June 11, 1979

TRANSCRIPT OF PROCEEDINGS

IN THE MATTER OF :

Advisory Committee on Health-Related Effects of Herbicides

Veterans Administration
Washington, D.C. 20420

THE VETERANS ADMINISTRATION

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ADVISORY COMMITTEE ON HEALTH-RELATED EFFECTS

OF HERBICIDES

The Veterans Administration
Room 119
810 Vermont Avenue, N. W.
Washington, D. C.

10:00 a.m.
Monday, June 11, 1979

ADVISORY COMMITTEE MEMBERS PRESENT:

PAUL A. L. HABER, M.D., Chairman
Assistant Chief Medical Director
for Professional Services
Veterans Administration
Washington, D. C.

GERRIT W. H. SCHEPERS, M.D., Vice Chairman
Medical Service
Veterans Administration
Washington, D. C.

JAMES R. ALLEN, JR., Ph.D.
Professor of Pathology
The University of Wisconsin
Medical School
Department of Pathology
Madison, Wisconsin

IRVING B. BRICK, M.D.
Senior Medical Consultant
National Veterans Affairs
and Rehabilitation Commission
The American Legion
Washington, D. C.

J. DAVIDSON ERICKSON, D.D.S., Ph.D.
Center for Disease Control
Birth Defects Branch
Atlanta, Georgia

BILL L. STEPHENSON
Environmental Protection Agency
Washington, D. C.

PHILIP C. KEARNEY, Ph.D.
Chief, Pesticide Degradation Laboratory
Department of Agriculture
Beltsville, Maryland

RICHARD A. LEMEN
Assistant Chief
Industrywide Studies Branch
Robert A. Taft Laboratories
Cincinnati, Ohio

ROBERT H. LENHAM
Special Projects Officer
Disabled American Veterans
Washington, D. C.

ADVISORY COMMITTEE MEMBERS PRESENT (Con't):

CAROLYN H. LINGEMAN, M.D.
Carcinogenesis Testing Program
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

JOHN A. MOORE, D.V.M.
Associate Director for
Research Resources Program
National Institute of Environmental
Health Sciences
Research Triangle Park, North Carolina

SHELDON D. MURPHY, Ph.D.
Department of Pharmacology
University of Texas Medical School
Houston, Texas

COLONEL J. W. THIESSEN, MC USA
U. S. Army Environmental Hygiene Agency
Aberdeen Proving Ground, Maryland

STEERING COMMITTEE MEMBERS PRESENT:

RICHARD A. LEVINSON, M.D., Chairman

JOHN J. CASTELLOT, SR., M.D.

STRATTON APPLEMAN

LYNDON E. LEE, M.D.

J. C. PECKARSKY

FRED CONWAY

MARGARET KILDUFF

DONELD HOWELL

ALEX KUTNER

PAUL LEGOLVAN, M.D.

I N D E X

P R O C E E D I N G S

DR. HABER: We would like to begin promptly. Without further ado, I would like to introduce to you our Chief Medical Director, Dr. Crutcher, an outstanding internist, a man who is more concerned I think with clinical practice of medicine in the Veterans Administration than any of his illustrious predecessors.

Dr. Crutcher has taken time from his very busy schedule to address us this morning, and I therefore introduce him to give you an official welcome.

DR. CRUTCHER: Thank you, Paul. The Administrator is receiving his doctorate degree from Emory University in Atlanta, and he is supposed to be making a benedictory appearance this afternoon, but air travel being what it is, he may not make it.

I personally wanted to open up this session because I think the problem of long-term effects of herbicides as it may affect our patients in the Department of Medicine and Surgery is one of significant concern.

I would like to congratulate Dr. Haber and his committee for having gotten such an expert panel, and I would thank those who are on the panel and advisory committee for taking the time from your busy schedules in order to contribute your experience, your talents, and your thoughts regarding this program.

From my perspective, I think the major area of difficulty here will be one of communication. Those of us in the biomedical field often say things and often our

patients don't understand what we say, even though we think it is very simple.

Those in the bioscientific field say things that those of us in the biomedical field hear but do not understand. Even those who are presenting their scientific treatise are not perfectly clear to those who are in the group.

I know from being on a research and development committee for many years that sometimes with some of the more specialized technologies, I couldn't understand the language, although I could read the words.

Those patients of ours who are neither biomedical careerists or scientists, but perceive signs and symptoms as they affect them, and its possible relationship to long-term effects of herbicides, have their own language and their own mind set.

I think that as a result of this, there is a possibility of having three groups of people, or perhaps four--the advocates of the veterans groups, having four interested groups of people, all well intentioned, all speaking with somewhat inexperience, ending up that there is a veritable Tower of Babble regarding this problem; and I think that the veterans groups and the veterans and the scientists and the biomedical people should probably be overly receptive to try and understand what the people are saying.

I have absolute confidence in the experience of this advisory council, but I am speaking as a physician. I have confidence in the scientific contributions that many of the members of this advisory committee have been

making in working on dioxin for many, many years.

At the same time, I have a tremendous respect for patients, and I feel that they have symptoms. They perceive symptoms that may be related to a specific cause, and then the ability to transmit or to change their attitude, or to change our attitude, becomes then a very difficult problem of who is saying what to whom, and what are we trying to do.

I think finally overall, though, that the Department of Medicine as part of the VA, is a very personal agency. We are dealing with people constantly every day. I dont think we are bureaucratic. Of course, it is up to us to prove the fact that we are not an insensitive, bureaucratic agency that is not receptive to what people are saying, but to put forth the picture that we are a group of dedicated individuals whose primary goal is to take care of those veterans that the law says we ought to take care of.

I think, Paul, with that as my overview, then I think this committee can work through these difficult communication problems, as well as gathering together some type of logical scientific data and chronology of whatever effects there may be, at what time, of those who served in our armed forces.

DR. HABER: Thank you very much, Dr. Crutcher. We appreciate it.

DR. CRUTCHER: It is good to see you all, and those that are in the audience.

DR. HABER: I would like now to move on with the agenda, and this calls for introductions, and I would like to ask the Committee and the Steering Committee to introduce themselves. We are arranged in alphabetical order.

Would you please give us your name, your academic or governmental affiliation, and in a few words, what you do, what is your own particular expertise, whether you are an epidemiologist or a biochemist or a clinician or whatever other appropriate designation you need so we can address you appropriately, and maybe we may begin with you, Dr. Allen, heading the alphabet.

DR. ALLEN: My name is James Allen. I am a professor of pathology at the University of Wisconsin Medical School. I have been there for approximately 20 years and during this period, have been interested in research on the halogenated hydrocarbons and the dioxins.

DR. BRICK: I am Dr. Irving B. Brick. I am a professor of medicine and Chief of the Division of Gastroenterology at Georgetown University School of Medicine, and also a senior medical consultant to the American Legion.

My interest is primarily clinical gastroenterology, and in particular liver disease. I am going to be interested myself to learn what these experts are going to teach me about the effects of these herbicides, particularly on the liver and other organs in which I am particularly interested.

Also as a representative of the American Legion, in handling many claims of veterans before the Board of Veterans Appeals particularly, the impact of the findings of this Committee will have great future effect I think on veterans' claims.

All of us in the American Legion are dedicated to trying to find out the truth over and above the emotional connotations that have been aroused by the particular subject that we are going to study.

Thank you.

DR. ERICKSON: I am David Erickson. I am Deputy Chief of the Birth Defects Branch at the Center for Disease Control, Atlanta, Georgia, and I am an epidemiologist by training and occupation and avocation, and I am primarily interested in the population dynamics and etiology of birth defects in humans.

DR. KEARNEY: My name is Philip Kearney. I am the Chief of the Pesticide Degradation Laboratory, U. S. Department of Agriculture at Beltsville, Maryland.

My major interest in this area deals with the chemistry of the dioxins and their environmental aspects. I have followed this for about nine years, and I have visited Italy in '76 and have had a lasting interest in the environmental treatment and chemistry of the dioxins.

DR. HABER: I am Paul Haber, Assistant Chief Medical Director for Professional Services whose responsibility it is to help direct patient care programs, and Agent Orange is something very much in our minds.

It is my job to try to get to the bottom of this for the VA and to advise the Chief Medical Director and the Administrator, on appropriate steps that need to be taken in order to solve this problem.

DR. SCHEPERS: I am Gerrit Schepers. I work for the Medical Service in the Veterans Administration. I am an internist and pathologist by training. I have worked in the field of toxicology, particularly carcinogenesis, for the past 25 years, and for the past year, I have been almost what one might call project officer for our Agent Orange problem.

Recently we have received all this extra help so that I need not call myself project officer any more. Thank you.

MR. LEMEN: My name is Richard Lemen, and I am with the National Institute of Occupational Safety and Health, and my background is in occupational epidemiology, and I have done my doctoral training at the University of Illinois.

I am in charge of the Industrywide Studies Branch, which is the primary area where long-term chronic epidemiology is done, and our interest is in the occupational effects of dioxin and what we might be able to help learn as far as the environmental effects by looking at occupational groups.

MR. LENHAM: I am Bob Lenham, the special project officer for the Disabled American Veterans Organization. I do not have a scientific background. I am here representing

the veteran as a veteran consumer. I am a Vietnam combat veteran, a hospital corpsman, that was assigned to the Marine Corps over there, and I, too, share with Dr. Brick the concerns and the input that we will have from this Committee and how we shall deal with this input in the claimants that we represent that come before us, before the Disabled American Veterans.

DR. LINGEMAN: I am Carolyn Lingeman. I am a pathologist. I work for the National Cancer Institute and have for the past ten years worked in environmental carcinogenesis. We are particularly interested in chemical compounds which cause cancer. I am also at the present time working at the Armed Forces Institute of Pathology on a special project involving attempts to collect pathologic materials from humans exposed to chemical carcinogens, and the problem is to document exposure to a toxic chemical and to determine whether or not a person does indeed have cancer or other disease that could be attributed to that chemical compound.

DR. MOORE: I am Jack Moore, Associate Director of the National Institute of Environmental Health Sciences, which is an institute of NIH that is concerned about the effects of environmental chemicals on the health of man.

As a toxicologist, I have been involved for the last nine or ten years with research trying to understand what typical benzodioxins as well as other dioxins may do on biological systems.

DR. MURPHY: I am Sheldon Murphy, professor of toxicology at the University of Texas Health Science Center

for approximately the last two years, and 14 years before that at the Harvard School of Public Health.

I have had a long time research interest in pesticide toxicology, and more recently, association with the herbicide dioxin problem largely through committees of the EPA and the National Academy of Sciences.

COLONEL THIESSEN: My name is Thiessen. I represent the Department of Defense, and in every-day life I am Director of Occupational and Environmental Health at the Army Environmental Hygiene Agency.

My interest in herbicides is relatively recent. I was involved as technical adviser to the Defense Logistics Agency in the disposal of Herbicide Orange.

I would like to make the statement that I do represent a large agency. I do not hold that I know all the details of the investigations that are going on and the discussions that are going on in the Department of Defense.

Of course, I will be glad to act as a focal point and get you all the answers that you need out of the Department of Defense.

DR. HABER: Thank you. As an Advisory Committee, the most important of our efforts is to secure information, but I must also inform you that we have a Steering Committee in the Veterans Administration which gives us direct advice.

Its Chairman is Dr. Richard Levinson, --would you stand when identified--who is Deputy for Clinical Support Services; Dr. John Castellot on the Committee who is Director of our Medical Service, a Vietnam veteran and a

veteran of Korea as well--just Vietnam; Ms. Margaret Kilduff of the administrative staff at the library to give us advice about the library; Mr. Donald Howell, representing Ms. Dinunzio, Office of Management Services, and Dr. Paul LeGolvan, Pathology Service; Dr. Lyndon Lee of the Veterans Administration who is in charge of one of our research programs; Mr. Tim Conway representing the General Counsel; and Mr. Charles Peckarsky, Director of Compensation and Pension Services, Department of Veterans Benefits.

I would like to call to your attention a couple of people who are going to be helping us--Ms. Williams, who labored mightily to produce this volume of paper and who will help us process the material as we go along.

I would like to charge the Committee and to give you some information about what I think our job is and some information about the way in which we will proceed.

I would like to call your attention to the fact that this Advisory Committee has been duly recognized and registered, complying with all the rules and regulations attendant upon such committees, and has been duly published in "The Federal Register," and future meetings will be advertised in "The Federal Register" to apprise all concerned of the occurrence of such meetings.

Let me read briefly from the charter of this Committee. The official designation is Advisory Committee on Health-Related Effects of Herbicides, and I will briefly read this.

"It has recently been brought to light that

enormous quantities of herbicidal chemicals were used during the Vietnam War, and that there is a possibility that large numbers of Americans, many of whom now qualify as veterans, may have encountered these chemicals to an extent that long-range, significant health problems may have been initiated.

There is considerable controversy in the published literature and it is probable that much information remains unpublished.

The Veterans Administration has not previously been required to resolve toxicological issues of such a complex and highly controversial nature.

The Committee will, therefore, assemble and analyze the information which the Veterans Administration needs in order to formulate appropriate medical policy and procedures in the interests of the involved veterans.

The Committee will have an entirely fact finding and advisory role and will not be required to develop policy. The Committee will adhere to all the provisions of U. S. Public Law No. 92-463, 5 U.S.C. App. I, Executive Order 12024, and Presidential Circular A-63 of March 27, 1974, and subsequent applicable revisions.

It is anticipated that the Committee may achieve its objectives within 24 calendar months. However, if an extension is needed, this will be properly negotiated.

The Committee will report to the Chief Medical Director, Dr. Crutcher, through the Assistant Chief Medical Director for Professional Services.

The Agency responsibility for providing the necessary support is the Veterans Administration, and the duties and functions will be quarterly sessions at the Veterans Administration Central Office in accordance with an appropriate schedule of dates set at the preceding meetings.

We will publish a structured agenda. This meeting will be entirely open today. It is likely that subsequent meetings will have both an open and a closed portion.

I would like to give you a few bits of information now about procedure. As published in "The Federal Register," we will adhere to our agenda. If revisions of that agenda are necessary, I will call those to the attention of the group.

We will go through presentations this morning, beginning with a presentation by Dr. Levinson on the Steering Committee, a statement of where we are on herbicide research in the Department of Medicine and Surgery, and we will then ask for individual reports beginning at eleven from the members of the Advisory Committee, brief statements of what your agency or office is doing with respect to herbicides, and the determination of their toxicity.

This will continue through the afternoon. We will have an hour and a half break for lunch, and then there will be the presentation and discussion of written questions from the VA Steering Committee to the Advisory Committee. Our Steering Committee has prepared some questions to which they want the Advisory Committee to relate,

and these will be announced so that everybody can hear.

Then we will get written questions from the floor. There will be time for a few statements from people from the floor, and we will begin that at three o'clock. It is expected that our Administrator, Mr. Cleland, will join us sometime later this afternoon, and he may wish to address those questions himself.

I would like to tell you that we encourage any questions of this group that you may wish to submit. We would like those questions written, and they should be submitted to Mrs. Grace Meyer in the back of the room, and we will then read these at three o'clock. I will read those, and there may be time, as I say, for a few statements.

All of these questions will be answered. All of those that require answers of a general nature will be answered, and they will be answered through a mechanism which I would like to outline, by the members of this Advisory Committee, and that will be done through small task forces. If there is a particular area of expertise in pathology or carcinogenesis we would ask the official member of the Committee to help us prepare a paper in answer to that, a position paper.

Obviously that can't be done today. It will take weeks and so on, and my office will endeavor to provide assistance in framing those answers, or we will prepare the paper itself, and then circulate it among the Advisory Committee for its answer.

The results of those papers will be available to

the public, and we will make it possible so that any question, any legitimate question which is posed to this group can receive a duly considered written answer which will represent the findings of this Advisory Committee.

Let me then briefly charge you. You are I hope impressed, as I am, with the fact that this does represent a multi-disciplinary group; many kinds of professional, scientific and technical expertise are represented in the group.

It is also a multi-disciplinary group from the standpoint of advocacy. There will be various shades of conviction about the possible connection between herbicides and long-term pathogenesis. Some of the Advisory Committee have already distinguished themselves for having contributed significant works to this body of literature, and I think that we will hope out of this enlightened discussion to arrive at the answer.

We in the Veterans Administration consider this a matter of extreme seriousness. The potential link between exposure to herbicides and long-term pathological effects is something that has seized the public interest, we think rightly, and has consumed a prodigious amount of our own time and expertise.

We are grateful to the agencies and organizations represented around this table for their willingness and commitment to help us find these very illusive answers, and the answers let me assure you are illusive.

We are well aware of the fact that a tremendous

amount of literature has been produced. We refer to the classic study of the National Academy of Sciences in 1974 accomplished with great input from a variety of disciplines and viewpoints which did not definitely come up with any evidence of long-term pathological effects in humans upon exposure to dioxin and the herbicides.

A subsequent study mounted by the United States Air Force, which was completed last October I believe and announced by General Dettinger at a hearing before the House Veterans Affairs Committee looking into this subject similarly failed to come up with hard evidence of the fact that there was a relationship between exposure to dioxin and long-term pathological effects in humans.

Nonetheless, the controversy continues in the minds of many. The definitive answers are not yet in, and I think that must, therefore, characterize my charge to the Advisory Committee. Many are not yet convinced that such a link between exposure and pathology does or does not exist, and we have, therefore, to address ourselves mindful of all the research that has been done heretofore, but perfectly willing to take a fresh, a new look at the evidence already in the files or that may yet be adduced by appropriate research or introspect.

The Veterans Administration has been concerned with this for the past 15 months, and we continue to be concerned. Our efforts in this regard can be summarized under four headings. One is to acquire and exchange information. This Advisory Committee is the keystone in

that process.

Secondly, to disseminate such information to all of our field installations, hospitals and regional offices alike.

Thirdly, to build and maintain a complete record and registry of all veterans about whom we know or who come to us for treatment, or for adjudication of claims for compensation.

Finally, to conduct and offer assistance into further research into this area. All of our efforts, and there have been many, come under one or another of those headings.

