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 arteriosus, 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
got 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 environmental 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 a 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

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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 other 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 com-
pounds 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 occurred 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 Moses, 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 carcinogenicity
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
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 '50s, 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

Acme Reporting Company
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 in claims 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 due 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 mutagenicity
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...