were better than anticipated and the study is proceding to the main data collection phase. Concerns were raised by the Science Panel that self-reported health data, including information on reproduction outcomes, should be verified from medical and/or vital records or not collected at all. Some

plans for utilization of these data are currently being developed at CDC and will be discussed at a Science Panel meeting in the near future.

2. The Agent Orange Study is to determine whether Vietnam veterans who were highly likely to have been exposed to Agent Orange while in Vietnam are at greater risk for poor health than are Vietnam veterans with similar experiences while in Vietnam but very unlikely to have been exposed to Agent Orange while there. The study will identify, from Battalion Daily Reports, 6,000 one-term Army Vietnam veterans who were likely to have been exposed to Agent Orange on several occasions, 6,000 similar Vietnam veterans who were not likely to have been exposed to Agent Orange, and 6,000 Vietnam veterans known to have served in areas where Agent Orange was never used. All of these will be followed for mortality or given a telephone interview and 2,000 from each group will be examined as in the Vietnam Experience Study.

   The questionnaire for this study is similar to the one being used in the Vietnam Experience Study. The pilot has not been completed but should yield similar results to the one which has been used for the Vietnam Experience Study. Since the identification of Agent Orange exposed and unexposed subjects who are similar in other ways is crucial to the successful completion of the Agent Orange Study, the selection of the three study cohorts will be reviewed by the Science Panel when this stage has been completed and before the main study begins.

3. The Selected Cancers Study is to determine whether Vietnam veterans are at greater risk for certain cancers than the rest of the population. The study will select post 1985 diagnoses of soft tissue sarcoma, Non-Hodgkins Lymphoma and other cancers from newly identified entries into the Surveillance, Epidemiology, and End Results (SEER) Registries sponsored by the National Cancer Institute. These registries cover approximately 10-12 percent of the U.S. population including both rural and urban residents. Cancer cases from the appropriate age group will be interviewed via telephone and their Vietnam experience compared to that of age matched controls selected from the same communities by random digit dialing.

The questionnaire for this study has been reviewed and cleared by the OMB. Data collection begin in 1985 and the names of identified Vietnam veterans are submitted to the Army and Joint Services Environmental Support Group for records review and assignment of an "Exposure Opportunity Index". This study should provide a good estimate of whether service in Vietnam and/or at least minimal exposure to Agent Orange is associated with an increased risk for Soft Tissue Sarcomas, Non-Hodgkins Lymphoma and certain other cancers 15 to 20 years later.

CDC - Birth Defects Study

The CDC Birth Defects Study was a Case-Control Study designed to determine if the fathers of babies with major birth defects were more likely to have served in Vietnam than fathers of healthy babies. The study was conducted among all identified severely affected cases from a population based Birth Defect Registry in the Atlanta, Georgia, metropolitan area and included almost 5000 major defects and 3000 normal babies born in the same hospitals at nearly the same time. Results of this study indicated that the risk for having a major birth defected child, diagnosed up to the first year, was no greater for Vietnam veterans than for other veterans, or for other men in general. In addition, there was no statistically significant increase in the relative risk for a Vietnam veteran fathering a baby with any individual type or group of defects compared to other men.

In addition to measuring the risks associated with the Vietnam experience per se, the investigators at CDC worked with the Department of Defense Army Agent Orange Task Force in assigning some measure of the likelihood for an opportunity for exposure to Agent Orange for as many Vietnam veterans as had available information. Two such indices (EOI) were created which were similar, but not identical. The analyses reported by CDC using these indices indicated an increased risk for fathering babies with three different defects with increasing opportunities for exposure on at least one of the indices. The three defects were spina bifida, cleft lip with or without cleft palate, and a group of neonatal neoplasms. Whether these findings are the result of chance occurrence when multiple comparisons are made, which is highly probable, cannot be determined with certainty. It is also quite possible that the indices themselves were sufficiently inaccurate as to render them uninterpretable, particularly since they were in the developmental stage at the time. It is not possible to make a definitive evaluation of these findings at this time.

At the suggestion of Congress, and as a matter of appropriate public interest, the Science Panel, through its Research Agenda Subpanel, is preparing a statement on the state-of-the-art of Reproductive Outcome research on the offspring of Vietnam veterans fathers. The purpose of this report will be to develop a research agenda of further research which needs to be done on this issue.

Soft Tissue Sarcoma - International Studies

The Science Panel reviewed international studies of the possible association between exposure to phenoxy acid herbicides and their contaminants and soft-tissue sarcomas. It was determined that these studies were inconclusive, that it would not be useful to engage in further in depth analysis of the already published data and that there are several studies currently underway that should enable a more definitive assessment of the possible association between soft tissue sarcoma and other cancers and exposure to phenoxy herbicides and contaminants to be made in the next several years.

NATIONAL CANCER INSTITUTE - CASE-CONTROL STUDY OF SOFT TISSUE SARCOMAS AND LYMPHONAS AND THEIR RELATIONSHIP TO HERBICIDE APPLICATORS IN KANSAS

The purpose of the Case-Control Study of these two cancers is to determine, by interview, whether cases of Soft Tissue Sarcoma and/or Lymphoma are more likely to have been occupationally exposed to phenoxy acid herbicides and contaminants than a matched comparison group. Cases were obtained from a population based tumor registry covering the whole state of Kansas and controls were matched for age, sex, race and residential area of the state. Kansas was chosen as a site for this study because, in addition to the existence of a tumor registry, the agricultural practices in Kansas wheat growing areas have included considerable application of 2,4,5-T without other concomittant pesticide use.

The Science Panel reviewed the original protocol for this study which is nearing completion under contract to the National Cancer Institute. The Science Panel is particularly interested in the outcome of this study since it should be useful in evaluating the possible associations between certain cancers and herbicide exposures which have been suggested from several studies conducted in Sweden.

National Cancer Institute - Study of Soft Tissue Sarcomas and Non-Hodgkins Lymphoma in Thirteen counties in Washington State

The Batelle Corporation, under grant from the NCI, is conducting a study of Soft Tissue Sarcoma and Non-Hodgkins Lymphoma in the 13 county area around Seattle, Washington which is covered by a population based Tumor Registry. The study will interview in depth for occupational exposure, residential history and home use of herbicides, especially 2,4,5-T. It is intended to verify such use from employment records, reported to be available in this region where much 2,4,5-T has been used. A comparison of the amount and rate of exposure of cancer cases will be made to a comparison group, the nature of which is unknown (to us) at present.

The Science Panel reviewed a very early version of this proposal in 1981, but was not involved in the formal review process. The Science Panel is interested in the outcome of this study since it should help in further evaluating the relationship between certain cancers and exposure to dioxin contaiminated herbicides.

AIR FORCE RANCH HAND STUDY

The purpose of the Ranch Hand Study is to determine whether the 1247 Air Force personnel who were involved in the spraying of Agent Orange (and other herbicides) in Vietnam were more likely to suffer ill health than a comparable group of Air Force personnel who were not involved in herbicide spraying activities. The aerial spraying of herbicide in Vietnam was code named Operation Ranch Hand and thus all of the Air Force personnel involved in the loading, operating and maintaining of the C123 Aircraft used in this operation were termed Ranch Handers. The comparison group consists of Air Force personnel who operated and maintained C130 aircraft in Southeast Asia and who were not involved in herbicide activities. The comparisons are matched to the Ranch Handers by age, race and military rank and specialty. The study will include comparing mortality from various causes between the Ranch Handers and the comparisons (since their service in Southeast Asia) with annual updates every year. It will also include comparing morbidity between the two groups based on an initial telephone interview and an extensive physical, laboratory and psychological examination every 3 to 5 years. The study is intended to continue for 20 years from 1981.

The Science Panel originally reviewed the protocol for the Ranch Hand Study in 1981. The study is of particular interest since the Air Force estimated at that time that many of the Ranch Hand personnel were exposed to Agent Orange at a rate 1000 times greater than almost any of the rest of the Armed Forces in Vietnam. The first Baseline Mortality Results from this study, published in 1983, indicated virtually no difference in mortality between the Ranch Handers and their comparisons through 1982. The Science Panel reviewed this report in the light of a critique which had been prepared by the Vietnam Veterans of America and suggested that a lay-language version of the report would be easier to understand than the rather detailed version which was released. The second interim report is scheduled for release in the very near future and is currently under review by the Advisory Committee for Special Studies.

Data collected during the interview and the first examination were released as the Baseline Morbidity Results in early 1984. The most interesting findings from this report included:

1. an increase in non-melanoma skin cancer among Ranch Handers. This finding will be further studied at the second examination to determine if exposure to sunlight has played a significant role since exposure to solar radiation is the acknowledged primary cause of skin cancer in the U.S.;

2. there was a significant increase in abnormal pulses of the extremities among the Ranch Handers. This will be further explored during the second examination since it is poorly understood and currently has no direct health related consequences; and

3. an increased number of minor birth defects (mostly birth marks) neonatal deaths and physical handicaps to children were reported by Ranch Hand parents than by comparisons. Each of these is currently being verified through the compilation of appropriate medical and vital records for all study subjects as requested by the Agent Orange Working Group. A progress report on this should be available imminently.

PROPOSED STUDIES OF INTEREST TO THE SCIENCE PANEL

Female Veterans Study

The Science Panel reviewed a proposal to study female Vietnam veterans which had been prepared by CDC. The proposed study would interview all, and examine 2000, of the approximately 7000 female veterans who served in Vietnam, who can be located, and who agree to participate. The Science Panel feels that, even though the study appears logistically feasible, it may not be the most efficient nor appropriate design to test possible adverse health effects among female Vietnam veterans. The Panel recommends that specific hypotheses relating Vietnam exposures and adverse health effects among female veterans be formulated, and then a suitable research design developed and evaluated.

Veterans Administration - Twin Study

A concept proposal for a study of identical twins - one of whom served in Vietnam and one of whom did not - was reviewed and approved by the Science Panel in 1982. The purpose of the study would be to compare physical and psychological health of the two members of an extremely closely matched pair of subjects who differed in their exposure to the Vietnam Experience - including possible exposure to Agent Orange. The final protocols for this study has subsequently been fully developed and we understand is currently under review.