It has been said that the democratic principles in which one is presumed innocent until proven guilty should not apply to chemicals, that is to say, that dioxin should not be believed to be innocent of pathological effects until proven guilty, and that certainly is true, but I would urge all of us to remember that the Veterans Administratic cannot undo what history has done. Try as we will, we cannot reverse the fact that dioxin is a contaminant and was sprayed on the fields of Vietnam, and what we now have to do is not to lament that fact, but to consider whether or not that spraying did carry with it the possibility of long-term pathological effects.

We know, of course, that dioxin is extremely toxic in acute situations. There is no question about that, and we are well minded on that issue, but whether or not it does produce long-term effects is something that does

concern us, and we have to go on about it.

We have got to establish that there is a clear link between pathology and long-term pathologic effects. We must weigh the evidence. We must consider all the information. We must conduct a scientific inquiry, although this is a subject on which emotion swirls about us, and we are all concerned about the plight of Vietnam veterans, and if such a link is established, we want clearly to act on it quickly, prodigiously, and in the appropriate fashion.

We must not be projected into establishing such a link until it has been made clearly evident through scientific inquiry.

We want to excite new research if that is necessary for the Committee. We want to advise the Chief Medical Director and the Administrator, and indeed the whole country. I need scarcely tell you that this has seized the popular imagination, and the public press has paid a great deal of attention to this issue.

We want to provide answers to the questions. I would like to say that one thing which I find reassuring in all this is that at least in the Veterans Administration, the Department of Medicine and Surgery, we are not waiting for the answers in order to treat people. That is to say, if veterans come forward exhibiting pathology or having symptoms, we would treat them if they are otherwise eligible immediately. We do not wait for the deliberations of this Committee in order to diagnose and treat. An individual

complaining of carcinoma would be treated in the Veterans Administration whether that was due to prolonged use of tobacco or exposure to other agents, or exposure to Agent Orange, so that that decision we don't have to make.

Anybody who is now ill, whatever the cause, if eligible for treatment, would be treated. That does not minimize the importance of our finding the possibility of such links, and in a way, gives us only temporary respite from the tremendous responsibility thrust upon us.

That concludes my charge to the Committee. I would urge you all to read again the "Federal Register" to familiarize yourself with the particulars, and I think now we will move ahead with the summary of the VA Steering Committee's activity.

Tell us where we are in the Steering Committee's activities.

DR. LEVINSON: Thank you. I will stick to the time schedule, but during this period, I would like to introduce, or at least call for brief remarks from members of the Steering Committee who are most expert in the particular aspects that I mention

First of all, the Steering Committee was formed last June at the time when the VA became aware that there was a major problem concerning the possibility of herbicide toxicity among Vietnam veterans, and recognized the fact that our response to this particular situation would have to be broad based and utilize expertise from throughout the agency.

Accordingly, the Committee was constituted with members from the Department of Medicine and Surgery, which of course is the health care delivery arm of the Agency, but also included representatives from the General Counsel, which is the legal arm, the Department of Veterans Benefits, which handles the compensation claims, as well as other matters, from Management Services, which is our administrative liaison with other agencies, and from our Research and Development Branch, which is also part of DM&S.

The Committee was charged with the task of helping the Chief Medical Director and the Administrator develop appropriate policies regarding the diagnosis of herbicide-related illnesses, the appropriate therapy that is necessary for any of the illnesses that might be discovered, and other related matters which might flow from the demonstration of a distinct connection between herbicides and permanent human disease.

This very broad-based charge was then implemented through a series of separate steps which I will describe to you briefly. Before I do that, I would like to quickly list some of the specific charges that the Committee had and which we hope to be able to fulfill before our tenure is terminated.

I mentioned that we provide advice to the DM&S management, as well as the VA-wide management on policy and actions related to the herbicides.

Second of all, we are charged with stimulating

and coordinating development to new approaches to the evaluation and treatment of individuals who might suffer from illnesses arising from exposure to herbicides.

Related to that, we had a very specific charge and that was to develop a program for examination of veterans who were potentially exposed to herbicides while in Vietnam, and to evaluate any potential illnesses that they may demonstrate. I will describe that more later.

We attempted also to act as a liaison not only through our membership, but also through other actions with the rest of the Agency both in the Central Office and in the field, and we are available as a resource to conduct special studies, prepare position papers, and answer questions posed to the Administrator, the Chief Medical Director, and others about this general matter, so we are an interagency clearing, steering and coordinating committee.

Just a word about our program for examining veterans. As has been said, the VA has not dealt significantly in the past with environmental exposure, and we have to feel our way slowly, using the best advice that we could obtain. We will, of course, be asking this Advisory Committee to give us additional specific directions in this program, but what we did as a first effort was to set up an official program for the detection and the examination of veterans currently in our patient population who, A, were in Vietnam during the period when the herbicides were used, and B, claim exposure to them.

The program consisted of following the

identification of these veterans, taking a detailed medical history which also emphasized the matter of exposure to the herbicides, and then a physical examination supported by appropriate special tests which were geared to detect diseases in the organs that various people had suggested might be affected on a long-term basis by herbicides.

The number of veterans, as you can imagine, in this category was large. It soon became apparent that we would have to accumulate this data in some central source and continue following these people for a number of years to reach any kind of conclusion about their disease and its connection to herbicides, and so we proceeded to set up a registry which we are now in the process of automating to provide this long-term followup, and to provide a data base for any long-term studies hopefully of a proper epidemiological and scientific nature that might arise from it.

We also are attempting with some difficulty to quantitate the exposure of these individuals to herbicides. We are doing this by utilizing the spraying tapes which are available from the Department of Defense that were used by the NAS in their earlier studies, and information about the unit histories of the ground troops who saw action in Vietnam during the period when the herbicides were used.

Our hope is to be able to match these various sources of data through the computer and to come to some kind of reasonable conclusion about the presence of a

person in Vietnam, and their exposure to herbicides.

This has proven to be an incredibly difficult matter, and we will need your help in attempting to interpret the sort of data we have. We have many, many questions about it.

We have also been involved in a coordination or stimulation sense with a series of research projects, and Dr. Hobson, a member of our Committee and the Depty ACMD for Research and Development, will address future research in this area separately.

I might just mention that Dr. Lyndon Lee, who was introduced as a member of the Committee, has been coordinating, directing actually, our study on determining dioxin levels in fat. This, of course, was suggested as a potential diagnostic test of great significance.

We have done a pilot study. Dr. Lee has been involved in its direction, and I hope we will have a chance to hear from him briefly about this matter.

Dr. Lee, would you stand and perhaps just say a few words?

DR. LEE: My background is in general surgery and pharmacology.

In October, Dr. Haber spoke to the Committee, and Congress, and promised that there would be several and various studies, one of which was the biopsy of fat for the assay of dioxin in both exposed people and in controls.

In November, he asked me if I could coordinate this, and I agreed. We developed a protocol which went

through the usual human experimentation approvals, as well as the research committee approvals in the hospitals, four of which were in the Chicago area because of several points.

First, we had a good many applications from veterans in the Chicago area who felt they had been injured by exposure.

Second, it was felt that perhaps these people who came from the more or less urban rather than suburban or rural area might at least have had less exposure as civilians than others from the farm areas.

And lastly the men were interested and could be persuaded to follow the program.

We also added one further hospital in Lincoln, Nebraska, because that was where the chemist who was to do our assays was centered, at the university, and we needed liaison, so we added one man there.

We have approached the National Academy of Sciences National Research Council through their followup agency for statistical participation, and that is being carried out. The protocol has been approved. We now have taken biopsies from 16 individuals; 14 of these have been exposed anywhere from 13 days to 6,600 hours of documented exposure, and these biopsy reports are not yet available.

There have been two controls which have had biopsies, and there are four more individuals to be biopsied this week, two additional who have not been scheduled, and that is the report at the present time.

Obviously we have not broken the code. These various materials have been sent to the biochemist coded so that he does not know what types of exposure, if any, the individuals have had, and will be prepared I think to give a more full report on this within probably another month.

DR. LEVINSON: Thank you. May I ask Dr. LeGolvan to just say a word to you? He is the Deputy Director of our Pathology Services--to say a word or two about the program with the Armed Forces Institute of Pathology with regard to the storage of biopsy and autopsy tissues from veterans exposed to herbicides who come through our hospital.

DR. LeGOLVAN: I am a pathologist in the Pathology Service with Dr. Williams. Our negotiations with the AFIP resulted in the establishment of a registry of tissue pathology for the cases that might appear at the AFIP, and listing possible exposure to herbicides.

In this registry, any tissues that are sent to the AFIP will be so coded for future study. These cases all are such that all hospitals have been notified that any cases that appear for routine surgery of any type or for any other studies in which tissues are obtained will be sent to the AFIP for this registry.

Thank you.

DR. LEVINSON: Thank you. Another function of our Committee is to attempt to increase the understanding of particularly our professional staffs in our hospitals and clinics about the matter of herbicides and other environmental toxins, and to make them more aware of the best

ways in which to examine veterans who claim or who should perhaps be claiming possible illnesses related to these agents.

We have done this in a fairly formal way through hot lines and circulars and other publications. We are planning some major educational activities in the near future, again hopefully with the help of this Committee, the Committee's expertise to offer more detailed educational information about the appropriate matters.

We have also attempted to answer appropriately the many requests for information from the press and radio and television. In that, we have the great help of Mr. Stratton Appleman, the man sitting in the back, who is a member of our Steering Committee, and hopefully, we are increasing the amount of specific and appropriate information of the public at large through most of these news releases.

Another matter that we are concerned with is compensation. Compensation for Agent Orange related matters is the province of the Department of Veterans Benefits. One of our members, Mr. Peckarsky, is from the Department of Veterans Benefits, and I will ask him to just say a few words to you about our present status in that matter.

MR. PECKARSKY: For me, this type of session is an extreme learning process. We are fortunate in that the law with regard to veterans benefits does not require the establishment of a causal relationship between subsequently experienced disability and any incidence of service.

In that regard, any disability that is incurred or aggravated at a coincident point of time with military service receives the status of service connection.

Nonetheless, it is important in the lapse of time that has taken place since the exposures in service that we learn as much as we can concerning the effects in the out years of exposures to dioxin. This we expect to get from our participation in this Committee's work.

DR. LEVINSON: Thank you. Just in conclusion, I would like to point out that the Steering Committee will continue to carry out its various missions and perhaps add additional ones as they appear appropriate.

In doing so, of course, we need all of the expert scientific and medical information that we can obtain on this matter towards that end. Our group compiled a series of questions which you will hear about this afternoon, in areas that we feel answers are very important, and we stand ready to assist you in any way in better carrying out your advisory function.

Thank you very much for your time.

DR. HABER: Thank you, Dr. Levinson. We really would be quite powerless to implement the advice of the Advisory Committee were it not for the existence of the Steering Committee.

We look forward to their continued input and the ability to translate some of this advice into specific rules and regulations so we in the Veterans Administration can implement the advice of this Advisory Committee.

On our agenda next is a discussion of herbicide research. I would like to introduce Dr. Lawrence Hobson. Dr. Lyndon Lee described the fat biopsy study, I would indicate to you that the basic idea for the protocol emanated from Dr. Hobson, and he might wish to tell you a little bit about what he had in mind on that, as well as what the Office of the Assistant Chief Medical Director for Research and Development will be doing to help us in the VA to research into this area.

DR. HOBSON: In a sense, I am bringing the coals to Newcastle by talking to this group since many of you are much more expert in this particular area than I am. I will just very briefly sketch why the fat biopsy program is undertaken.

The claim was made in a television interview that fat would retain dioxin for decades in an inactive form, and that anything that mobilized the fat, for example, a reduction program, during or at the end of those years, would release dioxin in the circulation and produce a problem of dioxin intoxication.

This, of course, requires that dioxin be stored in fat, and the most direct way to determine that is by a sensitive assay method to detect the dioxin.

We sought the advice of EPA as to what assay technique was best and who was the best one to apply it and were given the name of a man who had shown the best results in the sense of consistency, sensitivity, in this assay, and we, therefore, contracted with him to carry out

the determinations in part because he had the best test and because he is not in the VA or in the federal government and therefore would not be biased in his result and we further stipulated that the samples be submitted to him blind so he has no knowledge of what exposure the individual may have.

As Dr. Lee has said, there is a variety of exposures here so that when the assays are completed, we will be able to say whether in fact it is possible to detect this material in fat, and if so, to what level, and if it is detectable, whether there is any difference in the amount of dioxin determined in the fat of individuals who had military exposure, and the balance of us who have simply been in the civilian population or were in the military but not in the areas in which it was being used.

This is not an attempt to arrive at a definitive epidemiological study at this stage of the game: until we find that this most sensitive method can detect dioxin it would be rather foolish and fruitless to have a large number of people examined.

These are biopsy specimens and they require an operation so that we are not anxious to subject individuals to that to no end at all.

The other research that has been proposed to us in large part has been accomplished already. Dioxin itself and the herbicides have been the subject of extensive research, as all of you know I'm sure. The one area that has been suggested might be unique for the VA is

epidemiological studies of individuals who have been exposed.

The difficulties here, as I am sure all of you appreciate, are in the documentation of the precise level of exposure because the mere presence in Vietnam of an individual does not mean he was anywhere near the sprayed area, and presence in a sprayed area does not necessarily mean that he was there at the time when dioxin was present, so that we are really in a very difficult position in attempting to do definitive epidemiological studies of this material under those circumstances.

We feel that much better studies can be conducted in the sense of knowing at least the time, approximately the amount of exposure in industrial accidents or industrial exposures such as those that have occurred in the past, but not within the veteran group.

The one symptom or sign that seems to be generally accepted as evidence of exposure to dioxin is the appearance of chloracne, which is a skin condition.

As you know, the difficulty with using this as a criterion is that the military in most instances under field conditions did not record chloracne as a significant finding. It didn't endanger the individual's health. It was often confused with other skin conditions which were equally benign if treated, and there was not much made of it so that the record of individuals who may have had chloracne in Vietnam is really very scanty and probably non-existent. At least we have been unable to recover them.

Lacking that, the level of exposure, the amount of material to which the individual was exposed, let alone absorbed, is a matter of conjecture and we are not going around and exposing people to highly toxic material in an attempt to find out what is going to happen to them, so that we are quite handicapped.

I would raise one other point here which I am afraid is a very negative one and rather unpopular with known scientists, and that is that scientists are not all-powerful. We can't do everything. One of the things we can't do is to prove a negative. We can't say that something did not or cannot occur, and yet we are constantly being asked a question which is a very reasonable one in lay terms, namely, prove that nothing did happen or that nothing can happen, that you can't get cancer from this or you won't get sick from that.

This is, as I said, scientifically impossible to do. Let me demonstrate that very, very briefly. If you examine 100 people, and none of them had an effect, for whatever reason, you can say well, there was no effect, but somebody can say, but the 101st man may have got it, so you do 1,000, and you still don't find any effect, and they say well, but the 1001 may have got it, and you can continue this kind of endless chain in perpetuity and never be able to say that it cannot happen.

The best you can hope to do is to say that there is less than a certain chance that it would happen, not that it cannot.

The result of whatever kind of scientific studies that are carried out are going to be couched in terms that are going to disappoint some people because it will not say flatly that a certain thing did not or could not appear.

I think you have to keep this in mind when you look at research plans and research that has been conducted and not expect that you are going to get a flat answer that it cannot or won't happen.

We are at the present time dependent on an epidemiological study on the identification of individuals who were presumably, and with a strong level of presumption, exposed to dioxin, where there are certain groups where we know that was true; people who handled the defoliants and who were not particularly careful about it undoubtedly got exposed to the defoliant, and presumably to dioxin.

People who went into areas where the spraying had been done were only presumptively exposed, and it will probably wind up that that is the best epidemiological group we can find, but it is rather unsatisfactory from the scientific point of view, and it certainly will not, as no other study would do, establish the negative if we find that there is no ill effect in whatever group it is that we examine.

DR. HABER: Thank you very much. Dr. Hobson has been the recipient of a memorandum from me asking that our Research and Development Service consider the likelihood of other kinds of research, and we will be getting an answer

from him and their own advisory committee as to the feasibility, likelihood, and necessity of the Veterans Administration initiating additional studies in certain specific areas that were suggested to him.

We look forward to his continued operation and cooperation in this activity.

I would like to call attention to the presence of Dr. Stephenson representing Dr. Griffith from the EPA, and we welcome you, Dr. Stephenson.

DR. STEPHENSON: Thank you.

DR. MOORE: Dr. Haber, may we interrupt for questions?

DR. HABER: I think that what I would like to suggest is that if you have procedural questions, any time is appropriate. If they are substantive questions, I would like to delay that until either your presentation, which we are about to ask for now, or until the time for the questions.

DR. MOORE: It is a question that is prompted by the presentation. I will pose the question and if you want to hold it, fine.

DR. HABER: Yes.

DR. MOORE: With regard to the biopsy specimens that have been taken and that have been coded to be analyzed, is it possible to find out what levels of detection they are going to attempt to look for, PCD or put in positive controls of that type? Is that type of information available, or can it be made available?

DR. HABER: I would defer that to Dr. Lee.

DR. LEE: The level at which they can determine the presence of dioxin is one part in a trillion. They will report in units, giving us an idea, if there are any dioxin units present, how many these may be against controls which obviously may themselves show dioxin levels, but we are not certain about that.

DR. HABER: Okay. I think this question needs to be dealt with more fully, and we will this afternoon. I quite agree. I think at this juncture now we would like to go around the table and begin the process of reporting.

We will not be able to observe the alphabetical regularity with which we asked you to be seated because some of you have to leave earlier.

I would like to ask you to take 10 minutes or 15 minutes if that is required for the purpose of giving us a brief on where your particular agency or office is at this point, and I think also what questions you would like to see this group address as well, and in brief to let us know where you come from and to share with us a summary of your experience.

As I indicated, since some of you will have to leave earlier, I would ask your forebearance in departing from the otherwise assigned alphabetical listing, and with that, I would like to ask Dr. Brick representing the American Legion, and himself, to begin.

Dr. Brick, would you tell us what you are doing and what you would like to see solved in this area?

DR. BRICK: I am interested in the general problem of the long-term effects of dioxin as outlined in the charge to the Committee.

Representing the American Legion, we are interested in that particularly from the point of view of the compensation angle which is represented here by Mr. Peckarsky, and as he pointed out, he is interested, too, to know whether these problems are real, imagined, what the extent of the problems is, and that type of thing.