THE STATE OF AGENT ORANGE RELATED RESEARCH IN THE FEDERAL GOVERNMENT

The FY 1985 Report of the Science Panel of the Cabinet Council Agent Orange Working Group

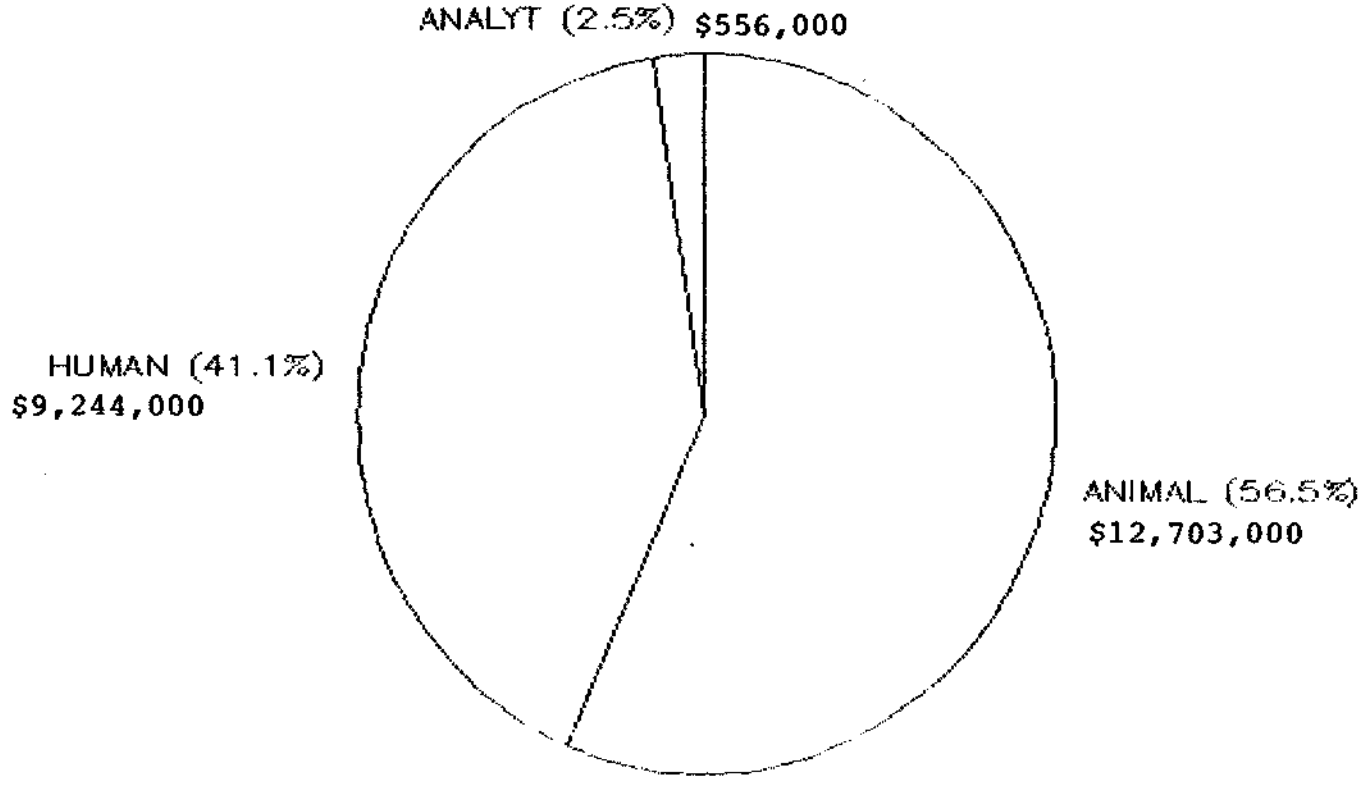
September 1985

The State of Agent Orange Related Research in the Federal Government
The FY 1985 Report of the Science Panel of the Cabinet Council Agent Orange Working Group

OUTLINE

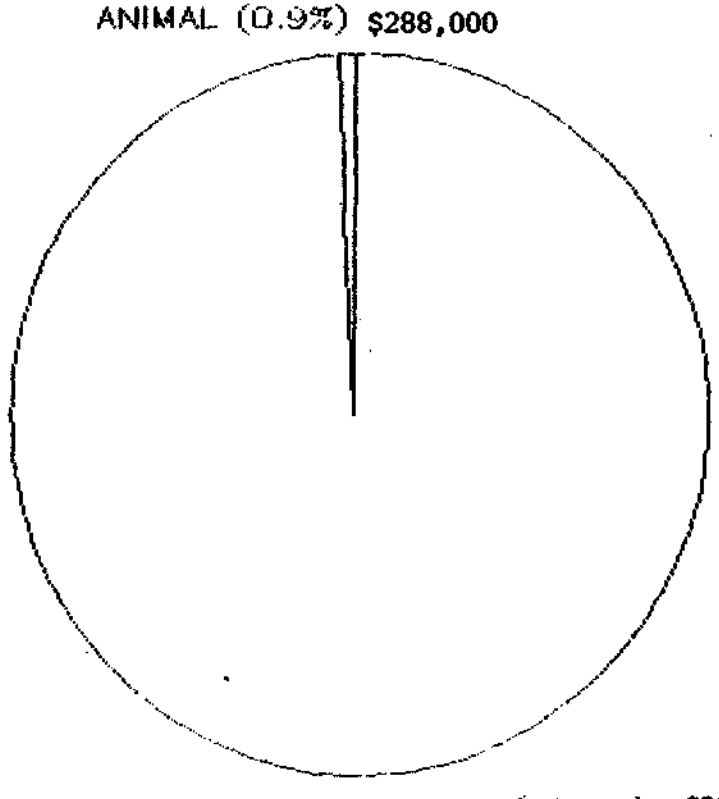
HHS A.O./DIOXIN EXPENDITURES

$22,503,000 TOTAL EXPENDITURES



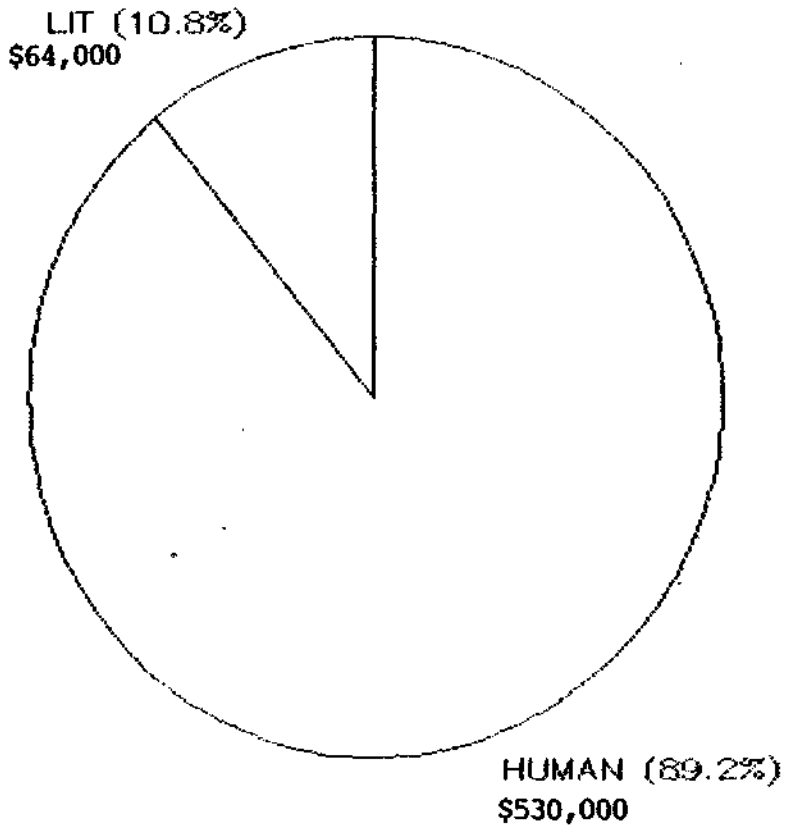
DOD A.O./DIOXIN EXPENDITURES

$33,605,500 TOTAL EXPENDITURES



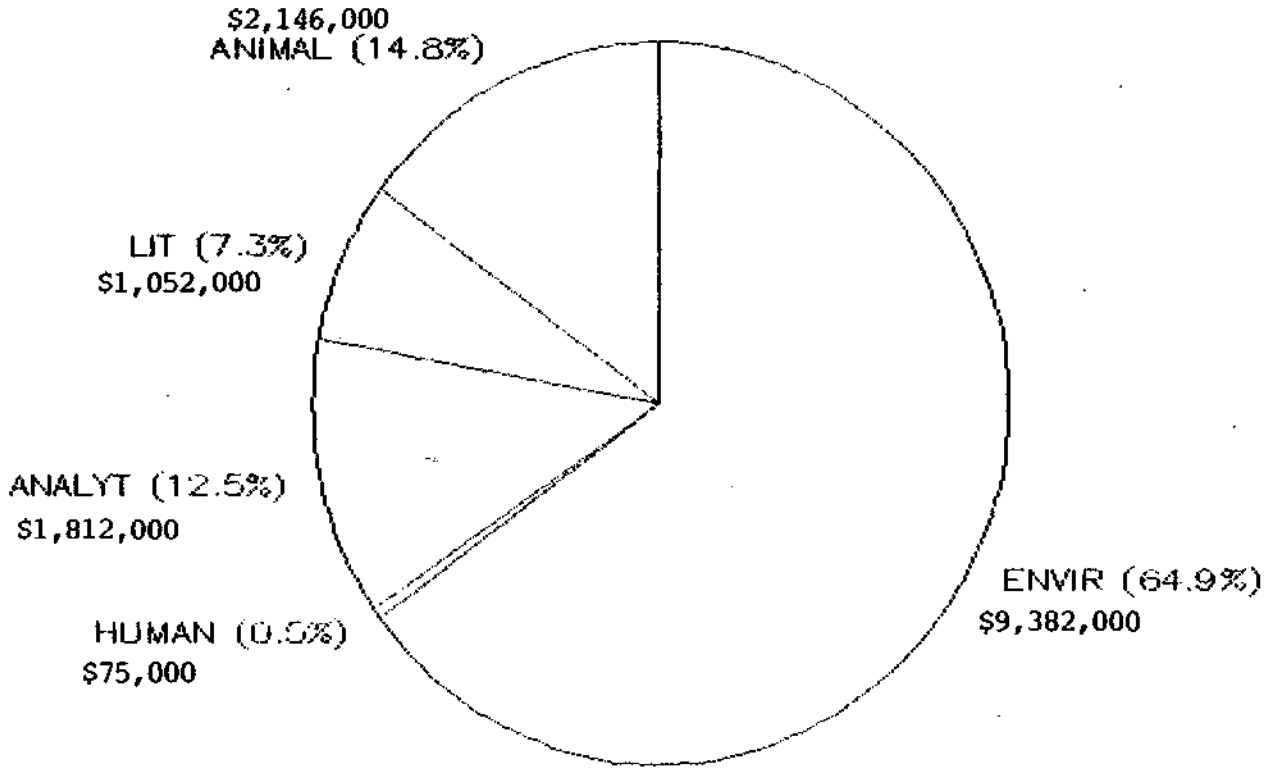
USDA A.O./DIOXIN EXPENDITURES

$594,000 TOTAL EXPENDITURES



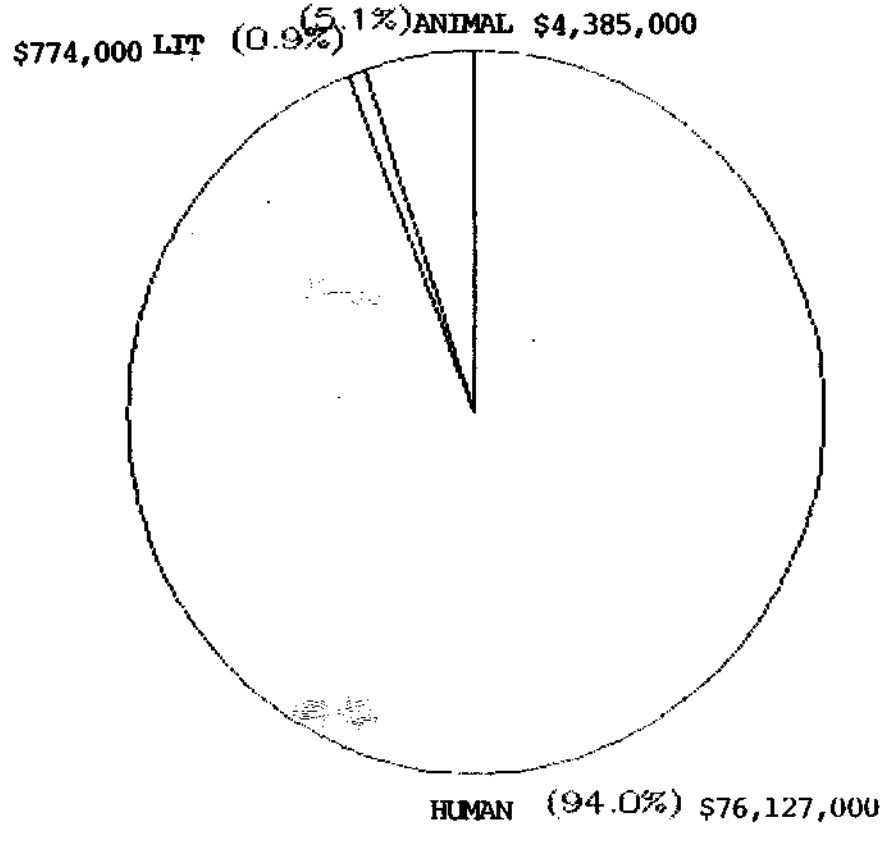
EPA A.O./DIOXIN EXPENDITURES

$14,467,000 TOTAL EXPENDITURES



V.A. A.O./DIOXIN EXPENDITURES

$81,286,000 TOTAL EXPENDITURES



APPENDIX C

AGENCY SUMMARY STATEMENT OF AO-RELATED RESEARCH EFFORTS

ENVIRONMENTAL PROTECTION AGENCY

Research Program Associated with Chlorinated Dibenzo-p-dioxins (CDDs) and Dibenzofurans (CDFs)

The US Environmental Protection Agency (EPA) has been concerned with CDDs/CDFs, particularly 2,3,7,8-TCDD, since the early 1970s. Much of the early work was related to 2,3,7,8-TCDD as a contaminant in the herbicde 2,4,5-T and included analytical methods development and its application to monitoring data.

While the Agency's research work with humans has been limited, it has been important. In the late 1970s, a controversial epidemiological study triggered immediate regulatory action by the Agency. During the same period, the Agency conducted an investigation of 2,3,7,8-TCDD in the human milk of mothers living in areas in which 2,4,5-T had been used. No confirmed positive residues were detected in any of 100 samples. The Agency has detected trace amounts of 2,3,7,8-TCDD in some human adipose tissue samples. Ongoing collaborative efforts with the Veterans Administration is aimed at analyzing samples of human adipose tissue collected during the 1970s to determine whether or not Vietnam service personnel have greater residues of 2,3,7,8-TCDD than do a comparable group of individuals who did not go to Vietnam. In addition, EPA has conducted assessments of the potential human risks associated with exposure to 2,3,7,8-TCDD and some of the other CDDs/CDFs. These "ballpark" risk estimates have been useful in reaching regulatory decisions.

During the 1980s, the EPA research program for CDDs/CDFs has focused on environmental and risk management concerns. Specifically, Congress directed the Agency of conduct a National Dioxin Study, the aim of which is the investigation of potential "hot spots" across the country and the determination of background levels, if any, of 2,3,7,8-TCDD in the environment. This current effort builds on more limited, but more focused, Agency efforts searching for 2,3,7,8-TCDD in envivonmental samples. In an attempt to conduct such investigations more quickly and inexpensively, the Agency has sponsored research to develop new methods of analysis of CDDs/CDFs. In order to better understand the significance of reports of CDDs/CDFs in the environment, EPA is conducting studies in the environmental transport and fate of these compounds, with a particular emphasis on the bioavailability and possible movement into the human food chain. Large-scale combustion is under special investigation as a possible source of CDDs/CDFs in the environment.

A major thrust of recent EPA efforts has been in the direction of controlling, managing, and/or destroying CDDs/CDFs once they are found in the environment. Methods have been found which successfully destroy 2,3,7,8-TCDD in contaminated soil and liquids. Procedures are being developed to minimize the emission of CDDs/CDFs from combustion sources.

VA/AFIP Soft Tissue Sarcoma Study

The possibility that exposure to phenoxy herbicides may induce rare forms of cancer in humans such as soft tissue sarcoma (STS) has been suggested from recent studies in Sweden. Subsequently, there is much concern in the United States that many veterans who served in Vietnam might have had a significant exposure to the phenoxy herbicides including Agent Orange and, therefore, might be at increased risk of developing STS.

In view of the concern raised by many veterans and conflicting findings in the scientific literature, the VA, in collaboration with the Armed Forces Institute of Pathology (AFIP), is conducting a case control study in which 250 individuals with STS are compared with 750 individuals without STS with respect to Vietnam service, probable Agent Orange exposure and other host and environmental risk factors.

The study is conducted in two phases. Phase I of the study will investigate whether service in Vietnam during 1965-1971 increased the risk of developing STS. Military service information, in particular Vietnam service status, for each case and control patients will be obtained from a review of the patient's military personnel records archived at the National Personnel Records Center in St. Louis, Missouri.

Phase II of the study will investigate other host and environmental risk factors for the development of STS based on information obtained from telephone interviews with the subjects or their next-of-kin. Information on risk factors such as occupational and non-occupational exposure to phenoxy herbicides, ionizing radiation asbestos, arsenic, vinyl chloride, and genetic synodromes will be obtained from the interviews and analyzed individually and jointly with respect to the risk of developing STS.

As of July, 1985, 58% of the study subjects (616/1,066) have been located and have completed the telephone interview. Data collection will be completed by March, 1986 and the final report is expected in late 1986.

VA Mortality Study

The Vietnam Veterans Mortality Study is designed to assess mortality patterns of U.S. servicemen in the Army or Marines who served during a portion of the Vietnam era. A sample of 75,000 veterans deaths has been selected from the VA BIRLS files. For each of the deaths, military service and cause of death information are being collected and coded. The two types of data will be merged and analyzed to compare the mortality experience of veterans who served in Vietnam with veterans of the same era who did not serve in Vietnam. Various analytical approaches are planned including classical proportionate mortality ratio (PMR) analyses as well as categorical data analyses.

As of August 1985 the military records search and abstracting have been completed for 98% of total cohort of 75,000. Ninety nine percent of the expected 72,000 death records have been received. However, about 15% of the records received did not include the cause of death information. Extensive tracing efforts have been made using both internal records and records maintained by other government agencies for all veterans whose VA claims folders lacked the cause of death information.

Completeness, accuracy and consistency of data on numerous variables (e.g., age, race, year of death, cause of death, branch of service, rank, MOSC, years of active duty, separation year, length of service in Vietnam, industry, occupation) are being checked in preparation for analysis. The final report is expected in late 1985.

Alternate Methods for Assigning Agent Orange Exposure Status to Vietnam Veterans Exposure Opportunity Index (EOI)

Some time ago the Joint Services Environmental Support Group (then the Army Agent Orange Tast Force (AAOTF) began to develop methods to estimate potential exposure to Agent Orange among Vietnam veterans. The method to be used in the proposed Agent Orange Morbidity and Mortality Studies currently underway by CDC involves detailed day-by-day tracking of both military units and individuals while in Vietnam. Amassing the information necessary to do this requires considerable effort and yields simultaneous information on all of the members of a given military unit. The method is thus suitable for identifying cohorts, but is extremely inefficient for determining potential exposures of individuals selected by other means. Furthermore, the necessary records apparently do not exist for many units in Vietnam, particularly non-Army units, and is the major reason why the CDC Epidemiological studies are confined to veterans of the Army.

In order to obtain some information on the possible exposure to Agent Orange of veterans identified through other sources, an alternative method was proposed by the AAOTF.

The Science Panel was briefed on, and reviewed in depth the alternative procedures for assigning Exposure Opportunity Indices (EOI) to Vietnam veterans. These procedures are based on the place, time and job specialty of veterans while in Vietnam as indicated in personnel records, military unit quarterly reports and herbicide application records from Vietnam. The method was proposed by the Department of Defense, and was developed by the Army and Joint Services Environmental Support Group in conjunction with the investigators of the CDC Birth Defects Study. Even though the alternative method is somewhat subjective and confounds combat status with exposure to herbicide, all of the members of the Science Panel agree that the method as developed, can provide an individual estimate of the relative likelihood for at least some exposure to Agent Orange while in Vietnam. Attempts to establish whether such exposures are capable of compromising health status is the business of ongoing health and mortality studies.

AGENT ORANGE LITIGATION

In 1979, a class action was commenced in the United States District Court, Eastern District of New York, charging the United States and a major portion of the chemical industry with deaths and injuries to tens of thousands of Vietnam veterans who came in contact with herbicides used in the war in Southeast Asia. The suit also claimed that as a result of the veterans' exposure, their children suffer severe birth defects. After five years of numerous motions and extensive discovery, a settlement amount of $180,000,000 was negotiated between the plaintiff-veterans and the defendant-manufacturers and approved by Chief Judge Jack B. Weinstein on June 11, 1984.

Following this settlement, a $10 billion class action was filed against the United States on behalf of the servicemen, their wives and children. The class action alleged, among other things, failure to warn, and pre-induction, in-service, and post-discharge negligence. At the same time, the defendants expressed their intention to press third-party contribution and indemnity claims against the United States, to recover all costs associated with their defense of the litiga- tion, including the amount of the settlement.

The United States moved to dismiss the plaintiffs' class action and, on December 10, 1984 Judge Weinstein denied class certification and dismissed all claims brought by the service-men. The Court also found that there is no credible medical or scientific evidence supporting claims of male-mediated birth defects or miscarriages, but reserved final judgment on these claims for ninety-days. The United States will also seek dismissal of all third-party claims pending against it.

Judge Weinstein has established a 28 member advisory board to advise the Court on how the settlement trust fund proceeds might be best utilized. The Justice Department has refused to allow federal personnel to participate in any way in the settlement process. Judge Weinstein has reserved final approval of the settlement pending review of the settlement distribution plan and resolution of all counsel fee disputes.

Veterans Administration Advisory Committee On Environmental Hazards

The Veterans Administration Advisory Committee on Environmental Hazards and its Scientific Council were created by the Veterans' Dioxin and Radiation Exposure Compensation Standards Act, P.L. 98-542, enacted on October 24, 1984. The functions of this Committee and its Council are not perceived to encroach on, or duplicate the efforts of the Agent Orange Working Group (AOWG).

The Veterans Administration Advisory Committee is distinguished from the Agent Orange Working Group in that the Agent Orange Working Group is solely concerned with risk assessment and the Veterans Administration Advisory Committee and its Scientific Council are concerned with risk management.

P.L. 98-542 requires, inter alia, that the VA Administrator prescribe regulations on adjudicating claims based on dioxin and radiation exposure after considering the recommendations of an advisory committee and its scientific council.

The Advisory Committee on Environmental Hazards created by the Act consists of fifteen members appointed by the VA Administrator. Eleven of these, of whom none may be from the Armed Forces, the VA, or Defense and not more than three may be federal employees, are appointed in consultation with the Director, NIH. These members must include three authorities on dioxin, three on ionizing radiation, and five on epidemiology or a related field. These eleven members also constitute the Scientific Council of the Committee. The Council is divided into two eight member panels which will, respectively, evaluate studies on dioxin and radiation exposure. The Scientific Council reports to the Committee and to the Administrator directly.

The balance of the Committee is made up of four individuals from the general public with special concerns regarding exposure to dioxin or radiation. The Chief Medical Officer and Chief Benefits Director of the VA are ex officio members.