From a professional point of view, I am particularly interested in the effect of dioxin and its effects on the liver and whether or not any of the liver diseases that we commonly encounter have anything to do with the exposure that may have been obtained in Vietnam.

I am not as familiar with the literature as some of the experts here. I don't pretend to be, and have a question about whether or not the National Academy of Science's report, and the Air Force report might be made available to some of us in the Committee who have not seen these reports. I think that might be helpful.

Also a question, Dr. Haber--minutes are being taken of this meeting, and will they be available to the members of this Committee?

DR. HABER: Absolutely.

DR. BRICK: Not all of us are going to be present at all of the meetings, and/or all of the meetings in toto, and if such materials are made timely available to us, I am sure that many of us will, in our own leisure, study these

and have questions and possibly some suggestions.

That is the end of my presentation.

DR. HABER: Okay. Dr. Moore, I understand you may have to leave. Would you, therefore, please address us and tell us what you have been doing and what questions you would like to see answered and so on?

DR. MOORE: As I mentioned in introducing myself, we have done work with tetrachlorodibenzodioxin, TCDD, and other dioxins for nine or ten years.

Our original work was trying to establish whether or not the benzodioxins can produce teratogenesis or other effects, or birth defects.

Since that time, we have tried to look into the types of effects that the benzodioxins may cause. We have not restricted ourselves to TCDD. Indeed, TCDD is but one member of a family of dioxins, others of which can cause toxicity.

I would like to point out to the Committee's attention if they are not aware of it, the evidence that is accruing over the last few years is clearly showing that a variety of chemicals that are called halogenated hydrocarbons may have the same target site for whatever effect they do produce, and so therefore, if one is looking for illness as a consequence of dioxin exposure, the expression of that illness may be a total insult, if you will, from TCDD, other dioxins, chlorinated dibenzofurans, possibly azoxybenzines, hydrochlorinated biphenyls. In other words, you can't consider TCDD exposure in a vacuum

is basically what I am saying.

I would like to point out two publications that have not been mentioned heretofore, and I think the Committee should be aware of their existence and may want to look at them.

One is a publication that came out of Sweden which is a culmination of a conference which was hosted by the Royal Swedish Academy of Sciences two years ago on chlorinated acids and their dioxins.

Aside from wanting to look at the recommendations that the various groups may have had in there, it is a fairly up-to-date background reference to what is in the literature and what may or may not be of interest.

DR. HABER: We are in debt to you for bringing that to our attention. I would hope that others of you if you know of significant publications would bring them to our attention. We will try to make them available if we can.

DR. MOORE: The second one is much briefer in size, and it is a technical report of a meeting that was held in January of 1978 in Lyon, France under the sponsorship of the National Institute of Enviromental Health Sciences and the International Agency on Research in Cancer, which is part of the WHO.

The one-week meeting was to in essence see if one could come to grips with the long-term hazards of polychlorinated dibenzodioxins and polychlorinated dibenzofurans. There are some recommendations in this, but aside from

the recommendations, I would again urge the Committee members to look at this as well because it does give a fairly good summary of the previous occupational exposures, the date they occurred, the numbers of populations that were involved in the exposures, and what is the current monitoring aspects of them, and I also tend to feel that if one is going to get insight fairly soon as to the chronic effects of exposure to dioxins or herbicides, it is going to be from some of these worker populations where their exposures are now approaching 20 to 30 years.

Unfortunately, the numbers are very small.

DR. HABER: Dr. Moore, is it fair to ask is your office engaged in any of those long-term follow-up studies now underway, the group at Nitro, or have you any input into that?

DR. MOORE: Indirectly. The Nitro, West Virginia group that was followed up, the clinical examination I believe, at least in part was done by the Mount Sinai School of Medicine, which is funded through our grant program.

DR. HABER: You will be getting those answers, will you not?

DR. MOORE: Yes. I believe NIEHS has a formal affiliation.

DR. HABER: That is one of the things I would like to do, to try to pinpoint who would be likely to find out.

Thank you very much, and we are indebted to you for calling those publications to our attention.

I think next, Dr. Thiessen, if you would be good enough to address us and we would like particularly if you can help us with that information, I understand your earlier statement about the complexity of the Department of Defense's research assistance on this, but if you can give us any information about the Air Force projected study, that would be most helpful.

COL. THIESSEN: Let me again reiterate that I am not familiar with the details of the Air Force study. The Air Force has been so kind as to give me a general statement that I would like to read into the record.

Let me make it clear that the Department of Defense intends to and has in some cases involved institutes such as the Armed Forces Institute of Pathology that has been mentioned before. The Armed Forces Epidemiology Board will discuss the study protocol that is being developed by the Air Force.

The study protocol will be brought before this Committee for at least advice, if not approval, and all these actions should take place pretty shortly, if they haven't taken place already.

Now the Air Force will conduct a study of the health of Ranch Hand personnel involved in the aerial spraying of Herbicide Orange in Vietnam. Operation Ranch Hand was a code name attached to the Air Force air crews between 1962 and 1971, when the operation ceased.

These personnel would have been the most likely

to have had significant exposure.

The purpose of the study is to determine if any causal relationship can be established between exposure to these herbicides, and changes in the long-term health status of the individuals involved.

The study will involve both veterans and active duty personnel; former Ranch Hand personnel exposed to Herbicide Orange, approximately 1200, will be carefully matched to a control group not exposed. Detailed telephone health surveys will be given all members of the study beginning in early October 1979. Comprehensive physical examinations will be given to a selected number of both exposed and non-exposed individuals. Health surveys and scheduled physical examinations of selected individuals will be conducted for a minimum of six years to see if any long-term health problems emerge.

The entire study will be completely reviewed by both government and civilian scientific personnel. This is to preclude any bias, and to ensure the scientific validity of this complex project.

The study details, as I said, will be presented to this Committee during this review cycle.

That concludes my statement.

DR. HABER: I would like to suggest to the Committee that in a prior meeting that I had with General Dettinger on the study, I asked of him permission for this Committee, this Advisory Committee, to get the protocol, which was granted, so when that protocol is delivered to us

we will circulate it among the Committee. I think this is really only in the interest of scientific exchange, though some of you may have some suggestions about this and possible suggestions of revision of the protocol which I think would have to be done fairly soon if we were going to do anything about it, but I must tell you the Department of Defense and the Air Force have their own scientific review process, and it strikes me that they are well along in this process.

Isn't that right?

COL. THIESSEN: Yes.

DR. HABER: What are the bodies that would review this?

COL. THIESSEN: The Armed Forces Epidemiology Board for the Armed Forces in general, and the Scientific Advisory Board of the United States Air Force for the Air Force.

DR. HABER: Then it will have been subjected to at least two prior in-depth reviews, but I asked for the opportunity for our group to see it and review it, and I think we should avail ourselves of that. In some subsequent meeting, you may wish to go on record individually or collectively as, hopefully, approving the study.

COL. THIESSEN: Let me also state for the record, sir, that the Armed Forces Epidemiology Board does not consist of Army representatives, but of national experts.

DR. HABER: I am well aware of that, and

General Dettinger was quite informative on that subject.

Okay. I think with those presentations, we ought to now proceed to ask the other members of the group in alphabetical order. Dr. Allen, I guess that puts you up first. Will you please tell us where you are in your research and what your plans are and what you would like for us to help you with if we can?

DR. ALLEN: I would like to say that I am an experimentalist. I have done no research at all on human populations that have been exposed to dioxins.

I have done no research on Agent Orange per se. My research has been limited primarily to the tetrachlorinated dibenzodioxins and their effects on non-human primates, the Rhesus monkey and on rodent populations, primarily the laboratory rat.

We have found that a relatively low level of exposure to the dioxins, namely, TCDD, is extremely toxic. In some of our initial studies, we found that levels, when consumed at 500 parts per trillion in the diet for a period of nine months, produced mortality in over 50 percent of the experimental animals.

Within a period of three months, the animals began to lose their hair, had swollen eyelids, dry, scaly skin, and indications of hematological abnormalities.

At these levels of exposure they had consumed in the neighborhood of 1 microgram per kilogram of body weight.

By the sixth month of exposure, and after having

consumed in the neighborhood of 2 micrograms per kilogram of body weight, the animals developed what we would consider a severe pancytopenia, decrease in circulating white cells and red blood cells, and a marked decrease in blood platelets.

At this time, we attempted to breed the eight experimental animals; three of the eight became pregnant. Two aborted early in gestation, which is an indication or suggestion of difficulties that we have observed in other studies, in the halogenated hydrocarbons and its effect upon the reproductive capability.

At seven months of exposure, we lost our first experimental animal primarily due to excessive bleeding all over the body. By the ninth month, we had lost our second animal due to widespread hemorrhage, and by the 12th month, we took the animals off the experimental diet.

At nine months, they had consumed in the neighborhood of between 2 and a half to 3 micrograms per kilogram of body weight.

During the succeeding three months up to the 12th month, we had lost three additional animals, making a total of five of the eight experimental animals that died from dioxin intoxication.

Some of the more pertinent lesions that we found in these experimental animals, in addition to the loss of hair, loss of eyelashes, swollen eyelids, dry, scaly skin, keratinized hair follicles, there was a marked thickening of the gastric mucosa, ulceration. There was marked dilatation of the gall bladder, and hypertrophy

and dysplasia of the epithelium of the gall bladder, as well as the common, cystic and hepatic ducts and the bile ducts within the hepatic tissue.

There were hypoplasia and metaplasia and dysplasia in the sebaceous glands, the salivary glands, metaplasia and hyperplasia of the transitional epithelium of the urinary bladder, and also metaplasia and hyperplasia of the lining of the mucosa of the stomach.

In subsequent studies, we have reduced the level of dioxin in our experimental diets to 50 parts per trillion. These animals now have been on this diet for over two years. After six months of exposure and after having consumed in the neighborhood of about 3 tenths of a microgram per kilogram of body weight, we attempted to breed the experimental animals.

Of the eight experimental animals, six became pregnant. Four aborted early in gestation, and two were able to carry their infants to term, thus further clarifying or substantiating the observation of the effect of dioxin upon the reproductive capability of non-human primates.

The animals have been on the diet for approximately two years. They have consumed in the neighborhood of one microgram per kilogram of body weight, and are beginning to show the same signs and lesions that developed in the 500 parts per trillion animal of three months, both groups having consumed in the neighborhood of one microgram per kilogram of body weight.

Thus in these studies it would appear that there

are very distinct changes that occur. When the levels of exposure to the dioxins are higher some changes occur much more rapidly than when the level of exposure is quite low.

It would appear that the same effects develop in the experimental animals, regardless of the time that is required, whether it be three months at 500 parts per trillion, or at 50 parts per trillion over a two year period.

This pretty well brings you up to date as to what are the effects that we have observed in our non-human primates. We now have studies that are on going where we are feeding animals 25 parts per trillion of tetrachlorodibenzodioxins. They are being bred at the present time to determine if these levels will have effects upon the reproductive capability, and the general body health of these experimental animals.

I would like to mention just briefly our preliminary work with the possible carcinogenic effects of the tetrachlorodibenzodioxin. We did a pilot study approximately three years ago where we had fed rats levels of dioxin ranging between 5 parts per billion and 5 parts per trillion.

Those animals that died during the course of the experiment had approximately a 37 percent overall incidence of tumors. Those that were sacrificed after two years on the diet had approximately a 36 percent incidence, overall incidence of tumors.

The tumors that were observed were quite variable,

involving the liver and the lung. Those two organs were the more severely affected.

These observations have been substantiated at a somewhat higher level by the Dow Chemical Company scientists and certainly there are indications from the Illinois Institute of Technology that there are carcinogenic effects of tetrachlorodibenzodioxin.

Recent reports at the American Association for Cancer Research meetings in New Orleans strongly indicated the promotional activities of the tetrachlorodibenzodioxins on cancer. Thus it would appear that we are working with an extremely toxic compound that has widespread effect on experimental animals.

DR. HABER: Thank you. I am sure there will be questions about it this afternoon. We would like to ask you to elaborate.

DR. ALLEN: In our evaluations of populations that have been exposed to dioxin I do not think that we can eliminate those that have been chronically exposed or have low-level exposure.

In work done at the National Institute of Environmental Health Sciences, they were able to show that some of the same signs and lesions were produced at levels of 70 micrograms per kilogram of body weight that we observed in the neighborhood at levels of 2 to 3 micrograms per kilogram of body weight over an extended period of time.

There may be heavy exposure which produces the effect, but this does not eliminate the possibility of low-

level exposure that may occur over an extended period of time that may produce this same effect, and these are what I consider extremely pertinent points, and I have received unofficial reports since, that in some of the peripheral areas that are involved, some of the people are beginning to show ill effects that were not observed in the more acutely exposed areas.

DR. HABER: Thank you, Dr. Allen. We certainly appreciate your statement.

I would like to move on. Dr. Erickson, can you please tell us what your laboratory has been doing and can you shed any light on this problem for us?

DR. ERICKSON: As I said when we introduced ourselves, I come from a group that is interested in the occurrence of birth defects in humans.

We have no experience whatsoever in dealing with this problem from the angle of herbicides. We got into the business that we are in, I think, because of another environmental exposure---that was thalidomide. There was a good deal of interest generated in the early '60's by the disaster which happened in Europe and in the other parts of the world, the epidemic of limb reduction deformities that were a result of maternal ingestion of thalidomide.

This epidemic wasn't discovered until a few years after it began, and the people got the idea if there were monitoring programs in place that the epidemic of this thalidomide syndrome babies would have been discovered earlier, and so at the Center for Disease Control, we

monitor the incidence of birth defects in human populations.

This monitoring of the trends is useful for two purposes I would think. One is to detect an epidemic of birth defects which might be due to the introduction into the environment of a new teratogen or due to the change in the prevalence of an old teratogen.

The monitoring programs also provide a somewhat unique data source for the mounting of special studies into the etiology of human birth defects.

We have two main programs in our branch. One is called the Birth Defects Monitoring Program, and it is a quasi-national program covering about a third of the births in the United States each year.

The other program is in metropolitan Atlanta and is a higher quality system, a more intensive type of ascertainment, but monitors only about 25,000 births per year.

I would just like to make a couple of comments about the epidemiology of birth defects in humans. People talk about birth defects, but there are really probably several hundred different kinds of birth defects, and each of these is probably a unique disease or a somewhat unique disease; at least from what we know about animals, and their reaction to teratogens, and the few known human teratogens, we have the idea that each teratogen or defect-causing substance produces a fairly unique type of malformation or syndrome of malformations.

Also each different type of defect is individually

rare. The most common ones occur at a rate of about one per thousand births, and so studies to discover causes of these things are very difficult and very time consuming and very expensive.

The last point I would like to make is that so far as we know, birth defects have been around for a long time, and with a few notable exceptions, the rates have remained fairly stable, and they are relatively stable around different areas of the world as well.

The notable exceptions I would like to point out here in the United States are three. First, we think there is pretty good evidence that the defects of the central nervous system are decreasing.

Over the past decade, we believe they have decreased at an annual rate of about 5 percent per year, and we believe that this decrease is real. We have no explanation for it, however.

Two, heart defects, ventricular septal defect and patent ductus arteriosis, have been on the increase during the last decade. They have been increasing at the rate of about 10 percent per year.

We again have no explanation for this increase. We are unsure whether it is real or not, or whether it is simply a matter of increased awareness on the part of pediatricians who are caring for sick newborn babies who are surviving longer now, and they have immature hearts when they are born.

The last defect which seems to be on the rise is

renal agenesis, and this may be a real increase, or it may be due to increased use of diagnostic technologies which weren't used in previous decades.

I think that's all I have to say, Dr. Haber.

DR. HABER: We welcome your interest in this field. You have much to contribute.

May we go on? Dr. Stephenson, do you want to briefly tell us what it is you do for a living because we went around the table and introduced the group so we get some idea of what special interest you have.

DR. STEPHENSON: Thank you, Dr. Haber. My background is industrial hygiene in particular. I am standing in this morning for Dr. Griffith, who is an epidemiologist, and I didn't know that we were going to be asked to give a review, but I will tell you rather briefly what EPA has done and somewhat what they are planning to do.

The EPA has done a descriptive epidemiologic study in Oregon where they were looking at spontaneous abortions, and this was not a cause and effect type study, but merely descriptive, and I would like to emphasize that.

Through this study, the Agency saw its way clear to issue an emergency suspension of 2, 4, 5-T, which in essence gives the Agency an additional year to weigh scientific evidence to the effects of 2, 4, 5-T, and this fall, hearings for the cancellation of 2, 4, 5-T registration will begin, and at that time, more scientific evidence will be submitted for cause and effect type look by scientists

as to the results of 2, 4, 5-T exposure to the general population.

I believe, Dr. Haber, since we will be in litigation, that is about all that I have to say now. So far as the design and particulars of the study done in Alsea, Oregon, Dr. Griffith is certainly familiar with those, being the primary epidemiologist in that study, and certainly will be available to this most distinguished group to lend his support in additional meetings, so with that, I would like to close.

DR. BRICK: I would just like to ask a question. You said new studies were being done. Are they of the same sort as were done in Alsea.

DR. STEPHENSON: Well, what we would like to do are some follow-on studies of those, or I guess the things that were opened up in Alsea, Oregon.

Now I don't know exactly what the designs are that Dr. Griffith has in mind right at this time, but he is working also with Dr. Robert C. Duncan at the University of Miami School of Medicine, who is the primary biostatistician, and working together I think they are interested in looking at additional follow-on studies.

DR. HABER: Very good. Thank you, Dr. Stephenson. Dr. Kearney, would you care to tell us briefly where you are at in this problem and what you would like to be doing?

DR. KEARNEY: Yes. What might be of interest to the group is a meeting I attended earlier this month, June 3rd to the 7th, in Arlington, and it was a dispute

resolution conference that looked at the ability of science to interact in the decision-making process.

The model selected for that dispute resolution conference was 2, 4, 5-T and TCDD. I will not go into the philosophical aspects of the dispute resolution. Sixty-five scientists attended the meeting, with about 63 observers. There were several Italian scientists there who could comment on the Seveso situation. There were six workshops in the conference.

There was a workshop on carcinogenesis and mutagenicity headed by Dr. Jessie Steinfeld, former Surgeon General of the United States, now Dean of Medicine at the University of Virginia.