SENATE VETERAN AFFAIRS COMMITTEE

99TH CONGRESS

Republicans	Democrats
Sen. Frank H. Murkowski, (R-AK) Chairman	
Sen. Alan K. Simpson, (R-WY)	Sen. Dennis DeConcini (D-AZ)
Sen. Rudy Boschwitz, (R-MN)	Sen. Alan Cranston (D-CA)
Sen. Robert T. Stafford (R-VT)	Sen. Jay Rockefeller (D-WV)
Sen. Arlen Specter (R-PA)	Sen. George J. Mitchell (D-ME)
Sen. Jeremiah Denton (R-AL)	Sen. Spark M. Matsunaga (D-HI)
Sen. Strom Thurmond (R-SC)	

COMMITTEE ON VETERANS AFFAIRS

SR-414..... 224-9126

Frank H. Murkowski, Alaska, Chairman.

Alan K. Simpson, Wyo.
Strom Thurmond, S.C.
Robert T. Stafford, Vt.
Arlen Specter, Pa.
Jeremiah Denton, Ala.
Rudy Boschwitz, Minn.

Alan Cranston, Calif.
Spark M. Matsunaga, Hawaii
Dennis DeConcini, Ariz.
George J. Mitchell, Maine
John D. Rockefeller, IV, W. Va.

STAFF MEMBERS

Alpert, Cynthia PROF ST M SR-420A..... 46210
Alvarado, Tina RECP SR-414..... 49130
Billica, Nancy MIN RES ASST SH-202..... 40578
Boertlein, Judy ST ASST SR-412..... 46213
Brew, William MIN COUN SH-202..... 40787
Eckhardt, Kay ST ASST SR-420..... 49132
Hucks, Becky CHF CLK/LEGISLATIVE CLK SR-412..... 46236
Hughes, Charlotte MIN CASEWKR SH-202..... 44112
Maraz, Stacy ST ASST SR-420..... 40206
McTighe, Cathy COUN SR-420A..... 46268
Moore, Jim PRESS ASST SR-420A..... 44921
Moore, Lisa RES ASST SR-420A..... 46230
Phinney, Al COUN SR-420..... 47836
Potzer, Babette MIN PROF ST SH-202..... 46775
Post, Ingrid MIN CHF CLK SH-202..... 46204
Principi, Anthony J CHF COUN/ST DIR SR-410..... 49126
Schratwieser, Hugh PROF ST M SR-420..... 46263
Scott, Ed MIN GEN COUN SH-202..... 46262
Steinberg, Jon MIN CHF COUN/ST DIR SH-202..... 46202
Susman, Julie DPTY ST DIR/LEG DIR/DPTY CHF COUN SR-414..... 46293
Yoder, Chris PROF ST M SR-420..... 46212

(No Subcommittees)

CHAIRMAN
COMMITTEE ON VETERANS' AFFAIRS

Sen. Frank H. Murkowski
of Fairbanks
Republican—Jan. 3, 1981

SEN. FRANK H. MURKOWSKI (R AK)
Committee on Energy & Natural Resources
- Subcommittee on Energy & Mineral Resources
- Subcommittee on Energy Regulation, Chairman
- Subcommittee on Water & Power

Committee on Foreign Relations
- Subcommittee on East Asian & Pacific Affairs, Chairman
- Subcommittee on International Economic Policy
- Subcommittee on Western Hemisphere Affairs

Committee on Veterans' Affairs
Select Committee on Indian Affairs

ASSISTANT MAJORITY LEADER

Sen. Alan K. Simpson
of Cody
Republican—Jan. 1, 1979

SEN. ALAN K. SIMPSON (R WY)
Committee on Environment & Public Works
- Subcommittee on Environmental Pollution
- Subcommittee on Nuclear Regulation, Chairman
- Subcommittee on Toxic Substances & Environmental Oversight

Committee on The Judiciary
- Subcommittee on Courts
- Subcommittee on Immigration & Refugee Policy, Chairman
- Subcommittee on Separation of Powers

Committee on Veterans' Affairs, Chairman

HOUSE VETERANS AFFAIRS COMMITTEE

99TH CONGRESS

Democrats	Republicans
G.V. (Sonny) Montgomery, Miss. Chairman	
Don Edwards, (D-Calif)	John Paul Hammerschmidt, (R-Ark)
Bob Edgar, (D-Pa)	Chalmers P. Wylie, (R-Ohio)
Sam B. Hall, Jr., (D-Tex)	Elwood Hillis, (R-Ind)
Douglas Applegate, (D-Ohio)	Gerald B.H. Solomon, (R-N.Y.)
Richard C. Shelby, (D-Ala)	Bob McEwen, (R-Ohio)
Dan Mica, (D-Fla)	Christopher H. Smith, (R-N.J.)
Thomas A. Daschle, (D-S.Dak)	Dan Burton, (R-Ind)
Wayne Dowdy, ((D-Miss)	Don Sundquist, (R-Tenn)
Lane Evans, (D-Ill)	Michael Bilirakis, (R-Fla)
Marcy Kaptur, (D-Ohio)	Nancy Lee Johnson, (R-Conn)
Alan B. Mollohan, (D-W.Va.)	Guy V. Molinari, (R-N.Y.)
Timothy J. Penny, (D-Minn)	Thomas J. Ridge, (R-Pa)
Harley O. Staggers, Jr. (D-W.Va)	Bill Hendon, (R-N.C.)
J. Roy Rowland, (D-Ga)	John G. Rowland, (R-Conn)
John Bryant, (D-Tex)	
James J. Florio, (D-N.J.)	
Kenneth J. Gray, (D-Ill)	
Paul E. Kanjorski, (D-Pa)	
Tommy F. Robinson, (D-Ark)	

COMMITTEE ON VETERANS' AFFAIRS

335 CANNON HOB 225-3527

G. V. (Sonny) Montgomery, Miss., Chairman

Don Edwards, Calif.
Bob Edgar, Pa.
Sam B. Hall, Jr., Tex.
Douglas Applegate, Ohio
Richard C. Shelby, Ala.
Dan Mica, Fla.
Thomas A. Daschle, S. Dak.
Wayne Dowdy, Miss.
Lane Evans, Ill.
Marcy Kaptur, Ohio
Alan B. Mollohan, W. Va.
Timothy J. Penny, Minn.
Harley O. Staggers, Jr., W. Va.
J. Roy Rowland, Ga.
John Bryant, Tex.
James J. Florio, N.J.
Kenneth J. Gray, Ill.
Paul E. Kanjorski, Pa.
Tommy F. Robinson, Ark.

John Paul Hammerschmidt, Ark.
Chalmers P. Wylie, Ohio
Elwood Hillis, Ind.
Gerald B. H. Solomon, N.Y.
Bob McEwen, Ohio
Christopher H. Smith, N.J.
Dan Burton, Ind.
Don Sundquist, Tenn.
Michael Bilirakis, Fla.
Nancy Lee Johnson, Conn.
Guy V. Molinari, N.Y.
Thomas J. Ridge, Pa.
Bill Hendon, N.C.
John G. Rowland, Conn.

MAJORITY STAFF

Burley, Suzy FILE CLK 335 53527
Burnett, Arlene ADMIN ASST 335 59165
Cochran, Jill PROF STF MEM EDUC, TRAIN, EMPLOY 335 53527
Daniel, Barbara STF ASST HOSP, HEALTH CARE 336 59154
Evans, Semmes STF ASST 337 59164
Fleming, Mack CHF COUN & STF DIR 335 53527
Frone, Stanley STF ASST 335 53527
Grant, Bob PRTG CLK 335 53535
Holley, Jim PROF STF MEM PUB AFRS 337 53664
Kilker, Beth STF ASST EDUC, TRAIN, EMPLOY 335 59112
McDermott, Mary FIN CLK 335 58557
McDonell, Jack PROF STF MEM HOSP, HEALTH CARE 336 59154
Moon, Arnold COUN COMPENS, PENS, INS 337 53569
Parker, Pam STF ASST OVERSIGHT & INVEST 335 59044
Raymond, Vic PROF STF MEM 336 59154
Richardson, Jean STF ASST COMPENS, PENS, INS 337 53569
Royce, Gloria PROF STF MEM HOUS & MEMORIAL AFRS 337 53664
Ryan, Patrick COUN 335 59154
Shultz, Richard COUN OVERSIGHT & INVEST 335 53541
Sniffen, Candis Lee LEGIS ASST 335 53527
Tippett, Patricia RECEPT 335 53527

MINORITY STAFF

Brandes, Sharon A PROF STF MEM 333A 59756
Donohue, Patricia ADMIN ASST 333 53551
Forrest, Sue STF ASST 333A 59756
Smith, Kingston DPTY COUN & STF DIR 333A 59756
Wilson, Rufus COUN & STF DIR 333 53551

SUBCOMMITTEE STAFF

Caldwell, Anne PROF STF MEM, HOUS & MEMORIAL AFRS 2443 52665
Durishin, Michael PROF STF MEM, EDUC, TRAIN, EMPLOY 2455 52601
Fuller, Richard PROF STF MEM, HOSP, HEALTH CARE 2352 52011
Gallion, Edward MIN PROF STF MEM, COMPENS, PENS, INS 2342 55614
Sechrist, Timothy PROF STF MEM, COMPENS, PENS, INS 2464 56265

U.S. HOUSE OF REPRESENTATIVES

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

335 CANNON HOB 225-3541

G. V. (Sonny) Montgomery, Miss., Chairman

Don Edwards, Calif.
Kenneth J. Gray, Ill.
Sam B. Hall, Jr., Tex.
Timothy J. Penny, Minn.
J. Roy Rowland, Ga.
Tommy F. Robinson, Ark.

Elwood Hillis, Ind.
Dan Burton, Ind.
Don Sundquist, Tenn.
Nancy Lee Johnson, Conn.
Thomas J. Ridge, Pa.

MAJORITY STAFF 53541

MINORITY STAFF 59756

SUBCOMMITTEE ON HOSPITALS AND HEALTH CARE

338 CANNON HOB 225-9154

Bob Edgar, Pa., Chairman

Dan Mica, Fla.
Wayne Dowdy, Miss.
Lane Evans, Ill.
Marcy Kaptur, Ohio
Alan B. Mollohan, W. Va.
Timothy J. Penny, Minn.
Harley O. Staggers, Jr., W. Va.
J. Roy Rowland, Ga.
John Bryant, Tex.
James J. Florio, N.J.
Paul E. Kanjorski, Pa.
Tommy F. Robinson, Ark.
Richard C. Shelby, Ala.
Thomas A. Daschle, S. Dak.

John Paul Hammerschmidt, Ark.
Elwood Hillis, Ind.
Gerald B. H. Solomon, N.Y.
Bob McEwen, Ohio
Christopher H. Smith, N.J.
Michael Bilirakis, Fla.
Nancy Lee Johnson, Conn.
Guy V. Molinari, N.Y.
Thomas J. Ridge, Pa.
Bill Hendon, N.C.
John G. Rowland, Conn.

MAJORITY STAFF 59154

MINORITY STAFF 59756

SUBCOMMITTEE ON COMPENSATION, PENSION, AND INSURANCE

337 CANNON HOB 225-3569

Douglas Applegate, Ohio, Chairman

Sam B. Hall, Jr., Tex.
G. V. (Sonny) Montgomery, Miss.
Dan Mica, Fla.
Wayne Dowdy, Miss.
Lane Evans, Ill.
Tommy F. Robinson, Ark.

Gerald B. H. Solomon, N.Y.
Chalmers P. Wylie, Ohio
John Paul Hammerschmidt, Ark.
Dan Burton, Ind.
Guy V. Molinari, N.Y.

MAJORITY STAFF 53569

MINORITY STAFF 59756

SUBCOMMITTEE ON EDUCATION, TRAINING AND EMPLOYMENT

335 CANNON HOB 225-9166

Thomas A. Daschle, S. Dak., Chairman

Lane Evans, Ill.
Marcy Kaptur, Ohio
John Bryant, Tex.
James J. Florio, N.J.
Kenneth J. Gray, Ill.