I have the conclusions of that workshop. There was a workshop on teratogenecity headed by Dr. Marshall Johnson at the Philadelphia School of Medicine and I have the conclusions of that workshop.

There was a workshop on human exposure headed by Dr. Austin of California. I have no affiliation.

There was a workshop on ecological effects. This was headed up by Dr. Ken Kamlett of the National Wildlife Federation, and I have the results of that workshop.

I have a report of the chemistry workshop which I was chairman of, and I do not have the results of the benefit workshop headed by Dr. John Staub.

I would feel most comfortable commenting on the conclusions of the chemistry workshop since they are pertinent to some of the discussions and some of the trials

discussed this morning.

We had eleven chemists in the workshop who are actively engaged in TCDD analysis in various forms. The first five questions of the workshop were philosophical and dealt with the role of the chemist and his participation with the decision maker.

The second five questions dealt with matters of chemistry and substance, and I think some of these might be of interest to you.

First of all, we dealt with what is known about the levels of detection of TCDD in the environment. It was generally agreed there is no level of TCDD in the parts per million or parts per billion range in any sample we have examined thus far, except as it relates to chemical disposal or spills.

It was further agreed that levels at 100 parts per trillion or above have not been detected in any environmental sample associated with 2, 4, 5-T. Here we are talking about fish, beef and mother's milk. Below these levels, that is, below 100 parts per trillion, you have to consider each of the studies individually.

First of all, dealing with mother's milk; based on three separate studies conducted up to January, 1979, no validated TCDD residues above 1 part per trillion had been detected based on the analysis of 44 mother's milk samples.

They concluded that there are no confirmed detected levels of TCDD in mother's milk.

In beef fat, out of 85 samples that have been surveyed thus far, one sample of beef fat confirmed at 60 parts per trillion of TCDD, and two apparent, but unconfirmed samples at 20 parts per trillion. The remainder of the samples were below the level of detection, which is 10 parts per trillion.

We also looked at beef liver, bovine milk, fish and wildlife. These were available for your perusal and I will make copies of these conclusions available to the Veterans Administration if you would like those.

DR. HABER: Yes, we would indeed.

DR. KEARNEY: There are several other things which I think impinge on what is said here, and I will share those with you.

Concerning the manufacture of 2, 4, 5-T, the question was, is it not of interest to this group whether you can measure dioxin contents in commercially available samples of TCDD and make it commercially feasible, and the answer to the question is that yes, we can.

Are there problems in the disposal of the waste of this material? There would be problems, but we feel that we can overcome these, but I think germane to this discussion is, can TCDD be produced from 2, 4, 5-T? We concluded that a yield of 1 part per million of TCDD can be the result of combustion of 2, 4, 5-T, particularly when it is mixed with organic matter.

Another question which I think is very pertinent to the biopsy study is, is 2, 4, 5-T the sole source of

the 2, 3, 7, 8 tetrachlorodibenzodioxin in the environment? This is important, and the answer is that it is not, that there are other sources such as combustion of certain chlorinated organic compounds, whether in commercial or industrial wastes.

That brings up another question which I think complicates the situation, but you must be aware of the fact that the chlorodioxins are a family of compounds of which there are 75 members. Tetrachlorodioxin, for example, is represented by 22 positional isomers. The 2, 3, 7, 8 tetrachlorodioxin is believed to be the most toxic of that family.

It was assumed that the 2, 3, 7, 8 was the product of trichlorophenol. It appears there are other sources of the 2, 3, 7, 8 in the environment.

The question which the group also must consider is, can you detect the 2, 3, 7, 8 in the environment as opposed to the other positional isomers? The answer to that question is, yes, we can. It is very new technology. It requires very elaborate facilities, and it is a very highly sophisticated technology, and the cost of analysis is going to be about $1,000 or more per sample.

The question is do we need more sensitive methods? What are the methods of measuring it in commercial samples and environmental samples?

The methodology which is available to us depends on the substrata at which we are looking. Now the current

levels of sensitivity having the appropriate specificity range from as low as .3 parts per trillion easily analyzable samples such as some of the fruits, to as high as 20 parts per trillion in certain animal and fat samples, and this is based upon certain appropriate chemical technology, what we call a signal to noise ratio of 2.5 to one.

The group also dealt with the environmental fate of TCDD, and I don't think that is of interest to this group. However, that information is available, so Mr. Chairman, these reports and these conclusions are available. They are unpublished at this time. There will be great speed to publish those, but the chairman of the conference has agreed to make these conclusions available to you.

Some of them are rather detailed in the field of medicine for which I have no expertise, but I think the group might benefit by having these.

DR. HABER: Dr. Kearney, thank you for a very illuminating presentation. First of all, let me express my gratitude for your making those available to us. The dispute resolution conference is precisely what we are all about, and I would like to have that made available to all of us, but I would also point out that I think that your dismissal of the fate of TCDD in the environment is something that does concern us, and I think we would want to look with great interest upon the finding in that regard because that is really one of the questions of people who went into Vietnam, where they came in contact

with the herbicides, and the fate of the TCDD contaminants would be of extreme importance to us, so we would be most grateful for any information about that.

Thank you again. We will appreciate getting those from you. We will make them available to the group.

Mr. Lemen, if you would be able to give us the same kind of summary, we would find it most helpful.

MR. LEMEN: NIOSH has had an active interest in dioxin since early this year when Secretary Califano received a letter from Mr. Cleland of the Veterans Administration requesting assistance in looking at industrial exposures to provide some light about what might happen as a result of enviornmental exposure.

As you all may be aware, industrial exposures oftentimes are very ideal for looking for epidemiological findings of a chronic nature simply due to the fact that occupational exposures tend to be oftentimes more intense and the ability to gather together a cohort or a group of people to study is oftentimes much easier in an occupational setting than what it is in the general environmental setting.

In attempting to do this, we have found that there are two groups studying the accident Mr. Cleland referred to in his letter to Secretary Califano that had occurred in 1949 in Nitro, West Virginia.

This was a Monsanto facility that had manufactured 2, 4, 5-T. Dr. Raymond Suskind of Kettering Laboratories at the University of Cincinnati has been following the people from this accident since the early 1950's at the request of the company, Monsanto. At the same time, Dr. Selikoff of the Mount Sinai

School of Medicine was also looking at this same set of workers at the request of the local unions.

We have contacted both Dr. Selikoff and Dr. Suskind. Two and one-half weeks ago, Dr. Selikoff's group had just been on a field investigation utilizing some of our testing equipment to do a cross-sectional medical study of these workers. I have talked to him in the last several days, and he informs me that they will be ready to start putting together the analysis of the findings of this particular cross-sectional study shortly. They are currently waiting on some laboratory results and when they are received, we will be in touch with him to discuss the results of on the analysis.

Dr. Suskind has also been asked by the company to do a similar type of study, and he is planning to go into the field sometime in the near future and do essentially the same thing that Dr. Selikoff has done.

In addition, Dr. Suskind is planning to do mortality study looking at the mortality of the workers that were in this particular plant to determine if there is any excess of cancer or any other chronic long-term health effects as a result of their exposure to dioxin.

As you may know, carcinogenic effects generally take 20 to 30 years to manifest themselves after first exposure, and this population is just at reaching this period of time where one might be able to detect such chronic effects.

We at NIOSH are following the progress of these two studies at the Nitro,

West Virginia facility but we are not actively working in Nitro because we feel that there are two competent researchers in the situation now, and we will simply follow their progress and give them any assistance that we can.

We have decided to expand our investigation and are at the present time looking for other industrial accidents or exposures that have occurred over the years throughout the United States.

We have so far found several, the most recent being last week in Jacksonville, Arkansas. Dr. Selikoff and the State Health Officer, Dr. Young, contacted us about a particular plant which had manufactured 2, 4, 5-T for the past 20 years. The plant had stored the waste material in barrels which they had buried under the ground as well as some above the ground. The barrels now have begun to rust and the material inside (dioxin) has begun to leak and to begin contaminating the surrounding area.

There is a lot of concern not only for environmental exposure, but for protecting the workers that will have to clean this up and how do they clean it up?

We are in the process now of working with the state health department in trying to remedy this situation.

Basically, these describe the extent of the plans at the Institute at present. We are still in our developmental stages of developing and proposing studies to determine what adverse effects result from exposure to dioxin, and we will keep the Committee informed as we take further steps.

DR. HABER: Thank you very much. That is very

helpful.

I would like to ask Mr. Robert H. Lenham, the special project officer of DAV, to give us his views and what the DAV's interest is and what they have been doing.

MR. LENHAM: Thank you, Dr. Haber. Some 58 years ago, the DAV was chartered a disabled American veterans organization to set up to provide assistance to disabled veterans, and their families.

We are very concerned and have received correspondence in the mail from veterans throughout the country expressing their concerns over the possible exposure to the herbicide.

Immediately we set up a centralized system for handling these disability claims for dioxin poisoning and trying to collect evidence to substantiate these claims.

This is a problem because the medical records in most cases do not specifically reflect that a given veteran was exposed on such and such a date to any herbicidal spray that might have occurred in Vietnam, and we are aware of this, so when a claim comes in from a veteran, we refer this back out to our local national service officer who contacts a veteran, will assist him, sets up a special file, and then alerts us to any and all action taken on the local level by the VA Adjudication Service.

We have publicized in our monthly magazine the various effects that have been referred to us that could occur as a result of exposure to dioxin. We will naturally be interested in the reports that will be coming out of this

Committee and the other type of reports that will direct themselves to the problem that we are now confronted with.

This is a problem, alluded to earlier, that has gotten the attention of the nation, so in this respect, I am glad to be serving on this Committee to act as a veteran consumer and to be able to pass what information I might be able to have gained from our organization to the Committee members of maybe what the direct problems with which we are confronted by the veterans who are contacting us are, and hopefully maybe this will be of some assistance to the Committee members.

Thank you.

DR. HABER: Thank you very much. Dr. Lingeman, can you please let us know where you are at and where you are coming from?

DR. LINGEMAN: I would like to ask a question. Is this Committee interested only in the dioxins and the Agent Orange, or are we interested in other herbicides, which were used in Vietnam? How many others were used?

DR. HABER: I would say that our overwhelming interest is in solving the problem of exposure of American Armed Forces personnel in South Vietnam.

Now to the extent that we can help shed light on a world-wide problem, and to the extent that the Veterans Administration is increasingly aware of the fact of environmental hazards as a potential carcinogen or damaging agent, we, of course, are interested.

We have had intimations that

exposure of people during their Armed Forces career to asbestos might cause difficulties, and we are at the present time approached by veterans who have concerns about that, but I would say that is by far the less important objective.

Almost entirely we ought to concern ourselves with the potential damage done to American servicemen and women as a result of exposure to the herbicides that were used in Agent Orange in Vietnam.

DR. LINGEMAN: In other words, were significant amounts of otner herbicides used in Vietnam during that period?

DR. HABER: There were other herbicides used I believe. There was an Agent Purple and an Agent White which were composed of cacodylic acid and picloram, but they were so trivial that it would be almost impossible to try to determine--their use was so trivial and infinitesimally less than the millions of gallons of Agent Orange that was sprayed that we can ignore them for the purposes of this discussion.

We are interested in shedding light on the whole subject of environmental toxicity, in particular for herbicides, but our main focus is on Agent Orange and what it did to the American servicemen.

DR. LINGEMAN: Thank you. This makes my description a little more simple.

The National Cancer Institute has for many years been interested in chemical carcinogenesis and devising methods to test for carcinogenicity. This is not a simple matter. There are problems with species specificity and

numbers of animals that must be used to provide a statistically significant result. The present Carcinogenesis Testing Program has the responsibility of determining which of 45,000 chemical compounds should be tested for carcinogenicity by the National Cancer Institute. The financial resources are very limited, and at the present time, it costs $250,000 to test one chemical. The standard test in mice and rats involves a chronic study, usually oral feeding or installation by gastric tube of the chemical compound, sometimes other methods, depending upon the compound. At least two species of animals are required. At the present time, we use mice and rats, 100 of each. We keep them alive, if possible, for their lifespan, which in the case of the mice and rats is between two and three years, and this has to be done under standardized conditions. There have to be adequate controls. Before each assay is begun, it is necessary to determine for each chemical the maximum tolerated dose so that the dose will not kill the animals but will permit them to survive long enough to develop cancers. The Cancer Institute's primary mission is cancer. The emphasis has been there. However, when possible, we look for other toxic effects.

Recently, the National Cancer Institute's Carcinogenesis Testing Program has come under the National Toxicology Program, which

involves seven other government agencies, both regulatory and scientific, and is under the direction of Dr. David Rall of the National Institute of Environmental Health Sciences. From now on, our program will not be completely independent, and all chemicals nominated by us for testing will also be the concern of the National Toxicology Program.

I wish to tell you exactly where we stand with the dioxins and with 2, 4-D and 2, 4, 5-T since these are the materials of interest here.

The National Cancer Institute has a system whereby chemicals are nominated for test by means of a Chemical Selection Working Group composed of NCI staff and representatives of other government agencies. We hope to have a member of the Veterans Administration on this Committee soon. This is the nomination form which I will pass around. Anyone can nominate a chemical. We ask people to provide as much information as possible when they nominate a chemical. I think probably most of the chemicals of interest to this Committee have already been tested or are under test at the present time. When a chemical compound is nominated for test, the Chemical Selection Working Group meets with representatives from other government agencies who have an interest in this, including EPA, FDA and others. Members of these other agencies also serve on the Chemical Selection Working Group.

The Committee members vote on each chemical according to materials supplied by a contracting firm known as Stanford Research Institute, which provides information about each compound including amounts produced and imported, whether they have been tested previously, and other information.

There has been a class study on pesticides in general and several pesticides other than 2, 4-D and 2, 4, 5-T have been tested or are under test.

We have to set priorities. Out of 45,000 chemicals, which are most likely to be carcinogenic, we take into account the chemical structure and similarity to known carcinogens, and the amount of human exposure. This is difficult to obtain. I have a sample data sheet on benefin, another herbicide that has been nominated for test by the NCI. After the Working Group assigns a priority for those compounds selected for testing, each one is presented to a subgroup of the Clearinghouse on Environmental Carcinogens, composed of a group of advisers outside the NCI. They are the best experts we can find in the field. They meet approximately four times a year, and each of the nominated chemicals is submitted to this group for their opinions. These are open meetings. The subgroup reviews the evidence for each chemical, perhaps asking for more information, and then ranks them on the basis of 1-10, ten being the highest priority. We then have a list of chemicals ranked in order of priority to enter into the testing program.

This is a copy of the monthly report of the status of each of the chemicals which have been nominated for testing, those which are under test, and those for which tests are complete but the reports have not been published. We can make these reports available to the

members of this Committee.

The dioxins, TCDD and HCDD, are in final stages of the testing procedure. They are under pathology review. The protocols describing the results to be presented to the Clearinghouse subgroup on Risk Assessment/Data Evaluation are, being printed at the present time, and so I can't say anything about them yet because they have not been presented to the Clearinghouse. However, we expect that both of these compounds will be presented to the Clearinghouse in July or September, so that within the time frame of the work described for this Advisory Committee, these results will be available as technical reports. Here is an example of a technical report on another dioxin, DCDD, which was published this year. This and other reports are available either through the National Cancer Institute or through other government sources.

DR. HABER: That is excellent. Please continue.

DR. LINGEMAN: The International Agency for Cancer Research, under the auspices of the World Health Organization, meets periodically to discuss chemical compounds known or suspected of being carcinogenic. This is Volume 15, which was published in 1977 on the subject of some herbicides, which includes 2, 4-D, 2, 4, 5-T, and the dioxins, the compounds of concern to this group. This is a publication that Committee members should have access to, for it is an excellent summary of known health effects of these compounds in man and animals.

The other activities of the National Cancer Institute which have to do with this area involve the Epidemiology Branch, and I have not had an opportunity yet

to find out the precise details of all that might be going on there. As mentioned before, epidemiologic information documented with good pathology material is very difficult to obtain. By the time of our next meeting, I hope possibly to have some information about activities of the NCI epidemiologists in this area.

DR. HABER: Thank you very much. We are making very good progress. We are at the break time, but I think we have but one more presentation, and I would ask your forebearance for Dr. Murphy to make his presentation, and then we will break for lunch.

DR. MURPHY: I can probably be relatively brief since I have not been directly involved in research on this problem, and I do not really represent an agency. Although my name tag says consultant to the National Academy of Sciences, I really am not here representing the NAS.

I am merely speaking from the standpoint of a scientist who has been concerned with the toxicology of pesticides for some 20 years, with focus on primarily the insecticides, and have published several papers in this area.

For a number of years, I have from time to time served on certain expert committees of the World Health Organization dealing with pesticide residues in foods, and in the process of those deliberations, have gained some experience in going through the process of evaluating laboratory animal and epidemiological data with respect to ultimately coming to the conclusions concerning recommendations regarding the hazard or relative safety of

pesticide residues.

I am a member of the EPA Science Advisory Board's Environmental Health Advisory Committee, and as a function of that Committee membership, I chaired a study group on the contaminant pentachlorophenol, the contaminant in a particular pesticide which I think does have some use as a herbicide, but was not to my knowledge used in Vietnam, but the contaminants in that material of greatest concern are the halogenated or chlorinated dibenzofurans.

Dr. Moore was a member of that group, and we reviewed the knowledge base concerning the contaminant of pentachlorophenol. Tetrachlorodibenzodioxin does not appear to be a contaminant of pentachlorophenol, but the other dioxins that are, as Dr. Moore has indicated, produce very similar actions as that produced by TCDD, and there is a wide range of toxicities involved among the number of different isomers that are contaminants.

Some two years ago, I was a member of an ad hoc panel chosen by the National Academy of Sciences to meet with Italian health officials to evaluate and recommend possible collaborations in research on health effects associated with contamination of the environment around Seveso, which we have heard mentioned several times today.

The contamination resulted from an explosion of a reactor producing trichlorophenol near the town of Seveso. This Academy-sponsored panel met several months after the occurrence of the accident with the counterpart committee, and then subsequently this past March met again to review

the status of the studies that were largely being conducted by the Italian scientists in the area around Seceso, both laboratory and epidemiological studies.

In a very brief summary of the discussions of this meeting last March, from the studies conducted so far, there were three health effects that were observed that the epidemiologists' reported suggested association with this exposure to TCDD from the industrial accident.

These included chloracne clearly associated with the exposure, some suggestion of what was described earlier as hepatomegaly, and apparently some specific tests conducted showed some deficiency or slowing of nerve conduction.

The epidemiologists were developing plans for following a fairly large group of people over a long period of time in connection with the concerns for carcinogenic potential of TCDD, and one of the interesting observations was that the concentration of dioxins in the wild animals that roamed in the area did not appear to correlate very well with the incidence of chloracne that was reported, and I was very interested in Dr. Allen's comment concerning evidence of some effects reported in the peripheral areas of exposure, and I wonder what these relationships mean.

An interesting point that has come to my attention during these two committee activities, one in the EPA and this activity of the Academy, is what is the relationship between the dosage for effects in laboratory animals and

in humans, and this seems to be a rather illusive relationship.

In some respects, one would have almost anticipated that the Seveso incident would have been even more severe effects than apparently had been noted.

There was an attempt to evaluate the potential contribution to teratogenic actions in the human population, and so far, it appears that statistically nothing sorts out as a positive finding in that regard.

You asked for what kind of things we would like to see. Well, I would like to see the earlier NAS report after the Air Force report. I would like to see more about what is the nature of the designs of the studies that are now underway, and I wonder how much alternate designs have been considered, looking for clustering of possible effects and so forth.

What are the plans for long-term studies? You do have a group of human population that can be followed, but what are the plans for these, and to the extent possible, although as I said I don't represent NAS, I would hope to coordinate some of the information with the Committee on the National Academy of Sciences which has now been renamed to something like Committee on Response Strategies to Unusual Chemical Hazards, so they can respond to other things than Seveso.

DR. HABER: Thank you very much. That then concludes our morning. I must say that I am more optimistic at this moment than I have been for some months, that we

will find an answer, although that answer is not clear.

I would like to thank everybody for the morning's proceeding. Would the members of the Advisory Committee and the Steering Committee remain behind just a moment, please?

We will reconvene at 1:30 as per the agenda.

(Whereupon, at 12:15 p.m., the hearing was recessed, to reconvene at 1:30 p.m. the same day.)

AFTERNOON SESSION

1:30 p.m.

DR. HABER: Let me reiterate if you will, please. For those of you on the floor who have questions, give them to Mrs. Meyer, dutifully sitting back there. She will give them to me and I will attempt to read them. If they are relatively simple and are procedural,, I will endeavor to answer them this afternoon.

Those that are more substantive, we will have some discussion from the Committee if the time allows, but I will tell you that we will get a position paper on it because I don't believe that the Committee yet is prepared definitively to answer. There may be differences of opinion which obviously is our job to resolve. So, while you might have some discussion about the question, that should be regarded as a tentative answer only in that the Committee will obviously want to deliberate further on some of the complicated questions, and we will adopt a position on it at some point, which will be made public either through the use of subcommittees or circulating documents through the committees all together.

I would like now to move along with our agenda I think that because we did so well this morning in covering each of the participants on the Committee and their agency's specific orientation toward the problem,

think what I would like to do now is to engender some dialogue among the members of the Committee. Undoubtedly each of your comments excited some concerns, some questions, some suggestions on the part of the rest of the group.

I would like now to encourage us to go at that business to try to get some indications of what the substance of these deliberations are.

Dr. Allen, may I begin by posing a question to you? In your work with primates, you have reason to believe that there were birth defects, but were these confined to females who were pregnant at the time of exposure, or did you have any evidence suggesting that males could transmit damage that they sustained to the offspring of non-exposed females?

DR. ALLEN: Dr. Haber, I would like to answer this by first clarifying a point. We have observed no birth defects in the offspring of monkeys that have been born to mothers that have been exposed to the TCDD's.

There have been abortions, and most of these abortions occured early in gestation. Those animals that were born to the mothers that were exposed prior to and during gestation, had normal infants, with the exception of being small. Otherwise, they were, generally speaking, small.

We have observed alterations in the menstrual

cycles, increase in cycle length and duration of the menstrual cycle, and alterations in progesterone levels in the females that have been exposed to the dioxins. We have not done thorough studies on the male Rhesus monkeys.

In our early report published in 1967, we did observe a marked decrease in spermatogenesis in monkeys that were exposed to high levels of dioxins, including the tetras, the hexas, the heptas, and the octachlorodibenzodioxins. Those of you that are older might remember the toxic fiasco that we had in the '50's, so we would expect, and we certainly would feel, that it does affect spermatogenesis.

We have observed no indications of a mutagenic nor teratogenic change in the animals so far.

DR. HABER: I am indebted to you for clarification, and I'm sorry I interrupted. I will tell you that Dr. Ton That Tung, the North Vietnamese physician who had had some experience with this several weeks ago came and briefed us, and when we put that question to him, although he had talked about birth defects in offspring of exposed females, he did not extend that to the males. He said he had no evidence of that, so it is a question of some concern to us.

DR. ALLEN: I also had the opportunity to visit with Dr. Tung while he was visiting the United States, and I think that I would like to say that in most instances,

the data that were presented by Dr. Tung were those of a practicing physician, and they were meager as to the information that they were able to relay to us.

DR. HABER: I can only agree to your observation, and I think Dr. Tung himself disclaimed any epidemiologic certainty from his findings and stated to us that they were suggestive only, that he was not an epidemiologist and portrayed himself as a practicing clinician in these observations, but of course, they were useful to us as observers.

I wonder, Mr. Lemen, if you could tell us a little bit more about the work of Dr. Suskind and Dr. Selikoff, if that is possible? I guess it was you who first suggested that?

MR. LEMEN: Fine. First of all, as far as results are concerned, I can't give you anything because Dr. Selikoff is just analyzing this,and I might suggest that you invite Dr. Selikoff or Dr. Marian Möses, who is the physician that was doing a majority of testing, to come to the Committee and present the results to you.

I can tell you the design of the study was that of a cross-sectional medical study, looking at workers who had been in the 1949 episode. Some had developed chloracne, and they were looking for any medical findings

in that group of workers.

At the present time, Dr. Selikoff has discussed the possibility of doing mortality analysis on the total work force. However, he has not started that.

Dr. Suskind has been following these people, according to my talks with him, since about the early '50's, and he has been looking primarily at dermatological conditions in the workers that were exposed to the 1949 episode.

Dr. Suskind says that he is in the process of doing mortality studies. However, he does not have results on the mortality study to date. We will continue, as I said, to monitor both of these to try and get results as soon as they become available, but neither one of the two studies has any results that we can speak of today.

I think at the next meeting,

Dr. Selikoff's group would probably be able to talk to you about their findings.

DR. HABER: I think we might invite him to make a presentation to us. Does the group have any objection to that sort of thing if we were to invite people that you might suggest to make presentations to us?

DR. KEARNEY: I think it would be very helpful.

DR. MURPHY: I wonder, Mr. Lemen, in Dr. Suskind's studies, has there been any attempt to assess morbidity

from whatever cause other than dermatological? How about infectious diseases?

MR. LEMEN: Quite frankly, the information that we have received from Dr. Suskind has been a little bit, I don't want to use the word sketchy, but it is inconclusive, and I can't really answer that question.

He says that he is looking at the health effects in total among the workers, but in talking to him, it appears that it has been more of a dermatological evaluation. That is about the best I can do.

DR. MURPHY: Are Dr. Selikoff's studies designed to assess immunofunction?

MR. LEMEN: Yes, to my knowledge, they are. As you well know, though, in the cross-sectional type of study, it would be very difficult to detect any chronic long-term health effects such as cancer because those people tend to cluster in one population at the same time, so the type of studies without the aid of the mortality study would probably not answer the carcinogenecity question that you have posed, and also the question of teratogenic effect would have to be addressed in talking to family members and doing a fairly detailed questionnaire of the wives and offspring of those workers.

DR. HABER: I would like to comment, though, on this problem of chloracne, and invite any comments from the

Committee or questions about it.

The chloracne for us has a particular significance because it really constitutes a marker. If a serviceman comes to the Veterans Administration for treatment or for adjudication of a claim, if there are problems with substantiating the possible exposure, Dr. Levinson described this morning how we are trying to match the tapes on movements of various units in the Armed Forces with areas of known exposure to sprays, so that we can get some concurrence of data. One thing we do feel pretty confident about, is that if a veteran should have, any evidence of chloracne attendant upon his service in Vietnam, that probably would give us pretty clear evidence that he has indeed been exposed, so it would constitute a kind of a marker. We know that chloracne should occur within a matter of days or weeks or at least a few months after exposure; that it is not likely to occur years later.

Its first occurrence having taken place during the period in which he was in Vietnam or very shortly thereafter then gives us some feeling that there may be long-term other effects. Chloracne has been associated with systemic symptomatology and general pathology, so we feel a little bit more confident about that.

Is there any comment about this?

MR. LEMEN: I have one question, and maybe the Committee can answer it.

Are there any levels below which you come in contact with the Dioxin or 2, 4, 5-T that you do not get the chloracne?

DR. ALLEN:

This was the question that I was looking at. From an experimental standpoint, there can be reproductive abnormalities in the females without showing obvious signs of dermatological alterations.

I have a question for Dr. Moore.

DR. MOORE: Can I finish? I can add something to his comment. There was a report in the British literature several years ago in which there was accidental exposure of several chemists trying to synthesize or work with TCDD, and in those cases where they did come down with clinical symptomatology consistent with dioxin exposure, it occurred in the absence of chloracne.

DR. HABER: What we are saying is that chloracne is not a sine qua non for evidence of exposure. That has been our suspicion, that people could have dioxin poisoning, if that is possible, exposure, and not come down with chloracne, but if they do come down with chloracne, the burden of proof is upon him who says that it was not due to exposure, and I think it has to be thought

of in that way. Where we find chloracne, we have got to really be very, very concerned. Where we don't find it, it still may be. Could you tell us a little bit more, Dr. Allen, about the dermatological abnormalities you saw in these monkeys and how long after exposure did they occurred? What would you say?

DR. ALLEN: One of the first indications that we had was in the let's say, for instance, the 500 parts per trillion. After they consumed 1 microgram per kilogram of body weight, we began to see the development of alopecia, loss of hair and dry, scaly skin, and if you look closely, you could see the accentuated hair follicles within a period of three months after we began to see indications.

In the 50 parts per trillion group, after they consumed in the neighborhood of 3 tenths of a microgram per kilogram of body weight, there were no obvious changes. However, we began to have indications of reproductive abnormalities that were obvious in these females.

DR. HABER: From ingested toxin?

DR. ALLEN: Ingested, not from dermatological or inhalation exposure.

DR. HABER: We have to keep in mind both possibilities. The troops or an exposed person may have wandered through areas infested with the

dioxin and become contaminated.

The other concern we have, of course, is that, and I look to Colonel Thiessen about this, there weren't too many dermatologists in the front lines so that the condition of chloracne might not have been precisely identified, but rather some other dermatological abnormality, trenchfoot or something like that. So we would be inclined to say that any dermatologic abnormality, unless it is pretty clear that it could not have been caused by dioxin, would have to be suspect.

Do you have any comment?

COL. THIESSEN: Individual cases maybe; I am not so sure whether an epidemic quote, unquote, of chloracne or acne or any dermatosis would have gone unnoticed.

DR. HABER: I didn't mean that. I just mentioned in individual cases that somebody might have ascribed that. It is conceivable at least that someone would say chloracne is a pretty tough diagnosis, and you have got to be a dermatologist to do it, and they were just corpsmen, so how would you have made that diagnosis at that time?

COL. THIESSEN: If the soldier had complained about a disfiguring acne, I'm sure that would enter into the record. I am certain of that.

DR. ALLEN: Dr. Haber, I have a question of Dr. Moore. One of the charges of the World Health

Organization, the group was to study the various industrial accidents.

Is there any feedback on this? What is happening with that charge? Are they pursuing this?

DR. MOORE: A number of those groups are being followed. The hope of the exercise was that the various groups that were studying their exposure here and their exposure there would come up with an agreed-upon questionnaire, a case history, so that there would be some consistency in what was looked for and the way it was they went about looking for it so that one could have the benefit subsequently of trying to amalgamate these various groups to get a bigger statistical cohort to try to look at.

At the time we met, which was a year ago January, nobody had been looking to the Nitro, West Virginia group subsequent to the actual accident which occurred in the early '50's, and the recent flurry of activity that we have found in the Nitro, West Virginia group is that it is a recent flurry of activity.

MR. LEMEN: Can you tell us some industrial sites that you are looking at?

DR. MOORE: They are in here. We are not looking at any sites. The sites that were identified by various people include some in Germany, some in this country, one in Holland, one in Germany Obviously

the Seveso circumstance from a time standpoint was in its infancy.

DR. ALLEN: Are there epidemiological studies that are being financed by WHO?

DR. MOORE: No, not epidemiologic studies as such; basically morbidity, seeing what the cause of death is, et cetera, on some of these older groups, to see if anything will show up.

MR. LEMEN: We have been looking just to answer a little bit more, and we have not found, except for the Nitro situation, any epidemiological studies that are going on in the United States looking at dioxin exposures.

DR. HABER: At this juncture, it might be useful to have Dr. Schepers tell us something about this problem. He has looked into this, and has identified a number. Every time we consider it, it turns out there are more industrial exposures than anybody knew, and Dr. Schepers has what I believe is one of the more complete anthologies.

Would you please let us know about this, and maybe we ought to enter that into the record, the complete thing, and tell us about the exposures we know about.

DR. SCHEPERS: It is not terribly complete. I just happened to accidentally have it in one of my folders, but the first exposure of human beings to 2, 4, 5-TCL--it wasn't 2, 4, 5-T--was at the Nitro site, and that was in

1949. About 188 people were exposed there in the factory, and probably the children and wives, too, because there is recorded illness of those children and wives, so that the number of human beings could be quite sizable.

Now one of the problems with our group is to identify these individuals because after 30 years, they have been disbanded. I traced the actual Director of Personnel for the Monsanto factory to Mr. Baum through some friends of mine, and I am going to ask Mr. Baum if he has a record of all these people, and I think he has, so that we may be able to trace the human beings through him.

The next series of accidents occurred as four events in West Germany, from '49 to '74, and they can be found in the literature, and I would be glad to supply the Committee with details.

Then there was a group of two accidents in France from '56 to '66; 38 people were exposed to dioxin-containing materials there. They all developed chloracne, incidentally.

Then the next exposures were in the United States from the period '56 to '74, and these were the four separate events that most of you will know, that totaled to 81 people. This is in Arizona, the group out there in Missouri, the horse farm, and so forth, and of course the employees of different chemical factories.

Then in '62, there was a small accident in a factory with five people exposed in Italy. In Holland, there was a group exposed in '63 with 50 workers, and they are being followed,; hyperlipema and asthenia being the main features so far identified.

There have been two industrial accidents in Russia between 1964 and '72. All the people recovered. These two events were at intervals of eight years, all symptomatic. The follow-up study is not known, but we are trying to find out what happened to those people.

Then in England in 1968 there was a single big reactor leakage event, and most of the descriptions are related to chloracne, but there are obviously possibilities there.

In 1970, there was a single accident in Japan. We are trying to follow that.

In Czechoslovakia in '72--there were very severe industrial exposures, gross poisoning--six of the 55 workers actually died, showing the severity of the exposure. Now that should be an extremely interesting group to follow.

Then in 1976 in Switzerland and Italy, that is, of course, the Seveso incident, and that is the largest single group. I understand there are about 70,000 children under surveillance by the Italian government.

I totaled up the numbers of people in these incidents, and they come to almost 1,000 people, so that we have a fairly large group of human beings that can be researched collectively.

DR. HABER: I think one of the things that this Committee should be expected to do is to try to compile as complete a dossier as we can on the numbers of and kinds of such accidents therewith to stimulate the appropriate research by the appropriate agency, and hopefully to share in the results of such research.

DR. MOORE: Dr. Haber, one of the best groups is that Czechoslovakian group that Dr. Schepers mentioned in that it has at least appeared in the literature. All of it has appeared in the literature. We have had those articles transmitted, and we will give you a copy of the translation.

DR. HABER: I have asked our staff to do two things for us. One is to draw up a general chart of organization of the federal government and the private and academic sectors as well to see whether or not we can develop a kind of chart so that all of us can have a ready-made indication of who is doing what. This would be keyed with the number of studies, and I think each of us could use that so we could find out where the responsibility lies or who accepts responsibility for doing certain things.

The other thing that I think might be very useful is,if we could begin to see, try to indicate some time lines so that we would have some indications as to when these studies would be complete, and we get some idea,at least in gross,about when we might expect some definitive answers.

I know that some of it would take years to complete, but hopefully we would be able to get some clear indication that we can give to the public about the latest date the information would have been in. Maybe that can be improved upon.

I wonder, Dr. Kearney, if you could tell us a little bit more about that conference on the dispute resolution because really that is what we are about, and it is the kind of a process in which I think this Committee would be very interested. If you could, give us any general guidelines as to how we use the scientific method to resolve a problem that is plaguing all of us.

DR. KEARNEY: Well, I can provide you with the background paper. I think in a dispute of this nature, it is a question of how it could be resolved and what would be the outcome.

I suppose in some respects the first conference we had was largely discipline oriented, i.e., the field of medicine and chemistry dealing with specific subjects of

teratology and mutagenecity, carcinogenecity, human exposure.

The more philosophical question of how one deals with dispute resolution will probably be the next conference in which we would have local people, sociologists, political leaders, and others involved, but it does bring to mind something which I think is germane to these deliberations. It would be helpful to us the advisory panel to perhaps at some point clearly define what the Administration wants from us with regard to resolution of this dispute.

In other words, is teratology a legitimate subject for deliberation here? I don't know the answer to that question because were there females in the Vietnam area that are involved here inclaims for compensation? Are we talking about males primarily, the number of males, and perhaps what you want us to focus on, because some of the issues are peripheral as far as we are concerned.

I don't know that we can answer that question today. As we get into this thing, these things will begin to surface.