Bob McEwen, Ohio
Chalmers P. Wylie, Ohio
Gerald B. H. Solomon, N.Y.
Bill Hendon, N.C.

MAJORITY STAFF 59166
MINORITY STAFF 59756

SUBCOMMITTEE ON HOUSING AND MEMORIAL AFFAIRS

337 CANNON HOB 225-9164

Richard C. Shelby, Ala., Chairman

Bob Edgar, Pa.
Douglas Applegate, Ohio
Alan B. Mollohan, W. Va.
John Bryant, Tex.
James J. Florio, N.Y.

Christopher H. Smith, N.J.
Don Sundquist, Tenn.
Michael Bilirakis, Fla.
John G. Rowland, Conn.

MAJORITY STAFF 59164
MINORITY STAFF 59756

Veterans Administration

Synopsis of Scientific Literature on Phenoxy Herbicides and Associated Dioxins

No. 1 - (Volumes I-IV)

Department of
Medicine and Surgery

VA CONTRACT NO: V101(93)P-953

SYNOPSIS OF SCIENTIFIC LITERATURE ON PHENOXY HERBICIDES AND ASSOCIATED DIOXINS

Prepared for Contracting Officer's Technical Representative:
Barclay M. Shepard, M.D.
Director, Agent Orange Projects Office
Department of Medicine and Surgery
Veterans Administration
810 Vermont Avenue, N.W.
Washington, D.C. 20420

Submitted by:
Clement Associates, Inc.
1515 Wilson Boulevard
Arlington, Virginia 22209

PREFACE

In October 1981, the Veterans Administration published the first two volumes of a comprehensive report entitled *Review of Literature on Herbicides, Including Phenoxy Herbicides and Associated Dioxins*. A continuation of this important effort resulted in the preparation and publication in April 1984 of volumes III and IV. At this point it was thought that a summary in layman's terms, with emphasis on health effects would be helpful to the general public's understanding of the complex and often controversial issue of Agent Orange. Consequently this summary has been prepared to fill that need. It should be noted that this synopsis includes only that body of scientific literature published through December 1983, and therefore does not include the results of more recent research such as the study of birth defects conducted by the Centers for Disease Control and published in August 1984. Also not included is the mortality study of Australian Vietnam-era veterans published in September 1984. The results of these and other more recent reports will be summarized in a similar synopsis currently being developed by the VA for publication in the near future. It is hoped that these lay-language summaries will serve as useful supplements for assisting non-technically oriented readers in understanding both the significance and impact of such literature and thereby assist in the ultimate resolution of the many and varied issues related to the phenoxy herbicides and associated dioxins.

Agent Orange Projects Office
Veterans Administration
Washington, D.C.
1985

CONTENTS

1. Introduction

For the past several years the Veterans Administration, in response to the concerns of veterans who served in the war in Vietnam, has been conducting or sponsoring research on the health effects of Agent Orange, the principal herbicide used by U.S. military forces in that country and to which some American military personnel were exposed.

In April 1984, under contract to the Veterans Administration, Clement Associates, Inc., a research firm in Arlington, Virginia, completed a two-volume survey of the extant scientific literature on the health effects of Agent Orange. The material that follows is a lay summary of that survey and is published because the Veterans Administration believes that it will be of interest to Vietnam veterans and others who have been following the Agent Orange issue.

2. What is Agent Orange?

"Agent Orange" is a name that has come to be used to describe a particular type of chemical herbicide that was used in military operations in Vietnam from 1965 to 1971. The name came from the orange stripe that identified the 55-gallon drums in which the herbicide was shipped and stored. Agent Orange was not a single chemical compound but rather a mixture of chemicals containing equal amounts of the two active ingredients, 2,4-D and 2,4,5-T. These weed-killing chemicals enjoyed extensive commercial and private use in the United States and in many countries around the world from the 1940s well into the 1970s. 2,4-D is still used extensively in this country and abroad.

Like many industrial chemical mixtures, the Agent Orange that was manufactured during the Vietnam era contained small quantities of impurities. These impurities included chemicals used in the production of 2,4-D and 2,4,5-T as well as by-products which developed during the manufacturing process. Some of the impurities were a family of closely related compounds known as polychlorinated dibenzodioxins which, as a group, have often been called "dioxins."

One of these dioxins, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin or TCDD, has been extensively tested in experimental animals and is believed to be the most toxic member of the dioxin family. TCDD is one of the contaminating dioxins in 2,4,5-T. In the remainder of this report the term dioxin will be used to refer to any of a number of different polychlorinated dibenzodioxins, usually unidentified. The term TCDD will be used to designate the specific chemical 2,3,7,8-tetrachlorodibenzo-*p*-dioxin.

Agent Orange was produced by several manufacturers in a number of chemical plants throughout the United States under contract to the Department of Defense, which specified the composition of the herbicide. Therefore the nature and amount of the active ingredients were the same regardless of the manufacturer. Although Defense Department specifications set an upper limit on the total amount of impurities that could be present in a batch of Agent Orange, it is certain that both the exact amount and the nature of these impurities varied from batch to batch, from year to year, and from manufacturer to manufacturer. Furthermore, since very little attention was paid to the importance of the impurities in Agent Orange until

late in the Vietnam experience, there is relatively little information available on the amount of the impurities contained in the herbicide shipped to Vietnam.

Agent Orange was somewhat different from commercial formulations of this class of herbicides made and marketed in the United States and in other countries around the world. In addition, we don't really know precisely all the types and amounts of the impurities that were present in Agent Orange, and furthermore we don't have any accurate way to find out. Because there is considerable evidence that the health effects of these herbicide mixtures depend heavily on the amounts and types of impurities such as dioxins which were present in the mixture, we can accept, only with reservations, information on health effects obtained from studies of people exposed to other herbicide preparations containing 2,4-D, 2,4,5-T, or both. If we hope to understand the health effects of Agent Orange with a high degree of certainty, it is essential to identify and study people who were exposed to Agent Orange.

3. Who was exposed?

The only individuals who are known to have been exposed to Agent Orange are those who were exposed during its manufacture and distribution or as a result of its use in Vietnam. Because Agent Orange was considered relatively safe at the time of its use, however, there were no systematic studies to determine how much Agent Orange might enter a person's system as a result of exposure in a manufacturing plant, during spraying operations or other applications, or from entering an area that had already been sprayed.

Another way of determining exposure is to depend on people's memory of when and how often they might have been exposed. Unfortunately, several different types of chemicals were manufactured in most of the plants that manufactured Agent Orange. In addition, several other herbicide mixtures as well as insecticides and other chemicals were used in Vietnam.

It would be very difficult for most individuals to know when they were exposed to Agent Orange specifically and how much exposure they received. The Air Force did keep records of most of the aerial herbicide spraying missions. By combining this information with data from records of the location of military units, the probability of exposure from aircraft spraying can be estimated. Those people who were actually involved in the handling and application of Agent Orange were undoubtedly among the most heavily exposed, but it is not possible to determine accurately the amount to which they were exposed.

4. What do we know about the health effects?

As one might guess from the information above, we don't have precise and direct information on the human health effects of Agent Orange itself. Scientists cannot identify people who were definitely exposed to known quantities of Agent Orange in order to compare such a group to people who were not exposed to Agent Orange or similar herbicides. Furthermore, Agent Orange as such was not tested in experimental animals at the time of its manufacture and use.

5. How do we determine the health effects?

Since we cannot study the human health effects of Agent Orange directly, we must use other techniques to learn what health effects might result from exposure to this material. Several methods are available and all of them have been used during the last 10 or 15 years. Each has limitations that make it difficult for scientists to reach definitive conclusions about the adverse human health effects of Agent Orange. Nevertheless, if scientists and health professionals review the entire body of information that has become available from all these approaches, certain patterns emerge.

It is now possible to begin reaching tentative conclusions about the health effects of Agent Orange. However, these conclusions are still somewhat uncertain. The results of studies which are currently in progress or planned will go a long way toward removing this uncertainty, but, for the general reasons described above and for specific reasons described below, it is quite likely that we may never be completely sure of what the health effects of Agent Orange are. This same uncertainty exists for many environmental health issues and is a result of the normal limitations of science.

One of the most promising approaches to studying the health effects of Agent Orange is to evaluate the health of people who may have been exposed to it as a result of the Vietnam experience and to compare their health with that of people who were not exposed to these herbicides. A few such studies have been conducted and several more are in progress. Some of the limitations of these studies have already been mentioned.

We don't have reliable records of everyone who was exposed, so assumptions are made such as "any veteran who served in Vietnam was exposed to Agent Orange" (Australian Veterans Health Study) or "any individual who was assigned to Operation Ranch Hand was heavily exposed to Agent Orange" (U.S. Air Force Epidemiology Study). These assumptions may lead to the inclusion in the "exposed" group of people who had very little exposure. If enough of these people are mis-classified as to exposure, scientists will not be able to detect any real health effects that might be present in those who were actually heavily exposed. In other words, the greater the mis-classification rate, the less reliable are conclusions regarding health effects of exposure.

Another serious limitation is that it is very difficult to select a group of "unexposed" people who can be closely matched with the people in the "exposed" group. Ideally, the two groups should be the same except for their potential exposure to Agent Orange. This means that individuals in both groups should not only be the same in age, weight, and sex, but they should also have similar smoking habits, diets, jobs, life styles, and places of residence. Another problem inherent in these studies relates to the widespread use in the United States of commercial herbicides that are similar to Agent Orange. In addition, dioxins are known to be present in other industrial chemicals in the environment. It is therefore very possible that some individuals in the "unexposed" group have actually been exposed to the ingredients of Agent Orange at other times and in other places.

Another problem with studies of people who were exposed to Agent Orange is that a relatively short period of time has elapsed since exposure took place. The phenoxy herbicides contained in Agent Orange were first used in Vietnam in 1962. Heavy use and potentially heavy exposure to Agent Orange did not begin until three years later, so the time that has elapsed since most veterans were exposed has been about 15 to 20 years. Certain adverse health effects such as cancer, heart disease, and respiratory problems that result from exposure to chemicals may take many years to develop. Increased cancer rates due to smoking or exposure to toxic chemicals have been shown to reach a peak 20 to 30 years after exposure. Thus, a lack of evidence of increased rates of cancer and heart disease in populations exposed to Agent Orange might suggest that exposure to Agent Orange does not increase the risk of developing these diseases. On the other hand, it might be that they haven't had time to appear in sufficient numbers to be detected.

The studies of populations who were probably exposed to Agent Orange as a result of the Vietnam experience have not yet provided clearcut answers to questions about its health effects. This is the result of some of the limitations described above. Furthermore, future studies of this type will not be capable of answering all these questions. It is therefore necessary to ask, "Where else can we look for these answers?" One potentially valuable source of information is the study of human populations with exposure to commercial herbicidal mixtures that were similar, but not identical, to Agent Orange. A number of such studies are available. Most are of workmen who sprayed herbicides on the job, but some are of populations who lived in areas where herbicides containing 2,4-D and 2,4,5-T were used. Most of these studies are subject to the same limitations as those of the people exposed to Agent Orange.

In all of these studies, the determination that a person is or is not exposed is based largely on that person's memory of past events or, in many cases, simply on where the person lived or worked. Also, people may be included in the exposed group who worked at a job or lived in an exposed area for only a few weeks. On the other hand, people may be included in the unexposed group if they are currently working in jobs or living in areas where they are not exposed to herbicides but who may have been exposed to herbicides in some previous job or place of residence, perhaps even without knowing it. Either type of error decreases the ability of scientists to detect possible effects of exposure to the chemical.