DR. HABER: Well, I think that is part of the question I was asking Dr. Allen really because our concern is not exclusively directed towards males in Vietnam, as there were obviously women in the Armed Forces, and some

of them may have been pregnant at the time. Although such cases have not yet come to my attention, if the clear link is established that a pregnant female does produce a mutagen or a teratoma, and she can have claimed to have had exposure that would be something that would be useful for us to know.

On the other hand, a thousand, perhaps a hundred thousand times more likely just on the basis of the prevalence of people, would be the possibility that males thus exposed might transmit genetic damage to offspring by females not so exposed.

As I say, it seems to me that no clear evidence has been adduced to that effect, and I think that is something that, therefore, should concern us, but I would not turn my back on the other.

I think that we have an obligation first to look at our own problem, but I would say that we must not pass up the opportunity to contribute to the general knowledge if in so doing we don't obstruct our major objective.

I think it is appropriate for us to discuss teratology in pregnant exposed females, but it certainly should not loom very large in our discussions.

DR. SCHEPERS: May I comment on that?

DR. HADER: Please.

DR. SCHEPERS: You have answered many telephone calls, Dr. Castellot, and I perhaps more. This is probably the most distressing thing to the veteran. Many of the calls that I get is Doctor, I have just had a child, and the child is deformed. Is this de to Agent Orange?

They want an answer to that. Now Dr. Erickson told us today that he has perceived a decrease in neurological teratology an increase in heart and renal agenesis.

They mention club feet, cleft palate, the obvious things. Those are the things that distressed them.

We need to give them an answer on that. If there is an answer here, let's hope we find it, but it is a distressing thing, and I think this Committee should stay with that.

DR. HABER: Absolutely. I agree with Dr. Schepers, and I hope I didn't mislead anybody. I think that is a cogent subject for discussion, and one that we really should zero in on, and I think we have to focus on this to be able to reassure the veterans, if we can, which would be extremely useful.

On the other hand, if there is a reasonable doubt, I think we have to place that.

DR. MURPHY: I would like to ask a question of

Dr. Erickson and Dr. Allen in relation to this. With the kind of surveillance program that you have, Dr. Erickson, would the number of malformations that might be found in a group of, approximately 10,000 people, show up in this? Would there be a big enough blip in the ordinary incidence of things to show up?

I don't mean 10,000 malformations, but a whole population of 10,000 people.

DR. ERICKSON: It is possible . It is also possible that it would not.

DR. MURPHY: In general surveillance you don't focus on a select population, and I would worry about drawing conclusions from the kind of general trends you reported this morning.

The other question, Dr. Allen, you mentioned you didn't have any evidence of mutagenic or teratogenic actions. Is that correct?

DR. ALLEN: I think that, and I will refer this question after I have attempted to answer, to Dr Lingeman here, if a compound generally speaking is carcinogenic, more than likely we will find it to be mutagenic. I think there is very little doubt that in animals, that TCDD is a carcinogenic agent. Thus, with the proper tools, I think we will likely find it to be mutagenic.

Are you in agreement with that? I mean, generally speaking, we think of a carcinogen as also more than likely being a mutagen.

DR. MURPHY: This is precisely what I was wondering about, and I think it has been reported mutagenic.

DR. ALLEN: It is a very difficult compound with which to work, particularly in your system or whatever it might be .

DR. MURPHY: Do you have tests on this?

DR. MOORE: Carney in Canada did contaminant studies and reported this negative.

DR. HABER: Repeat that.

DR. MOORE: Carney in Canada has reported on a dominant lethal study which would be in effect for genetic damage in the male transmitted to the offspring which would be picked up by fetal absorption . His study was negative.

DR. HABER: Could you give us that citation at some point?

DR. MOORE: Yes.

DR. HABER: Thank you very much.

DR. KEARNEY: In that regard, the carcinogenesis work, we did address this. It did say that TCDD is a mutagen in two bacterial reverse mutation systems, and they cite the reference, but no correlates of mutagenecity

have been found

Citing the reference, they also say TCDD is a carcinogen for rats, and cite four references, and mice, and cite two references.

DR. HABER: Is there any further discussion among the members of the Committee? One of the things I would like to ask the group to consider is, one of the problems we have is to translate the kind of data that Dr. Allen has presented into possible field exposures.

It is very useful to have his other detailed observations upon ingestion or exposure of a chronic nature to these toxic agents over a long period of time, and then to be able to make post-mortem pathologic diagnostic studies of exposed animals. That is clearly the first step, and it appears that in non-human primates and certain other species, that is pretty well along.

One of the things that I would like to ask the group to speculate and ruminate about, and maybe suggest how one could go about it, is, how does one begin to translate that kind of quantitative data into how could we begin to get a grip on the likelihood of intensity of the exposure of human beings in the field?

In other words, how much exposure would somebody have to have to sprayed foliage and vegetation in order

to come up with dosages that might be comparable even in an order of magnitude to what Dr. Allen has been feeding his experimental animals?

What I am trying to get at is some feeling among the group as to how we could begin that process because I think that is an important element . Are we talking about the same order of magnitude or are we talking about-- Dr. Moore?

DR. MOORE: I would like to make one request, if somebody doesn't have any information, and I will get on the bandwagon; in response to the question, it is my understanding that the use of Agent Orange in Vietnam, or herbicides in general,markedly decreased in the early '70's, and the bulk of herbicide exposure occurred in the late '60's Keeping that fact in mind, it was only around 1970, '69, '70 that the concern about the level of dioxins in herbicides became an issue,and there was an overt attempt to reduce the level of dioxins which would suggest that the actual material that was sprayed would be higher than that which would be found on Johnson Island, which has been subsequently disposed of and was analyzed At least it was analyzed.

It is my understanding that samples of some of the pre-'69 or pre-'70 Agent Orange materials that were used do exist, and I would urge you to find if indeed

that is the case, and if it is the case, to see what the level of dioxins are that were in that material

DR. SCHEPERS: We have tried very hard to get a lead on where these samples could exist, and we can't trace them. If you know, let us know.

DR. KEARNEY: As you know, in '70 we did do some sample studies for manufacturers. We got back to '68 I guess, and then we asked for other samples, and we were unable to obtain them .

The problem also on Johnson Island, I think perhaps the Air Force has,is one could not identify lots to manufacturers in the rebarreling process. I think records became lost.

DR. ALLEN: Can you give us an idea? I know the Air Force reported as high as 47 parts per million I have heard unofficial reports that there were levels higher than this. Can you give us any insight as to what the levels of dioxin TCDD, was in the material that was being sprayed?

DR. KEARNEY: Dr. Allen, I wish I could. I am not sandbagging you. I simply don't know. I heard this figure of 50 also. We did not analyze the sample, but

apparently industry became aware of the problem and one manufacturer quickly tried to rectify it.

Others became aware of it later, and were unable to rectify it until the very end, toward the end of the situation.

I only wish we had those samples to analyze, but we can't get hold of them either. We haven't tried legal means, but we simply have not been able to get hold of them.

DR. HABER: I think this is a very important question, Dr. Moore. I think you are right on target. I think there are two parts of it. One is we need to-- Colonel Thiessen, maybe you can be of assistance to us-- Dr. Schepers has been unable to run down where such samples might exist, but if we could begin to isolate such samples, and then, allowing for decomposition and so on over this length of time, decide whether or not there was any TCDD at the time of the spraying. The second part of that would be to translate spraying information into the possibility of exposure.

That seems to me to be a mathematical possibility at least, but probably a very difficult epidemiologic task to perform.

COL. THIESSEN: As far as TCDD is concerned of course, all the information that is available is either in the Air Force report. I don't know if there are any of the samples still available that were used to determine the TCDD level.

On the other hand, though, I wouldn't be surprised

if a chemist, a manufacturing chemist could simply, looking at a production process, say something about a maximum level of TCDD possible. I thought you had a representative of Dow Chemical; he is not here any more, but I am sure that Dow could give that kind of information Certainly I have never heard a level that high, but 50, 50 PPM is, as I understand it, the level that was present in some samples; in most of the samples, the contamination was below 10.

DR. HABER: Can you tell us what steps we went through to try to get that information?

DR. SCHEPERS: Well, we went to the Army records; to the Air Force records. We went to the Dow Chemical Corporation, the Hercules Corporation, 18 different chemical corporations to see what records they have.

My genuine impression is that one, they did not know of this problem until around about the late '69, '68 era, so that they genuinely did not know what the dioxin content was of the earlier samples.

My other impression is that the manufacturing process was fairly standardized so that the way the ingredients of Agent Orange were made in the '70's is probably the same way that this same material was made five years or six years earlier. There was no real change in the manufacturing method. Therefore, the probability is that the incidence of TCDD in 1970 was probably the same range as it might have been in 1963.

Now a lot of emphasis is often made on the

occurrence of large quantities, relatively large quantities compared to the experiments Dr. Allen has made, and when we talk of 50 parts per million, this is about 50 million times as much as you are using in your experiments, but often, not enough is said about the fact that quite a number of the samples that were tested had zero TCDD in them, and we don't know what the distribution was of the barrel with 50 in them, and the barrels with nothing in them, whether the analytical methods were sharp enough to be able to measure the presence of TCDD below one part per million.

We, of course don't know. I should rather suspect that the analytical methods were not available, but it almost becomes a moot issue when you, Dr. Allen, produce results at 10 parts per trillion, whether there was exposure to 40 parts per billion or 30 parts per million.

I don't understand the dimension. I see no relationship. It is just that there was a heck of a lot of TCDD in Agent Orange compared to your experiments.

What I would like to get from you is whether you have ever tried to calculate quantitatively how much dioxin is needed to produce an effect in an animal, what is the least quantity that will produce it, and then for us to relate that to the least quantity that we can identify in the herbicides used in Vietnam. That would be an interesting mathematical calculation.

DR. ALLEN: The only thing that I can say is that in my more recent studies, we have found that 50

parts per trillion in the diet when comsumed over a period of approximately six months, and it is about 3 tenths of a microgram per kilogram of body weight, will produce reproductive abnormalities, and over a period of two years, a consumption of 1 microgram per kilogram of body weight will produce obvious signs, gross signs, of intoxication.

DR. SCHEPERS: Have you found a no effect level?

DR. ALLEN: Not in non-human primates, no. We are going down to lower levels at the present time, but we have not found a no effect level when the exposure has been extended over a period of time.

At six months when they have consumed 3 tenths of a microgram, we did not see any obvious signs of intoxicatio grossly with the exception of reproductive abnormalities.

If we waited two years, we did see signs.

DR. SCHEPERS: What about the experimental model to compare to the experience of a soldier who might have been in Vietnam say six months in an area, combat zone, where he might have been contaminated in one shape or another, either sprayed on his head or in his clothes or in his water or whatever, and then he leaves? Have you got anything in your experiments, animal experiments to match that? In other words, a short period of exposure in the life cycle of the animal and then wait and see; that is the one we are interested in.

DR. ALLEN: The only one, and certainly it is far removed from your particular example, is in the 500 parts per trillion studies we had three that survived. We

have followed these animals now for approximately three years after they have been removed from the experimental diets. They have shown a dramatic improvement in their physical status. However, there are still abnormalities that we are encountering after three years of the exposure being discontinued.

DR. SCHEPERS: That would be the closest?

DR. ALLEN: That would be the closest that we have in our laboratory.

MR. LEMEN: You indicated this morning, though, that you did have tumors after two years on the ones that were sacrificed.

DR. ALLEN: We are talking about rats versus monkeys.

MR. LEMEN: Okay, but in the rat, you are talking about in the rats you saw the tumors?

DR. ALLEN: In rats, in the rats we saw the tumors. Monkeys are somewhat like the higher primates in that they do not develop tumors rapidly, so it requires a long period.

MR. LEMEN: I understand that, but in talking about the dose effect, if we are going to find anything, carcinogenic effects in Vietnam veterans, it is not going to occur for another 15, 20 years?

DR. ALLEN: That is more than likely correct, unless we have promotion of existing tumors.

MR. LEMEN: Right.

DR. HABER: I wonder, Dr. Allen, I understand you brought some slides with you. Would it be possible for us

to see those now?

DR. ALLEN: It's up to you.

DR. HABER: How long would that take?

DR. ALLEN: Five or ten minutes.

(A discussion was held off the record.)

DR. ALLEN: (Showing slides) We will go through these rapidly. If we could focus that just a little bit, this is just one of the non-human primates, the Rhesus monkeys that we employed, and I want you to pay particular attention to the hair coat.

If we could have the next slide--this is an animal of six months of exposure, and you will note the near complete loss of hair, particularly about the head, and the abdomen, shoulders, and if you look closely, the animal has practically no eyelashes, and the next slide will show you really what the animal looks like.

Here is another animal at six months. You will note the marked edema about the eyelids, the absence of eyelashes. You can't see the dry, scaly skin, but you can see the development probably on the side there, little acneform lesions, and I think the particularly obvious edema at the upper lips and generally all over the face.

This is just an example of some of the hematological changes we saw. At the top, it gives you the normal values of the monkeys and you will note in the white blood cell count we had a very decided decrease from about 9,000 down to in some of the animals about 2,000; of course, with the platelets, average of 327,000 down to 234450. You will note

the very decided decrease in platelets, and this is why we got what we feel is extensive hemorrhage.

The hemoglobin dropped from 13 down to 4, 6 and 8, as you see here, and of course associated with this is a decrease in hematocrits.

One of the more striking things that we saw was a marked thickening and proliferation of the fingernails and toenails, and note the clubbing of the peripheral digit there. This we feel could have been associated with the very decided decrease in circulating red cells.

We also got dry gangrene. The peripheral digits would very frequently sluff off, associated with the dioxin intoxication.

Another thing we saw, rather striking, was the decided increase in the size of the gall bladder, maybe five or six times the average size, and here we have a probe introduced through the ampulla into the common duct, and you will note the tip of it, you can get an idea as to the size of this gall bladder and the ducts.

When we examined these, there was a marked thickening of the walls of the various ducts and the gall bladder associated with hypertrophy and hyperplasia of the epithelium.

This is just an example of the hemorrhage that we saw in the lungs of these experimental animals, and a rounding off of the heart, which was associated with the very decided anemia that these animals were experiencing.

This is just hemorrhage in the uterus. That was

very common in the animals that died.

The bone marrow, of course, there is the near complete absence of bone marrow, and the hemorrhage in the marrow.

The next slide shows hematopoesis and a predominance of lymphoid appearing cells. Both the myeloid and erythroid elements were affected.

One of the more striking lesions was a marked thickening of the gastric mucosa,and to a lesser extent, the small intestine and large intestine. You note the hemorrhage on the surface of the stomach

The next slide will show us the reason for this thickening. About three fourths of the way up is the muscularis mucosa, and toward the top is the lumen of the stomach and the increase in glandular elements in the submucosa.

Could we have the lights on, please, and the slides off.

DR. HABER: Thank you very much, Dr. Allen. We are enlightened by your presentation.

I would like to call attention to the fact that Mr. Max Cleland, the Administrator of the Veterans Affairs, has taken time from his very busy schedule, and has flown in from Atlanta so that he could address this group.

ADMINISTRATOR CLELAND: I would like to thank you all for helping us in the Veterans Administration make some sense out of what has become possibly a very serious public health problem to Vietnam Veterans, and myself included.

I want you to know that I have a personal interest in the resolution of the questions surrounding Agent Orange. The Veterans Administration is quite concerned about the aftermath of exposure to Agent Orange, and we have picked you all to help us and lead us and guide us in the resolution of the questions surrounding Agent Orange.

One of the most difficult things I have had to do in the last few months is to try and answer questions about Agent Orange in a vacuum of ignorance, and in an area where even the scientists who are most knowledgeable about herbicides disagree.

That puts us in a very ambiguous and difficult position. We hope that this Committee will move with the greatest speed to resolution of these problems, which we face daily.

There are many interested citizens in this country who are concerned about the effects of herbicides on people and we are especially interested in the effects of herbicides on veterans, and whatever the data shows to be the case, so you all have a great challenge because we are greatly challenged as an agency that deals with veterans, and purports to deal especially with the health problems arising therefrom.

You are challenged to help us meet this quite serious question of Agent Orange, so I just want you to know that I am personally interested in your deliberations. I look forward to reading the minutes that you all have

accumulated today. There are others who will follow every word, and each point raised with much interest.

You have a great responsibility. I know you will tackle your job very well.

I thank Paul Haber for leading this Committee in its deliberations. I know that there will be a great deal of give and take and a great flow of information, and ideas and sharing of opinions and views.

I urge you to do that because we look upon you as the mechanism by which we can air all the complaints or ideas or fears, and especially the scientific data surrounding the questions of Agent Orange and herbicides used in Vietnam, so I just speak as the head of the Veterans Administration, and also as a Vietnam veteran, urging you to tackle your job seriously, and especially as Administrator thanking you for your willingness to take time from your busy schedules to help us with this most serious question.

Paul, thank you very much for the opportunity to visit. I know you have some other items on your agenda and I won't interfere. I will now resume my duties, but I did want to visit with you personally and tell you where I was coming from and how much we needed you to guide us in the future.

Thank you very much.

DR. HABER: Thank you, Mr. Administrator. I am very encouraged by this morning's discussion. It looks like we are beginning to make real progress.

ADMINISTRATOR CLELAND: Thank you very much.

DR. HABER: Thank you, sir. Dr. Allen, would you care to resume your presentation?

DR. ALLEN: (Showing slides) This is just a typical example of the marked thickening that occurs, and the gastritis that develops in animals exposed to the dioxins. Very frequently there are ulcerations that are also associated with this hypoplastic gastritis, and in my instances, we feel that these severe changes in the gastro-intestinal tract are associated with the demise of the experimental animals.

Dr. Moore and his associates have done a considerable amount of work with the effects of the dioxins on the immune capabilities of the animals, and certainly in our experimental animals we got a marked decrease in the lymph nodes throughout the body. This is just a typical example of hypocellularity that occurred in the lymph node, and with the decrease in cellular population, of course, there was necessarily a decrease in the immunologic response of the experimental animals.

This is hair follicles. You note the swelling of the eyes that occurred in the experimental animals. This is what they looked like microscopically, and the hair shafts are filled with keratinized material.

This also occurs to a lesser extent in hair follicles over the surface of the body. One of the more striking things that we saw was the marked changes that occurred in the epithelium throughout the body;

changes in cell types suggestive of, quote, possibly transformation of one cell type to another.

This happens to be pancreas, and generally speaking, there are very few, if any, mucous secreting cells in the epithelium.

Here we have a marked increase in the cells. They would normally be in the epithelium. They would be stratified in the epithelium.

Here we have a change in cell type. The same thing occurred in the salivary glands, and also in the bile ducts, indicating a change from one cell type to another as a result of exposure more than likely to the dioxins in one way or another.

We also saw marked changes in the transitional epithelium of the urinary bladder, not only changes in cell types, but also a piling up of the epithelium.

I just wanted to show you the reproductive abnormalities that occurred. It would appear that this is one of the more extensive. If you look only on the left side here, there is the 50 parts per trillion study animals, you then note the 500 ppt; compare the two. Total impregnated, 3 of 8 on 500 ppt. and we got 100 percent in our control animals on both experiments.

Total impregnated with 50 ppt, six of eight abortions, with four of eight in the 50 ppt and two of eight were normal births on

50 parts per trillion, two of eight, and one of eight on 500 ppt.

Also one of the more critical things that we are

concerned about in our study is the effect upon fetal development, and as quickly as we are able to have sufficient numbers of infants survive, we will also be doing learning and behavioral studies in an attempt to see if there are any deficiencies.

We have found with other haloginated hydrocarbons alterations in the learning capability, and the animals show behavioral deficits, so we will be pursuing these particular questions.

That's it.

DR. HABER: Thank you very much, Dr. Allen. Those slides speak eloquently of your work. We are indebted to you.

DR. MOORE: Dr. Haber, could I just make a comment about dose which is where we were going earlier?

I think one of the things that I feel very strongly about is that despite all of the work that is available experimentally or anything else with respect to the benzodioxins, we do have some understanding as to the kinetics of TCDD in the rat. We have a bit of data of TCDD in the primates, but we don't have good comparative pharmacology, and until we get that type of data, we are going to be hard pressed or whistling in the wind in trying to extrapolate from primate or rat or guinea pig into dose the same as man because we don't have good dose response ratios.

DR. KEARNEY: That brings up another point. I notice in our schedule that the last five minutes will be

devoted to future meetings. I am wondering if it is in order in light of the fact that you have represented on this panel various sources of expertise and what they can get from their agencies. However, due to a number of things which are evolving, there are people who now have summary information on such things as human exposure, and I don't think the group is aware of it.

I only became recently aware of this myself. I am wondering if at some time we could spend more than five minutes talking about the future meetings, as to what sort of things we need to hear, for us to make some sort of an intelligent decision?

In other words, I think this thing of human exposure is very important. I think the Environmental Protection Agency has taken the point of view that if the risk is high, that is suspect as a carcinogen, and if the exposure is low, then the hazard is low. If the exposure is high and the risk is high, then the hazard is very high, and these kinds of deliberations go into making some sort of an option on the pesticide.

We may have to take that same thinking process to deal with this situation. What I suppose worries me a little bit I guess I don't understand what the levels of exposure in Vietnam were, and maybe we wont get to that, but I would like maybe the Air Force to give us their thoghts on this, if someone can do this.

I am aware of some exposure research underway right now on 2, 4, 5-T, which I think might be usable to us.

I am aware of someone who is beginning to summarize the teratology data. I think it might be helpful if we could bring these people before the group and gain what we can from them. I think this is rather important as to where we go from here.

DR. HABER: Let me explain the item that is labeled 3:25-3:30, future meetings. That was to decide only the date of the next meeting. It was not to attempt to address any substantive issues, but only to take five minutes to agree upon a date, but I think that the composition of the Committee is mandated by the charge we have in "The Federal Register."

That does not, however, prevent, and I would certainly suggest that we should bring before the Committee experts of whatever stripe or disciplinary background or persuasion that we can get in order to enlighten us.

In other words, this group is not yet complete. We have had a recent resignation for reasons that I won't go into here, and a replacement will be sought for that individual, but except for that, I think the group is pretty well set. It was chosen very carefully, and I think that I would only echo Mr. Cleland's confidence in the group.

Again, if we need outside expertise, that is not of the group, from whatever source, we can obtain it and should, and I would say that people who can provide us with it ought to be available.

I think this Committee will continue to meet periodically as we see fit, but again, we should be able to

make available to us all kinds of expertise, and I would be completely subject to the wishes of the Committee. I think that if any of you wishes to suggest a presentation by somebody, we can certainly arrange for that as soon as appropriate.

I would like at this point to distribute--there are a number of copies for the group here, and there may be enough for members of the audience as well--and these are some questions which we will refer to the Committee to be answered.

We will prepare position papers on all of these questions unless we feel a question is encompassed in another, along with questions from the audience.

If any of you have any written questions, would you please submit them to Mrs. Myer so that we can--because what I would like to be able to do is to address--let me go over this list of questions briefly, and I will endeavor to secure answers to these in the form of position papers. I will quickly read these questions, and if anybody has any comment or further question, please feel free to mention them.

These are questions framed by our Steering Committee through the Advisory Committee. Remember the Steering Committee, with Dr. Levinson as the chairman, are the action group, and we are the advisory group here. If they need information or advice about particular aspects of the Agent Orange problem, each work group is to find the answers itself or to get the answers from others.

I will quickly read these. One, do the available data on exposure of Vietnam veterans to herbicides permit the performance of scientifically valid epidemiological studies on the long-term health effects of herbicides in this group?

I think that clearly is a substantive question for which we will endeavor to get an answer. As I say, we will have position papers in answer to each of these questions which would be made available to the public and will form part of the record.

Two, what are the best human population groups in which to study the long-term effects of herbicides on health, and how may these studies best be conducted?

That relates to the question you just mentioned.

Three, of what diagnostic value are the following procedures in assessing possible herbicide toxicity: levels of dioxin in fat pad biopsies; study of immune factors; study of chromosomal patterns; and study of liver microsomial enzymes?

What additional diagnostic procedures should be considered?

The first of those will be answered by Dr. Lee's study, and he will be communicating that to us as soon as those studies are completed, and it may be that Dr. Lee and Dr. Hobson will have to advise us where those studies will lead and whether indeed they would generate other studies of a similar nature.

We have, as I have indicated, a number of suggested

items for research that Dr. Hobson and we will be responding to presently.

Question 4, is it possible for herbicides to have long-term adverse effects on the male reproductive system?

That question certainly surfaced. We recognize it, and we will continue to pursue that.

Five, what topics should be included in the educationa curricula being developed to upgrade knowledge of potential herbicide toxicity among VA staff members?

One of the things we have tried to do before is to make the staff of our field hospitals responsive to the needs of veterans who come in complaining of dioxin poisoning or toxic effects of dioxin.

This is a continuing process. We get out information to our field as quickly as possible. Dr. Lee's study will have some effect on this. Physicians had to be brought on board with respect to the possible toxic effects, and he has gotten cooperation from a number of hospitals in doing these biopsies, so this itself contributes to the general knowledge on the part of our professionals throughout the hospitals.

Six, what sorts of animal studies would make the most important contributions to understanding the potentially toxic effects of herbicides in humans?

Clearly it is an important question.

Seven, what additional data should be included in the VA's herbicide registry over that being currently produced?

Dr. Castellot, can you tell us about the herbicide registry and where it is now? Is that a fair question?

DR. CASTELLOT: I can't give you any specific data in terms of how many names have been entered into the registry, but at the present time, on a quarterly basis, each of the field facilities, and there are 172, are required to submit data on the individuals who have presented themselves or were sought out in their particular geographic area with regard to herbicide exposure, and as you heard this morning, the history and physicals and other laboratory data which are accumulated at that time are submitted to the Central Office for review. That review is an ongoing process.

Dr. Levinson has the specifics in terms of the numbers involved, but it is an ongoing process and will be accumulated and will eventually I'm sure be subject to rather specific analysis in terms of determining any trends that may be developed, but that is an ongoing process here in the Central Office and the multi-disciplinary board which is reviewing all of these, so it is not done by any single individual.

Many of the people on the Steering Committee are involved with that as well.

DR. HABER: Eight. What are the known facts on the persistence of dioxin and the herbicides used during the Vietnam War in water, soil and the atmosphere?

Can these media serve as a source of human exposure to dioxin and herbicides?

We have touched on that, and clearly we need more data on the chemical formulations and how they persist.

Nine, what medical tests should be utilized to help establish a diagnosis of chronic herbicide-induced toxicity among Vietnam veterans?

One of the most vexing problems we have when veterans come to us is when a veteran says I don't know. I think I have been exposed, and I don't know whether I am sick or not. Can you please study me and tell me whether indeed I am harboring long-term ill effects of dioxins unbeknownst to myself, and what test would one do?

Well, faced with a situation like that, all we can do is the general physical, complete blood count, X-rays, general EKG, electroencephalogram, and so on.

There is no laboratory test at this point which would say yes, you have been exposed or no, you haven't. Liver profile, sperm count, all of those things are done when people come in with symptoms referable to that particular organ system, but unless the biopsy or the fact proves out, and if it does, we may have albeit a difficult and not trivial biopsy procedure that will be of help, if our current pilot studies prove out.

Ten, can criteria be established for determining the level of exposure of military personnel to dioxin during the Vietnam War based on spraying tapes and unit histories?

We will undertake to try to answer that.

Finally, will it be possible to develop standards and criteria which define the precise relationship between

herbicides and dioxin with chronic adverse effects in humans?

Can these criteria also specify the reasonable limits between the time of exposure to herbicides and the development of disease?

These questions have been submitted by our Steering Committee, and as I indicated to you, we will get answers for them and position papers on each of them.

I have here several questions submitted by the floor, and I will undertake to read these. If the answer is quickly forthcoming, we will attempt to give it to you. If not, we will treat these questions in the same way that we would those submitted from our Steering Committee and provide position papers in answer to them.

One, what is the U. N. doing concerning Agent Orange which may have an effect on U. N. troops that served with us in Vietnam?

Does anybody around the table have any answer to that?

Okay. We will undertake to get an answer and give it to you. Who submitted this? Does anybody want to be identified with that? Do you have any further amplification?

MR. GERKEY: No.

DR. HABER: We will try to get an answer.

MR. DE YOUNG: There has been some rumors around that we have heard that Australia and the Republic of Korea have taken a claim to World Court; something having to do

with troops being poisoned. It is total rumor, to my knowledge. I think it is totally false.

DR. HABER: We will undertake to find out that at the same time.

Next question, when is it likely that significant results from the Ranch Hand study will begin to become available?

Colonel Thiessen, can you give us any answers on that?

COL. THIESSEN: The results of the retrospective study, which is basically the questionnaire type study of all 1200 people, should be available by the end of 1980.

The cross-sectional study is the physical study on selected individuals and should go on at more or less the same time. It should also result in data at the end of 1980.

Of course, the prospective study will take years, but there will be interim results at the end of '80, '81 and so on and so forth, until 1985 when the study is considered to be finished.

DR. HABER: That is something I would like very much for our Committee to be able to do. As I indicated to you, I have done that, so we would like to try to get some answers as to when the definitive study will be completed.

Obviously everybody needs to know that from a policy standpoint. It is extremely important.

DR. ALLEN: You are going to get us the

experimental protocol on this?

DR. HABER: Yes, sir. I have made that agreement with them, and General Dettinger was very forthcoming and said he would.

MR. LEMEN: I have one question. You said that the prospective study was going to be cut off in 1985?

COL. THIESSEN: That is as the plans are now. Our protocol will be before the Committee for approval.

MR. LEMEN: My comment is that if you are looking for carcinogenic effects, you probably would miss them if you cut them off the study in 1985.

DR. HABER: We are very mindful of that in the VA, and we intend to follow identified people.

MR. LEMEN: Have you got a group already identified.

DR. HABER: I think that when we get the protocol we can make that comment. I am sure they will have to match men with capability and money and so on, but on the other hand, I think that while we want quick answers, I think it is incumbent upon those of us who are following these people to be prepared to follow them for a long period of time.

Dr. Hobson has talked to me about that several times, so we are well aware of that: 4.2 million veterans reportedly may have been exposed to Agent Orange. I think that is probably not true.

I don't think 2.4 million people were in Vietnam. However, the question is, is gross

information on subsequent health of many of these individuals available, and might it be useful?

There is no question that it would be useful. I would say the information--who asked that question?

MR. STONE: I was just wondering with the protocol that has been made, of perhaps trying to contact very large numbers of the individuals who may have been exposed.

The 4.2 million figure I believe comes from VA testimony last October.

DR. HABER: I hope not.

MR. STONE: Before the Subcommittee on Health.

DR. HABER: I gave that testimony, and if it is in there, it is a misprint.

MR. STONE: Perhaps they had the figures reversed.

DR. HABER: I think so.

MR. STONE: The proposal has been made that perhaps a general notification process of veterans who may have been exposed would be justified, and that useful information might be forthcoming.

DR. HABER: That is certainly something that is very much in our minds. That would be an extremely tedious expensive and difficult action to take, but on the other hand, if the facts warrant that, and if that is the advice of our Advisory Committee, if that is what they think, then we would undertake to do that.

I think that is something that is very good. Dr. Schepers gave me a note.

DR. SCHEPERS: The question is whether we have health records on Vietnam War veterans. They are mostly

young people, and they are still employed mostly, and so they don't come to the veterans hospitals, but we are already currently seeing about 150,000 of these Vietnam War veterans in our hospitals annually, so we are developing en enormous amount of medical information of a general kind about them, and this information is available to the Committee through Ms. Kilduff.

DR. HABER: The VA expressed extreme scepticism about the possibility that dioxin would be traceable in human tissue of even heavily exposed veterans. What will be the significance of a finding from the present tests of no detectable dioxin cases?

Well, it is difficult for me to anticipate the answer, but I think, and I will ask Dr. Hobson to comment on this, what our present study is designed to do is to tell us whether or not a fat biopsy would be useful in distinguishing between people who have been exposed to dioxin in Vietnam, and controlled subjects.

If that turns out to be the case, then we have a potentially, maybe not definitive, but useful way of determining whether others who claim they were similarly exposed do indeed store dioxin in their fat tissues.

It does not specifically say no, you could not have been exposed, and we don't pretend it is. Larry, do you have anything you want to say?

DR. HOBSON: No, except that we would not, under

any circumstances be going beyond the data if with the detection methods we had available to us, we could not find any in the fat. If it is there, we would give the amount that we were able to detect.

DR. LEE: Quite evidently if you find dioxin in the fat, it means there has been exposure, but it does not say when or where. Neither does it say that there will be disease as a result of it, either currently or in the future.

If you do not find dioxin it does not say you were not exposed, and it does not say that you won't have future difficulty from the exposure if dioxin was there.

As Dr. Haber pointed out, the only thing this will do, if there is dioxin present in those exposed and not in controls, is to tell you that these are individuals who can and should be followed, and that they do have known exposure proven, simply by the fact that the dioxin is in their tissue.

I might also say that those people who are exposed agriculturally or in the manufacture, probably have the same problem. It may be that we should put in a third group that would be a control group from neither industry nor from the agricultural people to see if they have the same sort of thing.

At the moment, all we know is that we have 16 people who had had a biopsy, and if there is dioxin in any of them, we will find out if it is in the controls or the others, and it does not indicate that they are or will be

sick, or that they won't be.

DR. HABER: Thank you. We have here a number of questions addressed to specific members of the panel.

Incidentally, the gentleman who said the 4.2 million quotes correctly. That is what the testimony said. That was an error, and I want to retract that. It was 2.4 million. It was a typographical error.

MR. DE YOUNG: There is good reason from where we sit in Chicago to say that 4.2 million is probably an accurate figure, the reason being that many stateside bases under the Freedom of Information Act have admitted to using 2, 4, 5-T during that same period of time, and so it is very reasonable to assume that anyone who was in uniform at that time came into contact with it, possibly in lower dosage at stateside, but into contact with it.

DR. HABER: That opens up a whole new range of possibilities.

MR. DE YOUNG: We have reports from men in Panama who said the jungle was defoliated. In Louisiana, it was made to resemble Vietnam by defoliation and so forth.

DR. HABER: That is a very interesting piece of information that we will have to deal with, so we will take that under consideration, too.

A number of questions have been addressed to various members of the panel. To Dr. Erickson--what is the usual percentage of wasted pregnancies in the population?

DR. ERICKSON: It depends how hard you look. The best studies that I know of come from the Hawaiian Island

of Kauai where something on the order of between 25 and 30 percent of pregnancies were wasted. A typical figure I think is something on the order of about 15 percent. It depends how early into pregnancy one is able to ascertain the fact of pregnancy.

MR. LARSON: Please define wasted.

DR. ERICKSON: I presume that meant lost at term, live birth.

MR. DE YOUNG: I can define it. The toxicologist in Chicago used the term to mean any pregnancy that was not delivered of a healthy child, a pregnancy that was in some way abnormal, possibly a still birth, possibly spontaneous abortion, or a birth gross deformity.

The figure he gave was 10 to 15 percent, and I wanted to see what CDC's figures were on that, if you had any.

DR. ERICKSON: CDC doesn't have any figures of their own, but this Hawaiian study was of a population on a small Hawaiian Island where all the women of reproductive age were registered and followed on a monthly basis so that very early pregnancy losses could be determined and studies where you will find the figure of 10 to 15 percent, usually the ascertainment of pregnancy is later into pregnancy, and there is a quick falloff from a fairly high in early pregnancy to a lower level later in pregnancy.

MR. DE YOUNG: Thank you.

DR. HABER: The next question is addressed to Dr. Kearney, and it is, what are the other ways, quote, unquote,

of production of 2, 3, 7, 8, TCDD, other than TCP?

DR. KEARNEY: What are the other sources of the 2, 3, 7, 8 other than in the production of the 2, 4, 5?

DR. HABER: Right.

DR. KEARNEY: Well, there appeared, and I don't have the dates on this exactly, in '75, '76, reports from Europe that industrial incineration was giving rise to dioxin materials, and these are reports from Rappe, and Dr. Otto Hussinger from Amsterdam, and Dr. Boozer at Boshart in Switzerland.

It appeared that any situation where you had chlorine and industrial wastes that were incinerated at high temperatures, could be a source of dioxins.