Other potential sources of information about the health effects of Agent Orange are studies of humans who were exposed to some of the components of Agent Orange. There are a number of groups of people throughout the world who were exposed to dioxins as a result of industrial accidents or unintentional release of dioxin into the environment. Several of these groups have been followed for a number of years and much information has been gathered. It is difficult, however, to judge how relevant these findings are to people exposed to Agent Orange. The specific dioxins to which these people were exposed were not always completely or accurately identified, and they may be somewhat different from those found in Agent Orange.

One of the most widely publicized incidents in which humans were exposed to dioxins was the explosion of a chemical reactor at the ICMESA plant near Milan, Italy, in July 1976. A cloud of chemicals containing relatively large quantities of dioxins blanketed a portion of the

small town of Seveso immediately downwind of the plant. In succeeding weeks many persons living in Seveso showed signs of dioxin exposure, the most prominent being chloracne, a form of acne which includes the appearance of blackheads around the eyes and ears and in some cases covers much of the body.

No direct measurements were made of the chemicals in the accidental gas cloud itself but it has been possible to estimate the dioxin exposure of people in different areas by three independent methods. The first was a calculation of the distribution of the dioxin based on the nature of the chemical reaction, the quantity of ingredients, and the wind direction and speed at the time of the accident. The second method recorded biomedical changes, such as the death of birds and other wild and domestic animals and the appearance of chloracne in people. These changes were then correlated with the geographic location of each person or animal affected. The third method, performed somewhat later, was the actual analysis of the soil for dioxin. This gave results which were judged to be in agreement with those of the other two methods. In addition, reports by the exposed individuals provided supplementary and confirmatory information.

In the areas with the most intense exposure, animals and birds died; humans did not. People experienced a variety of symptoms shortly after the explosion including weakness, headache, loss of appetite and weight, insomnia, impotence, nausea and abdominal pain. There was also a burning sensation and an eruption of the skin, but the role of dioxin, as opposed to other more caustic chemicals suspected of being present in the cloud, is unclear. The symptoms cleared up within a brief period but one characteristic skin change, chloracne, persisted. Chloracne was present, especially in children under the age of 14. In the most heavily contaminated areas about 20 per cent of the children developed the skin disorder. The changes gradually cleared over the ensuing months.

Early after the exposure there were laboratory results suggesting changes in liver function, but the test results did not differ a great deal from those obtained in an unexposed, control population. Within a year after the exposure careful examinations showed some problems with the nerves controlling muscle function. These changes apparently disappeared within the following two or three years.

It is not clear that the exposure to dioxin had any effect on the pregnancy rate, the miscarriage rate or the birth rate since there are no good statistics from nearby communities with which to compare the exposed populations. There is no convincing evidence that the dioxin caused birth defects, interfered with growth, disturbed resistance to disease or increased the death rate. Some details of these results may be questioned because of the difficulties encountered in collecting the data. It is reasonable, however, to say that the Seveso accident did not result in a very serious or life-threatening effect on the health of exposed persons, at least in the near-term. It is too soon to draw final conclusions regarding possible delayed effects.

A final potential source of information about the adverse health effects of Agent Orange includes studies using experimental animals. Care must be taken in interpreting the results of animal studies because animals may respond quite differently from humans in the way they absorb chemicals, in the distribution of these chemicals in the body, in the way the chemicals

are broken down or stored in the body, and in the way they are eliminated. Differences in body size, diet, lifespan, and the way individual organs function may also cause animals to respond differently from humans. For these reasons responsible scientists are reluctant to base predictions of human health effects on animal studies unless the chemical has been tested in several species of experimental animals and there is a good basis for believing that the test animals are similar to humans in the way they respond to the chemical.

For reasons noted earlier, Agent Orange when it was first used was not tested in experimental animals and, because the amount and identity of the impurities in Agent Orange varied, it cannot be exactly reproduced for studies in experimental animals now or in the future. It is therefore necessary to rely on the results of experimental studies of herbicide mixtures similar to Agent Orange as well as studies of individual components of Agent Orange such as 2,4-D, 2,4,5-T and TCDD to serve as a basis for predicting the human health effects of Agent Orange.

The remainder of this report on the health effects of Agent Orange summarizes the information available as of early 1984 from all the types of studies described above. The section that follows provides a discussion of each of the suspected or potential health effects and in each case the available evidence is evaluated as a whole. For more detailed information regarding specific studies the reader is urged to refer to the *Review of Literature on Herbicides, Including Phenoxy Herbicides and Associated Dioxins,* Volumes I, II, III and IV, published by the Veterans Administration.

6. Summary of the studies on health effects

Cancer

To date only one systematic study of cancer in military personnel exposed to Agent Orange in Vietnam has been published. In this study of Air Force personnel who were engaged in Operation Ranch Hand (the herbicide spraying operation in Vietnam), there was no increased occurrence of serious or life-threatening forms of cancer, but a greater incidence of a type of skin cancer was found in the exposed group compared to a control group of military personnel who were not exposed to Agent Orange. This type of skin cancer is a very common, localized form that is known to be associated with exposure to sunlight. Further studies need to be done to determine whether Ranch Hand personnel were more likely to have been exposed to sunlight than were the members of the comparison group. There was also a slightly increased incidence of cancer of the mouth and throat in the Ranch Hand group, but this excess is so small that it may be due to chance.

Two other reports are available on cancer in Vietnam veterans but in neither report was there any confirmation of exposure nor were matched control groups used. In one survey, based on Vietnam veterans who registered with the VA's Agent Orange Registry, a somewhat higher proportion of mouth and throat cancer and of lymphoma (cancer of the lymphatic system) was found compared to the same proportion of cancers among U.S. males aged 25 to 39. In the other report, a physician in Atlanta reported three cases of soft-tissue sarcoma (a rare cancer) among his patients. All three of these patients had served in Vietnam but no other information was given about them.

Comparisons between groups exposed to the herbicides or to dioxins and unexposed groups have shown no overall increase in cancers. Attention has centered on certain types of cancers.

There have been 11 reports of studies of cancer in men who were employed in jobs that involved the spraying of herbicides similar to Agent Orange. Eight of these studies were limited to men who sprayed herbicides containing 2,4-D or 2,4,5-T. The other three studies were of workers exposed to agricultural chemicals in general, including herbicides. These three studies are not discussed here because of the uncertainty regarding exposure. The eight remaining reports are also based on groups of workers whose exposure was of doubtful duration and intensity. Two of the eight studies of 2,4-D or 2,4,5-T indicated that there was an association between exposure and the incidence of soft-tissue sarcoma. A third study showed an association between exposure and lymphoma, and one study showed an association between exposure and stomach cancer. Another of these eight reports described five cases of lymphoma with cutaneous (skin) lesions seen in an English hospital. Four of the five patients worked with 2,4-D or 2,4,5-T. A case-control study reported an association between herbicide exposure and cancer of the nose and throat. The remaining three reports showed no association between exposure and any form of cancer, although one suggested a slight association with soft-tissue sarcoma.

Of seven studies on populations exposed to dioxins either in the workplace or in the environment, two showed an increased incidence of cancers. A study of workers exposed to dioxin as a result of a reactor explosion in a 2,4,5-T manufacturing plant in Germany in 1953 showed an excess of stomach cancer. Another study of the residents of Midland County, Michigan, where Dow Chemical Company has a large plant, revealed an increased incidence of soft-tissue sarcoma in women between 1960 and 1980. This finding is unlikely to be related to dioxin exposure, however, because the excess cancer was seen only in women and several of the people with soft-tissue sarcoma had lived in Midland County only a short time before the diagnosis of cancer and had little or no connection with the company.

Three separate reports describe two cases of lymphoma and three cases of soft-tissue sarcoma in workers who may have been exposed to dioxin. These are isolated case reports, and they contained little evidence of dioxin exposure. Two studies of workers occupationally exposed to dioxin revealed no excess incidence of any form of cancer.

None of the studies of cancer in humans exposed to Agent Orange, related herbicides, or dioxins provides an answer to the question of whether Agent Orange might cause cancer in humans. When all the reports are taken together, however, certain patterns appear that provide suggestive evidence that exposure to dioxin-contaminated herbicides may be associated with an increased incidence of cancer. Thus, seven reports suggest a relationship between such exposure and soft-tissue sarcoma. Four reports point to a possible connection with lymphoma. Two studies show an association with stomach cancer and three reports suggest a possible association with cancer of the mouth, nose, or throat.

The results of animal studies lend support to the hypothesis that dioxins and dioxin-contaminated herbicides may cause cancer in humans. Six studies of the potential for TCDD to cause cancer in animals were positive when relatively large doses were given. TCDD painted on the skin of mice caused cancers related to soft-tissue sarcomas. Four studies in which rats were given TCDD by mouth showed that the rats developed cancer of the liver, mouth and nose, tongue, adrenals, and thyroid. In two studies in which TCDD was given to mice by mouth, liver and thyroid cancers resulted. Several studies suggest that when TCDD is given to mice with other cancer-causing chemicals, it increases the response to those cancer-causing chemicals.

As yet there have been no published studies which show that Agent Orange or similar commercial herbicides have a demonstrated potential for causing cancer in laboratory animals. A few studies designed to measure the effect of 2,4-D and 2,4,5-T on rats and mice have been negative for cancer, but these studies were not adequate to detect a small increase in cancer in the treated animals. The current evidence, though far from conclusive, justifies continued surveillance of people who have been exposed to dioxin and dioxin-contaminated herbicides in order to confirm or deny an increased incidence of cancer which can be attributed to that exposure.

Reproductive effects

The various possible causes of reproductive abnormalities are difficult to determine because there are fairly high rates of birth defects, stillbirths, miscarriages, and sterility in all populations. For example, between three and six percent of all children are born with some kind of defect. The percentage varies depending upon how serious a disturbance has to be before it is recorded as a defect. In addition, some defects are not noted at birth, but show up later in childhood or beyond.

Two systematic studies of reproductive performance and outcome among men who may have been exposed to Agent Orange in Vietnam have been published. In the first of these the Australian government sponsored a study to see whether birth defects were related to the father's service in Vietnam. No association was found, although there was a slightly increased risk of heart defects and Down syndrome among the children of Vietnam veterans.

In the study of Operation Ranch Hand personnel discussed in the cancer section above, a small increased incidence of miscarriages following Vietnam service was found among the wives of the Ranch Hand group when compared to wives of the control group. The same difference, however, was observed for pregnancies occurring prior to Vietnam service. There were also slight increases in deaths of newborn babies and minor birth defects. There may have been slight increases in learning disabilities and physical handicaps among children of Ranch Hand personnel. The significance of these findings is not clear because most of the increases are very small, and many of these differences disappear if the data are analyzed differently. In addition, these differences were based on self-reporting and at the time of the initial report had not been confirmed by a review of medical records.

Two studies have been reported of men who were exposed to herbicides similar to Agent Orange. A study of wives and children of herbicide sprayers in New Zealand showed no increases in birth defects, stillbirths, or miscarriages when compared to the population of New Zealand as a whole. There was a very small increase in the incidence of heart defects, but this may have been due to chance. Another study of children born to the wives of men who sprayed herbicides for the Long Island Railroad showed no increase in major birth defects but two relatively minor birth defects—minimally deformed feet and tear duct obstruction—were seen in excess.

Several studies have been conducted to ascertain whether there are increased incidences of spontaneous abortions, stillbirths, or birth defects in areas where herbicides similar to Agent Orange have been heavily used. In these situations there is the potential for exposure of both parents as opposed to exposure of only the father as in the four studies discussed above.