The Dow study went further than this. They repeated the European studies. They looked at mufflers. They looked at wood burning fires. They looked at industrial incinerators, and they looked at municipal incinerators, and there were dioxins associated with each of these, so this raises the question -- are there other sources of dioxins other than the production of trichlorophenol, and it raises a question as to the biopsy study--do you have proper controls so that you would see Vietnamese veterans not in Vietnam who were not exposed, although this question of the Vietnam veterans not in Vietnam being exposed raises another complication.

DR. MURPHY: Dr. Kearney covered it, but the question asks 2, 4, 5-T at least as you traced it, and I

think he pointed out trichlorophenol, which I think is important to recognize, 2, 4, 5-T is not the only product through which trichlorophenol, in the production of trichlorophenol that you get the TCDD, and werever you are producing that--many processes.

DR. HABER: My understanding was that it was a degradation product as well as a deformulation product. Is that true?

DR. KEARNEY: Now you raise a very interesting question. For example, I understood the question to say phenol, but maybe it said 2, 4, 5-T.

For example, in Italy what was being produced there was trichlorophenol for the production of hexachlorophine and most of the explosions in Westphalia were trichlorophenol-producing plants rather than 2, 4, 5-T producing operations, so that is a question.

You can get pyrolysis of certain phenols and 2, 4, 5-T, and you can produce TCDD. It is also possible that is a source, so that there appear to be a number of sources, and this does further confound the issue.

That's all I am prepared to say.

DR. HABER: Thank you. Dr. Lingeman, you have been asked to answer two questions. You asked about other herbicides used in Vietnam, and if the Committee was to address the story with Agent Orange; do you have any information on their health effects which leads you to ask, and are you recommending this study?

DR. LINGEMAN: Other herbicides are known to

be carcinogenic, including several arsenal compounds; some of the inorganic compounds are known and accepted as human carcinogens.

One of the others in Vietnam was picloram. It has been tested by the National Cancer Institute and there was a possible increase in hepatic nodules which are considered by some to be pre-cancerous conditions in rats, so yes, the answer to the question is other herbicides are known to be carcinogenic, and possibly toxic in various ways.

DR. HABER: I think the question would be are you recommending such a study?

DR. LINGEMAN: If other herbicides were used concommitantly with Agent Orange, I believe that they definitely would be relevant.

DR. HABER: Our information is the amount they used was almost trivial. Is that not true?

MR. LEMEN: Just to add on to what you have said one of the things that concerns me is the massive use of the related compounds, particularly the pesticides used in Vietnam that have thus far not been addressed.

I would like to agree with you to say that I think the pesticide issue is one that may well be just as big as the herbicide issue, and we should certainly look into it at the same time.

DR. HABER: I think that is important, and we should obviously address the official charter of this Committee, the VA Advisory Committee on Health-Related

Effects of Herbicides, but I am sure that narrow construction was because of our main concern about Agent Orange, but it would not stand in the way of our getting other information made available.

One final question from the group. This one was signed by Mr. Donald A. Larson. To what extent is information potentially available on the effects of Agent Orange on the indigenous Vietnam population?

I would like to answer that and that is to say that there is information available in the original National Academy of Sciences report, and then we have the report of Dr. Tung, and other people, which we have to look at more carefully and continue to see whether or not we can get updated information.

I think Dr. Tung is anxious to cooperate with us. Wasn't that your impression, John? You may have been here when he briefed us and expressed the desire that he could continue to work with us, and I think we will certainly try to make available from him any information which is of value.

I think Dr. Allen has already characterized it as lacking the quantitative sophistication that we are accustomed to, at least in this country, and one has to understand he was in a war-time condition and maybe some of the niceties couldn't be observed.

MR. LARSON: I meant general. That was an isolated instance. I meant general.

DR. HABER: As I said, we will endeavor to review

the minutes. If we feel the questions have been definitively answered, we won't deal with it any further.

If it was a more substantive question which could not have been answered precisely and must therefore only represent a tentative view, we will develop a position paper on this.

There are two people who I would like to specifically call on if they are present. Mr. Frank McCarthy, is he present, or is Mr. Michael Gerkey present?

MR. GERKEY: Did you have a question you wanted to ask me?

DR. HABER: I was informed by the Administrator that you might wish to make a statement, and if you do, this is the time and the place.

MR. GERKEY: Okay. Then I guess I will have to do it.

What I am basically concerned about is the effect of Agent Orange on the world, as there were people from different parts of the world who served with us in Vietnam who most likely, if we were affected, would have been affected.

They were part of the United Nations. I feel that if any research is to be done to help us, there should be research done to help them also, and they should be made aware of the effects of Agent Orange on the populations in their countries. There should be some sort of a world organization set up to work with scientists and work with people in the Veterans Administration and work with people at the local level, at the state level, at the

government level, along with the military level, and I believe one should look into this matter and pursue it.

DR. HABER: That's good. We are indebted to you. I think that is an excellent suggestion. There have been a couple of indications around the floor that the people in the U. N. may have been involved. I think it is only fair that we make some representation through the Administrator's office to the World Health Organization, or some other international body, and offer to share with them the possibility of our getting data on that, so we will do that.

In the future, we will have opportunities for those of you in the general public who wish to make prepared statements to the group, and we will, in our "Federal Register" notification, indicate that if anybody does wish to make such a prepared statement, if he submits it to us before, he would then be asked to read it before the general group, and we will make provision for that.

This being our first meeting, that has not been deemed possible, but I would suggest that if others in the audience wish to make brief statements not exceeding five minutes in length, we would be anxious to accommodate you, so if anyone wishes to make such a statement, will you please come to the microphone and identify yourself and please confine yourself to no more than five minutes.

MR. DE YOUNG: Frank McCarthy is not here today. I saw Frank in Kansas City last week and Frank said

essentially that he didn't feel it was worthwhile coming because he thought the purpose of this Committee was to whitewash the subject.

I no longer think that. I no longer think that. I came here specifically to watchdog this Committee from my point of view.

Let me get into my prepared statement, and maybe it will make some sense.

I am the Veterans Services Coordinator at Columbia College in Chicago. It is under the VISA program funded by HEW.

Eighteen months ago, an extremely agitated woman appeared in my office in Columbia College in Chicago. Her name was Maude DeVictor, and she was at that time a VA Benefits Counselor at the Chicago Regional Office.

She told me of 27 cases of cancer among Vietnam veterans she had seen there in the Chicago Region. They all had one thing in common besides cancer. All served in areas of Vietnam defoliated by the now almost mythical Agent Orange.

She went on to show me the research she had compiled- articles from scientific journals showing evidence of the herbicide 2, 4, 5-T's ability to cause skin problems, cancer, miscarriages, mutations, and birth defects; letters and notes of phone conversations with scientists and researcher who provided further statements documenting the contamination of herbicide with dioxin, that most toxic of all man-made chemicals.

She further told me that she had written the VA Central Office repeatedly about this and received no response. The claims for service connection for these men had not been granted.

We decided that the veterans of the Vietnam War had the right to know if Agent Orange had caused these problems 5, 10 and 15 years after their exposure, so we asked Mr. Bill Kurtis with WBBM-TV, CBS in Chicago to have his investigative team research Agent Orange and its dioxin contaminant.

For six weeks they traveled the country pulling in all the loose ends, and trying to weave together the pattern of dioxin poisoning that had emerged in so very many widely scattered episodes--dead horses in Missouri, and the sick owners who had sprayed dioxin-contaminated oil on their horse barn; dead Rhesus monkeys in an experiment done by Dr. Allen in Wisconsin; deformed goats and ducks and sick people in Globe, Arizona; sick residents of the national forests where Agent Orange like herbicides were still in use; and of course, veterans of Vietnam from Chicago.

In all those episodes, some common symptoms emerged--skin problems, hair loss, joint problems, headaches, nausea, fatigue, psychological changes, blood disorders, cancer, and birth defects.

The documentary that grew out of this, called "Agent Orange: Vietnam's Deadly Fog," was aired on March 23, 1978 in Chicago. WBBM referred calls to my office, and the ensuing weeks found me with an epidemic of calls from

Vietnam vets saying they, too, showed these problems--hundreds of phone calls from all over the midwest from vets talking about skin rashes persistent since Vietnam; severe headaches; joint pains and swelling, often mistakenly diagnosed as arthritis, and resistant to treatment; nausea and continued fevers, some for seven years; extreme debilitating fatigue; an endless progression of sick days, days they had not been able to work; and an unending series of colds, flu and other common ailments; mysterious stomach disorders, intestinal disorders, urinary disorders, kidney disorders, liver disorders, auto-immune responses; allergies and blood disorders; and nervous system problems, typically numbness of the hands, arms, feet and legs; a collection of psychological changes--tempers, violent behavior, depression, anxiety, brooding, memory loss, confusion, an inability to cope with the pressures of life, a loss of resiliency, and cancers and tumors in men 25 to 35 years old.

Some doctors have described those as almost unheard of in men that age.

They also reported difficulty in conceiving children after their return from Vietnam. Many of them reported a loss of interest in sex or physical impotence as well.

Some reported multiple miscarriages by their wives, often followed by the birth of a child with severe physical deformities, typically of the fingers and feet, heart murmurs, and cleft palate, as well as hyperactivity and learning disabilities of various sorts.

What was the VA response? "No firm evidence

exists to incriminate these herbicides." Men who were legitimately worried about their health and their children's health were brutally turned away with the statement that their problems couldn't be from Agent Orange, that it was all in their heads, and were sent to the shrink.

The news media in various cities picked up that story. The Chicago pattern was repeated first in St. Louis, then New York, Los Angeles, San Francisco, Denver and Detroit. Each time the media carried the reported symptoms, calls from Vietnam vets poured in.

Hundreds of claims were filed and denied. "No firm evidence exists." Months later, a tissue biopsy was instituted by the VA as a first step in determining whether these vets had been poisoned by dioxin. In Chicago, the tests were so badly handled that three vets in Chicago are suing the VA for malpractice.

The first VA advisory committee on toxic herbicides was established by the VA Central Office last year. It was so flagrantly in violation of the Federal Advisory Committee Act that it was abolished and this Committee formed, an action that took a year, and which we applaud.

VA Central Office promised to issue instructions to all medical facilities on how to test Agent Orange victims. As late as three weeks ago, VA doctors were still asking vets what is Agent Orange.

A document came to us which authorized the destruction of certain tumor and cancer registry records, and

at the same time spokesmen from the Central Office were assuring me that all medical records would be preserved and sent to the National Cancer Institute.

Mr. Cleland denied any knowledge of the destruction of those records. Veterans all over the country have called in to tell us of the run-around, ignorance, the futility, the red tape, the insolence, and the outright malpractice of the VA health care system. The VA seems to have lost all credibility with this country's Vietnam veterans. It has broken faith with us by not telling us the whole truth at first. We got PR statements carefully worded to avoid any conclusions or responsibility.

Is it any wonder vets have not been beating down the VA's doors in haste to get medical care? Until the VA gives vets their legally mandated benefit of reasonable doubt and aggressively researches the Agent Orange, vets will stay away. Until the VA gives vets their rightful first-class medical care, courteously, sympathetically, and with dignity befitting their status as the warriors of our society, vets will stay away.

The VA must take the lead in Agent Orange research. In the past, VA doctors have won international awards for contributions to medicine. I hope that is not over. The VA must act immediately not in its own interest or in the government's interest, but in the interest of the vet.

Information must be gathered, and the start has been made, not only from the manufacturers of the chemicals, but from scientists and doctors and researchers

without the vested interest of the petrochemical industry. The fox cannot watch the chickens.

Information must be sought from vets themselves, from service and fraternal veterans organizations, from environmental groups and individual citizens. The word must be put out to all Vietnam veterans--you may have been poisoned. Come in and get checked, but before we do that, we must have programs in place to do the testing, extremely subtle testing, checking more than just blood, chest and urine, and then we must provide treatment, and none of us knows where to begin on that.

Then there are children. Current claims by veterans that Agent Orange has deformed their children get administratively disallowed in that cold exactness of language so favored here in Washington.

These men want to know if their own government has crippled their children, and if they can safely have more children, and they need answers soon.

Because vets need these answers now, and because the VA has lost credibility, many of us of whom the Agent Orange questions were first asked a year and a half ago, veterans groups and citizens groups from all over the country have joined together to look for these answers, answers that can be believed.

We have organized an Agent Orange Task Force to seek out those answers and help those vets. This group is composed of representatives from ten veterans organizations nationwide, including the National Association of Concerned

Veterans, the Vietnam Veterans of America, the Vietnam Veterans for Self-Reliance, Vetline/Hotline, Agent Orange Victims International, Concerned American Veterans Against Toxins, and others.

We extend an invitation to other veterans groups to join us in this effort. We are gathering information on Agent Orange from veterans and researchers all over the country, and respond with the best answers we can as we go. These answers will not protect the chemical industry. They won't protect the government or protect the military or the VA. They will protect the vet.

Secretary Califano of the Department of Health, Education and Welfare has assigned the Assistant Surgeon General, Dr. James Dickson, to analyze our caseload data, looking for the patterns of illness emerging. Dr. Dickson will also listen to scientists, researchers, and doctors who have information on dioxin poisoning.

Secretary Califano has pledged his department's aggressive action to find answers to the questions of Agent Orange. We take him at his word, and hope this second herbicide committee will be as aggressive in the interests of Vietnam veterans.

The eyes of the nation are on this Committee. Twice as much of these herbicides were sprayed here in the U. S. as was sprayed on Vietnam. Whether they know it or not, the outcome of this Committee is important to every citizen of this country.

On top of the spectre of Three Mile Island, we

now have the spectre of Agent Orange, and I may add of Agent White and Purple and Blue and Green and Pink.

I am here today with John First of Southern Illinois University. I mentioned in my prepared statement that St. Louis was the next city after Chicago to report a large case. In about five weeks, John had 607 phone calls for more information about Agent Orange.

I would like him to take five minutes, if you wouldn't mind, and let him go through the data that he has collected on that.

DR. HABER: All right.

MR. FIRST: I would like you to know that we do not consider this scientific information. What we wanted to do more than anything was find out what the people were complaining about.

We asked them to tell us what they had experienced since Vietnam. In an effort to avoid pre-disposing their answers, we chose not to ask specific questions until they had nothing further to add to their spontaneous remarks.

We have two tallies here. I would prefer to call them accountings. Of the 607 reports that we got, 89 reported nothing but their name and address so that they might receive further information. We received no information from them.

Of that 607, 301 reported numbness and tingling. That is 49 percent; 305 reported various rashes. A significant number of those rashes were reported to have acne-like eruptions. They come and go with time. They

are often reported to increase in severity with heat.

This tally includes a list of birth defects that are reported. I am not a doctor. I do not know the significance of these. I make them available to you in the hope that you will know whether or not they are significant in the general population figures.

We totaled 55 veterans with full intake, at which time we now have 89 percent reporting a rash. This is not a scientific sampling. They called on their own response to published symptoms which they recognize, for which they had failed to receive adequate treatment.

I do have copies of this available for the Board.

DR. HABER: We would appreciate that very much. Incidentally, let me now say that we would appreciate any representations from any interested parties--scientific, lay, of whatever description, and would undertake to make this information available to the concerned members of the Committee.

Additionally, anybody who wishes to make a presentation to us at times other than the meeting, can do so by writing or calling my office and arranging for such an opportunity. We would grant him a hearing, in addition to which we will have opportunities at future meetings for public statements of the kind we just had, to be read into the record, and the questions to be exercised.

I see by the clock that we are right on schedule, and I wish to thank both the Committee and the audience for helping us meet that precise time limitation.

I would like now to take a few moments to simply set the date of the next meeting, which ought to give us time to prepare our papers and to circulate documents among us.

Notwithstanding the fact that we are in the midst of the summer and people's schedules are disrupted, I would like to set this meeting for early in August, and my first cut will be August 9th.

Can you all determine if that is not possible for you? Dr. Murphy? When would be?

DR. MURPHY: Late in August.

DR. HABER: Supposing we make it early September, September 7th. Is that a possibility? Can everybody make it?

DR. KEARNEY: I will be in Europe.

DR. HABER: I think this is going to be difficult to do this way. I therefore think that it would be best to circulate several dates to all of you by some written communication, and then we will ask you to circle the most propitious date, and when we get the greatest number of attendees, we will convene.

Is that satisfactory to the members of the Committee?

MR. LEMEN: Yes.

DR. HABER: Dr. Schepers reminds me if you cannot attend, your alternate who has been named could attend, but we would like to keep the group as much as possible to this representation. We will give you ample opportunity to

indicate any problems.

MR. LEMEN: I have a question. You said that we would develop position papers. Are you going to be writing to us then to ask us to comment on these?

DR. HABER: Yes. We will handle these position papers in one of two ways. We will endeavor to make a preliminary statement which we will circulate to the group for corrections, or if we feel incapable of doing that, we will ask a small group of you, or one or two of you to help us frame the original paper, and then circulate it. You will not be tasked until I specifically contact you.

Is there any further business of the members of the Committee? If not, please accept my heartfelt thanks for what is a challenging and difficult task. I think it is well begun. I think I have gotten several new ideas. I am indebted to all of you for the dispatch and scientific way in which you have approached this very, very difficult subject, and I have no question but that we will produce the answers sooner because of the existence of this Committee than would otherwise have been the case.

Thank you all very much, and we stand adjourned.

(Whereupon, at 3:30 p.m., the hearing was adjourned, to reconvene at an undetermined date.)

REPORTER'S CERTIFICATE

DOCKET NUMBER:

CASE TITLE: ADVISORY COMMITTEE ON HEALTH-RELATED EFFECTS OF HERBICIDES

HEARING DATE: June 11, 1979

LOCATION: Washington, D.C.

I hereby certify that the proceedings and evidence herein are contained fully and accurately in the notes taken by me at the hearing in the above case before the

VETERANS ADMINISTRATION

and that this is a true and correct transcript of the same.

Date: June 18, 1979

Kathy S. Doyle

Official Reporter

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Washington, D.C. 20005

I HEREBY CERTIFY THAT THE PROCEEDINGS AND EVIDENCE HEREIN ARE CONTAINED FULLY AND ACCURATELY, AS CORRECTED.

Paul A. L. Haber

PAUL A. L. HABER, M. D.
Chairman
Advisory Committee on Health-Related Effects of Herbicides

August 7, 1979

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