One of these general population studies gained a great deal of publicity in the late 1970s when it was asserted that women living in the vicinity of Alsea, Oregon, experienced a higher rate of miscarriage than did women living in other parts of Oregon where herbicides were not commonly used. Careful review of this study by expert scientists has resulted in a consensus that the results were misinterpreted and that the study did not show the claimed effect.

More recently, a study of people living in an area of New Zealand where herbicides containing 2,4,5-T were often used revealed an increase in the occurrence of clubfoot in children in the area. Other small and perhaps insignificant increases were found in heart defects and malformations of the penis. A study conducted in Hungary looked at the rate of five major birth defects in that country's general population over a five-year period in which the use of 2,4,5-T increased greatly. No changes in the rates of these birth defects were found.

Four studies have been conducted of men exposed to dioxin as a result of working in plants where 2,4,5-T was manufactured. None of these studies showed a clearcut effect on reproductive outcomes. Two of them did show a slight increase in spontaneous abortions in the wives of the workers. Two studies of the population exposed to dioxin as a result of the ICMESA accident at Seveso suggest that there may have been an increase in birth defects (particularly of the heart) and an increased incidence of spontaneous abortions in the year following the accident, but their validity is questionable because the reporting of birth defects and abortions was generally unreliable.

The studies of the reproductive effects of 2,4-D, 2,4,5-T, and TCDD in experimental animals are of limited usefulness in helping to predict the reproductive effects of Agent Orange in male Vietnam veterans. In almost all of the animal studies, the herbicide or dioxin was given to pregnant females rather than to male animals. In the one study in which the mixture found in Agent Orange was fed to male mice, it had no effect on reproductive performance or on the offspring. In two studies, relatively uncontaminated 2,4,5-T and TCDD were fed to both male and female rats and reproductive performance and outcome were recorded for three successive generations. These studies showed that both 2,4,5-T and TCDD decreased the number of live births and the weight of newborn animals, as well as causing an increase in birth defects of the kidneys. Numerous studies in which TCDD was given to pregnant females in relatively large

doses indicate that it can cause defects in the developing fetus. TCDD causes birth defects in pregnant rats, mice, rabbits, and monkeys when given by mouth or injection. It also causes an increase in the number of spontaneous abortions and a decrease in birth weight of newborn animals.

In summary, no study of reproduction in humans exposed to Agent Orange conclusively shows an adverse effect which has been caused by the herbicide. Scientists believe, however, that people with known exposure to TCDD-contaminated chemicals should be observed for possible adverse reproductive effects.

Enzyme effects

One of the best studied effects of dioxins in experimental animals is the ability of these compounds, especially TCDD, to alter the activity of certain enzymes. Enzymes are proteins that serve as catalysts in the formation or breakdown of various chemicals in the body. In some cases many enzymes are involved in the alteration of just one chemical, whereas other enzymes are capable of acting upon an entire class of chemicals.

It is very difficult to study the effects of chemicals on enzyme activities in humans. Most enzymes are located in tissues where metabolic activity is greatest, such as the liver, lungs, intestines, brain, and reproductive organs, and these tissues are the least accessible to study. Furthermore, there are large differences among people in their baseline metabolic activity. About the only approach available is to look at the levels of chemicals produced by enzyme reactions that appear in the blood or urine and determine whether they are different in people exposed to a specific compound when compared to people who are not exposed to that compound.

Only a few studies of enzyme activities have been conducted in animals which have been fed or otherwise dosed with 2,4-D and 2,4,5-T. These studies suggest that these compounds do not cause major alterations in enzyme activities, and some of the small effects seen may be the result of contamination of these chemicals with small amounts of dioxin. A number of studies of TCDD, on the other hand, have shown that it alters the activity of some enzymes in experimental animals.

The best studied effect is an increase in the activity of an enzyme known as aryl hydrocarbon hydroxylase (AHH). AHH is important because it makes certain chemicals more soluble in water and, thus, more likely to be excreted in the urine. Very small amounts of TCDD cause large increases in the activity of this enzyme in rabbits, mice, rats, guinea pigs, hamsters, birds, fish, and monkeys. In several studies in which living cells were taken from humans and allowed to grow in a culture medium, the addition of TCDD to the culture caused an increase in AHH activity in the cells.

It is interesting that in two studies of human populations exposed to dioxin as a result of industrial accidents (one at Seveso and the other at a 2,4,5-T manufacturing plant in England), scientists found elevated levels of d-glutaric acid in the urine of exposed people. This chemical

is believed to be formed by enzymes that are very closely associated with AHH. This finding adds support to the theory that TCDD may stimulate AHH activity in humans.

What are the health implications of stimulation of AHH activity? This is a difficult question to answer because the role of AHH is not yet fully understood. Evidence from animal experiments and some human evidence indicate that some of the aryl hydrocarbons that are altered by AHH are cancer-causing. Some experiments in which TCDD was given to animals several days before they were exposed to cancer-causing aryl hydrocarbons showed that it protected the animals against cancer. Thus, TCDD caused an overall health benefit.

Unfortunately, the picture is much more complicated than that because, if TCDD is given to animals at the same time as the aryl hydrocarbon rather than a few days earlier, the TCDD binds to the site of the AHH enzyme that is responsible for changing the aryl hydrocarbon and prevents the AHH enzyme from doing its job. Thus, administration of TCDD with aryl hydrocarbon causes more cancer than does the aryl hydrocarbon itself.

An additional complication is that there is evidence that AHH catalyzes other tranformations and that some of them may convert inactive chemicals into toxic ones. In the absence of complete information, the fact that TCDD stimulates AHH activity must be viewed as a potentially adverse effect.

Animal studies have also shown that TCDD alters some enzymes that are involved in the manufacture of heme, the portion of the hemoglobin molecule that binds oxygen in red blood cells. Animal studies indicate that TCDD *decreases* the activity of an enzyme known as uroporphyrinogen decarboxylase in the liver. This results in a decrease in the amount of heme synthesis and a build-up of the chemicals known as porphyrins from which heme is formed. As the porphyrin level builds up, more porphyrins are excreted in the urine.

A number of animal experiments have shown that the pattern and amount of porphyrins excreted in the urine changes after treatment with TCDD. Two studies of workmen exposed to dioxin have shown increased urinary excretion of porphyrins. The Air Force study of personnel involved in Operation Ranch Hand has also shown that there are more men with abnormally high porphyrin levels in the exposed group than in the comparison group, although this finding correlates more strongly with alcohol use than it does with potential exposure to Agent Orange.

Interference with porphyrin metabolism may result in a condition known as porphyria cutanea tarda (PCT) in which the skin blisters and later becomes dry and brittle, particularly on exposure to sunlight. Workers who were exposed to dioxins as a result of two industrial situations developed this condition but in both instances the men were also exposed to another chemical known to cause PCT.

The available medical evidence indicates that there are no lasting adverse human health effects that result from alterations in porphyrin metabolism due to exposure to TCDD. The body adjusts by producing sufficient heme to meet the oxygen-carrying needs of the body. PCT is a relatively rare manifestation of changed heme metabolism and may be caused by

other external factors, such as alcohol consumption. There is also a known genetic factor which influences the development of PCT. PCT resulting from exposure to such chemicals as dioxins and similar compounds is reversible and disappears after exposure.

Another enzyme activity for which there is indirect evidence of interference by dioxins is related to the conversion and storage of fats. Studies of workmen exposed to dioxins showed increased blood levels of fat molecules known as triglycerides. Although elevated levels of some triglycerides are known to be associated with heart disease, to date there is no conclusive evidence of an association between heart disease and dioxin exposure.

Although it appears that dioxins have the ability to alter the functions of a number of enzymes, at present none of these alterations has been shown to be associated with any serious or irreversible adverse health effects in humans. However, any influence that substantially alters the way the body handles internal and external chemicals must be viewed with concern. It should be remembered that as in the case of most of the effects of these chemicals, the active herbicide ingredients 2,4-D and 2,4,5-T by themselves are not known to affect the enzyme system in humans.

Effects on the immune system

Unlike such well-studied and relatively well-understood systems of the body as the cardiovascular and digestive systems, there is still much of the "immune system" which is not well understood. It is currently the subject of intensive research to better understand its chemistry, mechanisms, and functions. The immune system is involved in a large and complex array of processes that defend the body against foreign chemicals, disease-causing bacteria, viruses, foreign cells from outside the body, and abnormal cells from within the body. Virtually all of the body's organs and tissues participate in these processes to a greater or lesser extent.

Because of the lack of basic knowledge in some areas, it is difficult to assess the impact of chemicals on the immune system. One problem is that the system functions in many different ways. A chemical to which the body is exposed may activate only one or two of dozens of known defense mechanisms. Therefore, it may be necessary to run a large number of different tests to detect these changes. Since many of these tests are very complex and some require the examination of body tissues, it is especially difficult to study altered immune function in humans.

Two additional factors make it difficult to detect such changes in humans. First, there are tremendous differences among people in the manner in which their immune systems operate. For example, there is a wide variation in the way different people manifest an allergic reaction, which is one of the ways the immune system functions. Second, many activities of the immune system have no obvious or external manifestations. It is usually not possible to assess a person's immune function by a simple physical examination. These changes in immune function may only be reflected by subtle variations in indirect indicators, such as increased susceptibility to infections or increased sensitivity to materials that cause allergic reactions. One result of these problems is that the effect(s) of chemicals on the immune system of humans may

be very subtle and difficult to detect. Highly specialized and complex tests are often needed to detect these changes.

There is no evidence that 2,4-D or 2,4,5-T by themselves alter the immune function of animals. There have been no studies of humans exposed to Agent Orange or similar herbicides that show an adverse effect on the immune system, and there have been no reports of increased allergies or of increased susceptibility to infection, either of which might indicate altered immunity. On the other hand, there have been no studies reported that were designed specifically to look for such an effect in humans soon after exposure.

There is considerable evidence, on the other hand, that TCDD interferes with the functioning of the immune system in experimental animals. When TCDD is given to animals, a common effect is a decrease in the size of the thymus, an organ that is involved in the immune system. This effect occurs at doses lower than those that cause changes in other organs. At even lower doses, TCDD interferes with the ability of the animal to produce certain types of white blood cells in response to the presence of foreign materials in the blood stream. In some studies, this effect is paralleled by decreased resistance to bacterial and viral infections.

It appears that TCDD has the ability to suppress the immune system in unborn animals when the TCDD is given to pregnant females. Sensitivity decreases in newborns but significant effects can still be seen in adult animals treated with TCDD. In fact, immune suppression is the most sensitive indicator of TCDD exposure in mice, occurring at doses below those that cause changes in enzyme activity. Furthermore, although immune function improves after exposure ends, it remains relatively depressed for a very long time in experimental animals.

Most studies of humans who have been exposed to dioxins have not included tests of immune function. There has been a study of children who lived in the heavily contaminated area of Seveso, Italy. The results of this study showed that these children had higher levels of certain immunologically active blood components than did children from uncontaminated areas. The body also produced more white blood cells in response to certain foreign materials. These results suggest that exposure to dioxins *stimulated* immune function in these children rather than depressing it, as seen in the animal experiments. This finding is not inconsistent, however, with experimental findings that some chemicals which depress immune function at high doses may actually stimulate immune functions at low doses.

Another study of workers exposed to dioxin as the result of an industrial accident has been reported to have shown *decreased* immune function in the exposed workers 10 years after the accident, but this study has not been published and cannot be independently reviewed. These results, taken together, fall far short of providing convincing evidence that dioxin exposure can cause altered immune function in humans. Nevertheless, the evidence of such effects in experimental animals provides some basis for concern that exposure to dioxin may adversely affect immune function in humans.

Chloracne

Chloracne is a skin condition that is known to result from exposure to a group of structurally similar compounds in which chlorine atoms are bound to an aromatic hydrocarbon. One of

these compounds is TCDD. As its name suggests, chloracne, is similar in appearance to the common forms of acne that affect teenagers and usually appears within a few weeks after exposure to the chemical that causes it.

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 confined 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. 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 opens sores and permanent scars. The condition fades slowly after exposure. Minor cases may disappear altogether, but more severe cases may persist for years after the exposure.

It is well known that chloracne can result from exposure to dioxins. In seven reported situations where workers were exposed to dioxins as a result of industrial accidents or poor housekeeping practices, many of the workers and, in a few cases, members of their families developed chloracne. Chloracne was also diagnosed in 187 people, mostly children, living in the section of Seveso that was most heavily contaminated with TCDD as a result of the ICMESA accident in 1976. Two laboratory workers who were exposed during the synthesis of TCDD developed serious cases of chloracne.

There are no authoritative reports in the literature that document an association between exposure to Agent Orange or similar herbicides and chloracne. The Air Force study of Ranch Hand personnel showed no excess of acne in those individuals when compared to unexposed controls and no cases of chloracne were found. Most of the epidemiologic studies of occupational groups involved in the spraying of herbicides like Agent Orange do not report the presence of chloracne among the workers who were studied. A research effort looking for cancer among herbicide sprayers in Finland turned up a few cases of possible chloracne, one of which was diagnosed by a dermatologist. It would appear, therefore, that chloracne is not a sensitive indicator of exposure to herbicides like Agent Orange.

Animal studies are of little use in measuring the potential of Agent Orange for causing chloracne in humans. The ingredients 2,4-D and 2,4,5-T have not been extensively tested, but it appears that they do not cause chloracne or similar skin conditions in experimental animals. Different kinds of animals react differently to TCDD, but it causes skin conditions very similar to chloracne when applied to the ears of rabbits and to the skin of certain kinds of mice. Scientists disagree, however, as to whether these skin effects are identical to human chloracne. Some types of experimental animals fail to show any acne-like condition when treated with TCDD. It seems that only monkeys exposed to TCDD develop a skin condition that appears identical to human chloracne.

One conclusion that is gaining support on the basis of both animal and human studies is that susceptibility to chloracne may be genetically controlled. Two individuals equally exposed to TCDD may respond differently because of variations in inherited susceptibility. This would explain why some of the workers exposed to dioxins in each of the seven industrial incidents did not develop chloracne, even though there is no reason to believe that they were less

exposed than workers who did develop chloracne. Thus, whereas chloracne may be a sensitive indicator of exposure to dioxins in some people, it may not be in others. Therefore, 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.

Neurobehavioral effects

It has been known for some time that exposure to relatively large amounts of 2,4-D, such as might occur when it is being mixed or sprayed, can cause adverse effects on the nervous system. Workmen who splashed 2,4-D on their skin or who stood for a long time in 2,4-D spray mist developed a variety of symptoms including tingling or decreased feeling in the hands and feet and tightening of muscles in the arms and legs. Examination of these workmen showed the loss of the knee-jerk reflex and an increase in the time for nerve impulses to travel from the hands or feet to the spinal cord and back. Studies in experimental animals give results similar to those seen in humans. These studies suggest that 2,4-D interferes with the transmission of nerve impulses to muscles. If the exposure is minimal the nervous system recovers. However, sustained exposure of experimental animals to relatively large quantities of 2,4-D may cause long-lasting changes in the brain and spinal cord itself.

A few studies of humans and experimental animals exposed to 2,4,5-T have failed to show any nervous system effects such as those caused by 2,4-D. There is some evidence, however, that humans exposed to dioxins as a result of industrial exposures or accidents may suffer impaired nervous system function. A wide range of signs and symptoms have been reported in these people including pain in the arms and legs, numbness in the hands and feet, muscular weakness particularly in the legs, headache, loss of memory and concentration, sleep disturbances, nervousness, and emotional and behavioral abnormalities. The speed of nerve impulses was slowed in two groups of workers who were probably exposed to dioxins.

There have been very few studies of the effects of TCDD or other dioxins on the nervous system in animals. It is not clear why this knowledge gap exists, but one possible explanation is that the doses of TCDD needed to cause detectable signs of nervous system damage in experimental animals are higher than those that cause other serious toxic effects. Scientists have therefore tended to concentrate on the other effects.

Whether nervous system and psychologic effects have occurred in individuals exposed to Agent Orange as a result of the Vietnam experience is unclear and controversial. It has been suggested that Vietnam veterans experience a high rate of psychologic problems, with certain symptoms appearing quite frequently. These symptoms include nervousness, disturbed sleep, irritability and short temper, depression, and suicidal thoughts. Many psychiatrists consider that some of these comprise a distinct collection of symptoms or a syndrome known as post-traumatic stress disorder and that this syndrome is unrelated to any chemical exposure. Evidence in support of this conclusion is that individuals such as prisoners of war and hostages who have undergone sustained stress display similar symptoms.

Unfortunately, there are almost no systematic studies of nervous system function or psychological problems among individuals exposed to Agent Orange. The recent Air Force

study of Ranch Hand personnel showed no difference between the exposed group and unexposed controls in several measurements of nervous system function including the speed of nerve impulse transmissions. On the other hand, when Ranch Hand personnel were evaluated by analyzing answers to questions on some of the tests designed to detect emotional disorders or personality disturbances, psychiatrists concluded that they were different from the comparison group and showed tendencies toward traits defined as "hypochondria, depression, hysteria, and schizophrenia." Ranch Hand personnel were also said to feel more isolated and to have a higher degree of nervousness and anxiety, to be more easily startled, and to experience more psychosomatic illness than did the comparison group. These differences were minor and are difficult to interpret. The methods used in this study would not show whether the differences between groups were due to post-traumatic stress, Agent Orange exposure, or both.

The fact that self-perception of psychologic problems is an important component of such an analysis was shown in a study of 100 veterans who were asked about their exposure to Agent Orange and their current mental and emotional well-being. Their potential exposure to Agent Orange was independently assessed by comparing their service records with records of the time and location of herbicide spraying missions in Vietnam. The frequency and seriousness of psychologic and emotional problems correlated very closely with how much herbicide the veterans *believed* they were exposed to, whereas the correlation was much weaker when the comparison was based on how much herbicide exposure the records showed.

The issue of the effects of Agent Orange on nervous system and psychologic performance is probably the most difficult health issue to resolve. There is a great deal of human and animal evidence that both 2,4-D and TCDD can adversely affect the nervous system. All of this evidence suggests that these effects are the result of short-term high level exposure rather than sustained exposure to lesser amounts.

Other toxic effects

Studies of people exposed to Agent Orange or similar herbicide mixtures have failed to reveal any significant toxic effects other than those discussed above. Other effects have been attributed to TCDD, however. As was mentioned briefly in the section on enzyme effects, there is suggestive evidence of a higher incidence of heart attacks among workmen exposed to dioxins in industrial accidents. This evidence is far from conclusive, but it is sufficient justification for continuing to observe the health of people exposed to dioxin, especially since it may take many years after exposure for adverse effects on the heart to show up.

The most dramatic sign of fatal dioxin poisoning in experimental animals is an apparent loss of appetite which leads to general body wasting. The animals eventually die of a condition very similar to starvation. This effect is observed following a large single dose of TCDD. No similar effect has been described in humans, so it may be of little relevance to human health. The mechanism by which TCDD causes this apparent loss of appetite is unknown and is the object of much current research. Some results suggest that TCDD may interfere with an appetite regulating system in the brain or thyroid.

Animal studies have suggested another aspect of the toxicity of TCDD which may have implications for human health. It has become increasingly clear that some animals are relatively resistant to some of the toxic effects of TCDD compared to others. Recent research has shown that this difference in susceptibility is genetically influenced and that mice with just one parent in common can show large differences in susceptibility to the toxic effects of TCDD. The effects for which susceptibility appears to be genetically controlled include the appearance of birth defects in the offspring of female mice exposed to TCDD, the increased activity of several enzymes including AHH and uroporphyrinogen decarboxylase, depression of immune function, chloracne, and the lethal effects of TCDD. This suggests the possibility that humans as a group who are known to be genetically very diverse, may have a wide variation in susceptibility.

7. Summary and Conclusions

What can we say about the health effects of Agent Orange? From the evidence now available we can arrive at almost no definitive conclusions. The limited evidence available suggests that 2,4-D and 2,4,5-T by themselves are not highly toxic to humans. 2,4-D appears to be capable of causing nervous system toxicity but only in situations where there is very high-level exposure. 2,4,5-T may contribute to birth defects when pregnant females are exposed. There is no evidence that purified 2,4-D or 2,4,5-T cause cancer, change the activity of enzymes, affect the immune system, or cause chloracne or porphyria cutanea tarda in humans.

There is very little direct evidence that Agent Orange causes adverse health effects in humans, but this may be the result of our limited ability or inability to identify different groups of people or large numbers of people with well-defined exposure and exposure to a known amount of the substances of concern. If adverse human health effects are found as a result of present or future research efforts, it is highly likely that these will be the result of the effects of toxic impurities such as dioxins, especially TCDD. The limited evidence of TCDD toxicity in humans comes from studies of humans exposed to dioxins, and indirectly from studies of dioxin toxicity in experimental animals. These studies provide some support for the possibility, but do not prove, that exposure to dioxin-contaminated herbicides may cause adverse health effects in humans.

These adverse effects may include chloracne, cancer at several different sites, spontaneous abortion and birth defects in the offspring of exposed females, altered enzyme activity, altered porphyrin metabolism, and altered immune function. Effects for which the available evidence is very inconclusive but which should be the subject of further study are neurobehavioral effects, including psychologic effects and heart disease. Chloracne does not seem to be of significant importance since it has not been commonly observed even among individuals heavily exposed to herbicides. Therefore chloracne does not appear to be a sensitive indicator of exposure to dioxin-contaminated herbicides.

What will future studies tell us about the health effects of exposure to Agent Orange? Studies that are planned or in progress have the potential to reduce much of the uncertainty about the health effects of exposure to Agent Orange. However, because of very serious problems in determining the exact amount and nature of exposure and in choosing appropriate

exposed and unexposed groups to examine, these studies will never be able to demonstrate conclusively the *absence* of a toxic effect. The areas in which future studies may be able to provide the most information are the delayed effects such as cancer.

Studies in experimental animals can still be helpful in suggesting possible adverse health effects of Agent Orange. Particularly helpful would be studies of the purified components of Agent Orange separately and in known combinations. Other important areas of investigation include effects on immune function and the genetic control of susceptibility to the toxic effects of dioxin.

In the meantime, exposed individuals can get some degree of reassurance from the fact that despite their inadequacies, the studies which have been completed to date have revealed no widespread or major adverse health effects among the people who were exposed. There is no evidence that the psychologic disturbances seen in Vietnam veterans are the result of exposure to Agent Orange.

For many of the potential health effects, there is little probability that they will first appear years after exposure. These include reproductive and enzyme effects, chloracne, and neurobehavioral problems. It is possible that cancer may first appear years after exposure. Persons exposed to Agent Orange should take no exceptional precautions beyond those that are prudent for everyone, i.e., consume a balanced diet, exercise regularly, have regular medical checkups, be alert for tell-tale signs of cancer, abstain from smoking, and use alcohol moderately, if at all.